





A STUDY OF THE SIMILE IN MEDICINE

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ERRATUM

Page 409, line 20 should read :

f) ADAPTATION of species. Those unable to adapt themselves become extinct.

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PREFACE

While current medical literature reveals evidence of an unmistakable recrudescence of interest in the simile problem sober reflection on the general trend of contemporary medicine emphasizes this renaissance even more distinctly. Although frequently ascribed to various intrinsic factors, for example, more critical examination of the generalization and more thorough analysis of its implications by those occupied with the problem, it would seem, in view of the relative inaccessibility of these restatements and consequently a general unawareness of their existence, that the dominant role in this revival of interest can be safely assigned to some more universally appreciated extrinsic factors. Naturally more accurate delineation of the simile has served to make its contentions less unorthodox and more comprehensible within the frame of science; still there is considerable basis in fact for the conviction that re-orientation of medicine itself along hippocratico-biologic lines, the inevitable outcome of developments in many departments of medicine and biology, independently and unconsciously, led back to the simile and gave widespread impetus to its reconsideration.

To assert that tradition and its enveloping nebula of misunderstanding and distortion of the simile has long been and continues to operate as the most serious obstacle to wider interest, is hardly an overstatement. It is generally agreed that any conception can be evaluated more accurately when the history of its development is known; but in the present instance there is the additional and compelling reason, mentioned above, which necessitates the inclusion of a succinct outline of the history of the simile problem. Indeed what originally seemed but a brief preface introducing the modern conception gradually assumed decided importance as the devastating influence of traditional confusion became increasingly clear. Likewise it has seemed advisable to digress occasionally from pertinent phases of the subject and to consider seriously some perfectly irrelevant matters since their reiteration in past discussions and their rediscovery and injection into current literature continue to enshroud rather definite problems in a fog of irrelevancies. However, here as well as in the presentation and attempted appraisal of the modern conception, the study is intentionally incomplete. Perhaps the most difficult part of the task has been the selection of representative viewpoints out of a wealth of

material assembled during many years of investigation. Repeated revision of the manuscript, which constantly threatened to reach undue proportions, has caused further deletions in the interest of brevity.

While obligations, literary and otherwise, will become immediately apparent, it is a pleasant task to record with profound gratitude the names of some colleagues and friends whose ideas played important parts in shaping the thoughts and material which follow: Prof. August Bier (Berlin), Prof. Karl Kötschau (Jena), Rudolf Tischner (München), the late Prof. Hugo Schulz (Greifswald), Hans Wapler (Leipzig), Prof. Max Neuburger (Vienna) and Eduard Rentz (Riga). Even more valuable has been the stimulating criticism of Hugh M. Beebe (Ann Arbor) and the cooperation and assistance of Claude A. Burrett (New York). Needless to say none of the above necessarily concur with any of the opinions advanced.

The study is addressed to the Board of Regents of the University of Michigan at whose invitation the work was originally undertaken. It represents a sincere effort to fulfill a promise made several years ago, namely, to submit a statement reflecting my more mature judgment on the simile problem. However the work has no official status beyond furnishing information once and perhaps still desired.

If the problem has been more clearly defined, the sources of difficulty exposed, the way paved for understanding, mountains of chaff separated from nuggets of truth, paths broken through an almost impenetrable jungle of literature, indeed, if any single one of these aims is attained, the labor has been well expended. It is hoped that the study will prove helpful to those interested in the problem and that it will be regarded as another step towards a united medicine. More than this I cannot expect.

THE AUTHOR



PART I

THE EARLY CONCEPTION OF THE SIMILE

THE MAGIC SIMILE.—There is a widespread conviction, cherished chiefly by medical historians and fostered by their writings, that the magic and the modern simile are identical or at least essentially affiliated. Since busy investigators are not disposed to devote much energy to the serious examination and indirect promotion of outworn, discarded and retarding medical superstitions, their persistent disinclination to consider the simile is well founded, providing an actual identity can be proven. Therefore it is advisable to examine this alleged relationship at once. The material which immediately follows should serve to repudiate all well-intentioned suggestions of identity or essential affiliation. Furthermore it seemed advisable to supplement these remarks by a rapid review of the evolution of one justly prized, universally accepted procedure in medicine which admittedly had its remote origin in magic, in order to indicate that the modern simile would not necessarily suffer serious discredit should future discoveries prove an interrelationship between the two.

Since the major aspects of simile magic are well known and detailed accounts are available,¹ extensive discussion on the first point is unnecessary. Where primitive people populated the world with demons, many of their practices, and particularly their therapy of disease, are comprehensible on the basis of confronting magic with magic. The Indian wears an eagle feather head dress partly to evidence his prowess in hunting, partly for decorative purposes, but he is also motivated by the thought that the vision, speed, courage and other desirable qualities of the eagle will be magically acquired by wearing the head dress. The magic transference of bravery from a slain enemy to the victor by means of ingestion of the organs (heart) explains some aspects of cannibalism.² Too prolific women attempted to prevent conception magically by hanging sterile branches on their garments. Conversely sterile women have been compelled to drink decoctions prepared from the bodies of prolific animals (wasps, flies) in order to become pregnant. All these practices apparently are based on the principle of participation,³ the naive use of the causality principle, association of ideas, a primitive post hoc ergo propter hoc. *Materia medica animalium*

abounds with illustrations. Early examples of the treatment of "same by same" can be found in the Ebers Papyrus (1500 B.C.): ear diseases with ear, headache with fish head, blindness with swine eyes. Equally primitive or extremely complicated applications of this same principle are found in most pharmacopocias until 1800 A.D. At times the thought process is obvious: human calculi in bladder stone; again the connection may be obscure in the light of available knowledge. It would be pointless to enumerate the representatives of the animal kingdom, impossible to even list those of the vegetable. To remain with the first it may be asserted with confidence that there is hardly an important organ or tissue, secretion or excretion, scarcely a well known small animal, fresh, dried, or incinerated, hardly a large animal, at least its tissues, excretions or pathologic structures, the rarer the better, hardly a fossil known to antiquity which has not been employed according to this principle. The Egyptian may use the blood from a *black* cow for *grey-ness* of the hair,⁴ or the Grecian poet may require Telephos to be healed by rust from the spear which caused the wound, but the principle is the same as some recently cited practices.⁵ The appended bibliography may be consulted for the pertinent literature.⁶ Naturally inability to procure the *idem* frequently led to the use of the *similimum*: other factors also played roles.

Bastian's theory that primitive people show similar patterns of mental development because they have in common a human brain, finds considerable support in the magic simile and particularly in the quite universal doctrine of signatures. Ancient forms of this doctrine need not be examined since they are inextricably interwoven with the above mentioned magic simile.

The greatest modern representative of the doctrine of signatures, of signa naturae, was Paracelsus, though he had an immediate even if obscure predecessor in Agrippa.⁷ Just as in the magic simile where some extrinsic property of the object, its color, form, consistency, etc., permitted the field of utility to be anticipated, so in the doctrine of signatures these and other incidental properties furnish the clue. (Philosophically this could mean that form and function are two expressions of the same thing, but an analysis of this point is foreign to the present discussion). Well known examples are: sharply pointed objects for treatment of sticking pains; red drugs for cardiac and hematopoietic diseases; perforated leaves for penetrating wounds; testes-like Orchis root as an aphrodisiac. Location could also furnish indications (Chinese doctrine of signatures): upper parts of plants for diseases of the upper parts of the body, etc. As Paracelsus has been mentioned a citation follows:⁸

"Because through the art of chiromancy, physiognomy and

magic it is possible to recognize in the external appearance, the peculiarities and virtue of every root and herb by its signature, shape, form, and color, and it requires no further testing or long experience. Does not the leaf of the thistle stick like needles? Because this sign has been found by magic, there is no better herb for internal sticking than the thistle."

Schlegel⁹ states that Linnaeus subscribed to the doctrine of signatures since he regarded red plants as styptic; if so he did not stand alone.

Additional citations which illustrate practices followed or register prominent adherents might easily prove tedious and would certainly not furnish necessary information. Suffice it to say that almost innumerable variations of the magic simile (and the allied doctrine of signatures) are known. They have in common at least one factor which alone ought to have revealed the futility of attempts to associate them logically with the modern simile, not to mention an imputation of identity with it. They invariably utilize some completely incidental, accidental and arbitrarily selected association of external similarity which has nothing to do with the actual pharmacologic action of the substance concerned. In contrast the fundamental implication of the modern simile is: the similarity of a "drug" to a disease is determined by a complete study of the real physiologic actions ascertained by actual experimentation upon a reasonable number of subjects. A definite knowledge of the true physiologic and toxicologic effects evoked by the substance is placed into relationship with the actual phenomena in a given instance of disease.

The magic simile states: Euphrasia is useful in eye diseases because the flower looks like an iris. The modern simile in its most elementary form states: if a substance, for example, euphrasia, is demonstrated pharmacologically to possess the property of evoking ocular phenomena, it can be considered therapeutically in eye diseases which involve the same structures. What is the relationship between two doctrines, when one states that opium is useful in diseases of the "head" because it possesses a "crown," the other that pharmacologic proof that opium affects the cerebrum is an indication of its field of therapeutic activity?

For this single reason alone, and many others could be adduced, it is difficult to sustain logically a contention of identity or essential affiliation. Since the two doctrines are fundamentally different, future allegation of identity strongly implies an acknowledgment of superficial acquaintance with one doctrine or both.

Quite foreign to the subject and provocative of endless fruitless speculation is the interesting but unsolved question of possible un-

conscious stimulation from the magic simile in the primitive elaboration of the modern. However in order to cast ridicule on the modern simile, polemic writers frequently employ a rather obvious device, which would not require mention, if it were not for the surprising success it obtains. They imply the modern simile is unworthy of serious attention since magic stood in the background at its birth. The casual reader may miss the enormous difference between stating that the simile is magic and that the simile arose from magic. An analogous statement would be: astronomy is magic or astronomy arose from astrology. Peculiarly enough these facile pens do not belittle smallpox vaccination because it originated as a magic procedure among the Chinese. Nor is the well merited enthusiasm over the bacteriophage dampened by appreciation of the fact that Indian folk magic taught bathing in infected rivers. Certainly no one would minimize the importance of liver therapy in pernicious anemia because Persian folk magic recognized its potentialities. No one would cease to employ massage as a therapeutic adjunct because it possesses a remote ancestor in Egypt where patients were pummelled in order to render the body an unpleasant habitat for the invading demon. The value of abdominal massage in the treatment of certain forms of constipation is unchanged by knowledge that Solomon Islanders attribute the syndrome to swallowing cuttlefish which are eliminated by exercise and massage. It is difficult to determine why a different standard should be demanded of the modern simile.

The correction of the widely prevalent error of essential affiliation between the two similes, advocated here primarily in the interest of truth, co-incidentally would eliminate one great psychologic handicap under which the simile now labors. The importance of this obstacle may be legitimately inferred from the zeal with which polemicists have attempted to forge the connection. There follows immediately a brief outline of the evolution of the conceptions of antitoxins. Three factors motivated the selection of this topic: first, no informed student would seriously challenge the merit of antitoxin therapy; second, qualified authorities willingly concede the existence of a magic ancestor; third, the subject matter is relevant to a subject discussed later. It is intended to indicate, by analogy, that there is just as little justification for evaluating the modern simile on the basis of an alleged magic ancestor as there is for antitoxin therapy with an admitted magic forefather.

v. Behring,¹¹ the discoverer of diphtheria antitoxin, correctly suggested that the regimes of Lucanus,¹² Pliny,¹³ Celsus¹⁴ and Aelianus¹⁵ for the therapy of snake bite belong to the immunizing procedures. The same holds for many magic practices of African

and American primitives,¹⁶ universal antidotes of the Mithridates type, and attempted immunization against poisons and disease by amulets. Contrasted with these endeavors at active immunization are passive measures. The following are suggestive: diets supposedly identical with those of immune animals; widespread use of duck blood;¹⁷ ingestion of mice for protection against aconite;¹⁸ stork blood for snake bite;¹⁹ and many uses of hartshorn.²⁰ In the hippocratic writings greater emphasis is placed upon detoxification of poisons in infectious diseases by the body. Galen made the important suggestion that poisons may produce symptomatic pictures similar to disease,²¹ a viewpoint amplified by Paracelsus.²²

While the ancients regarded infectious diseases as demoniacal possession, poisoning from Apollo's darts, certain winds, real or fancied animals,²³ still these magic conceptions did not prevent drainage of swamps, care in preparation and selection of food, detailed advice on the selection and storage of drinking water, so that one might properly speak of the magic origin of hygiene. Perhaps more pertinent is the practice of burning sulphur which was deemed a specific for the epidemic diseases of the period.

With the writings of Nicander, Mithridates, Attalus, Pliny, Dioscurides and Scribonius Largus, "ambrosias," "mithridates," "theriacs," "alexipharmics" and other universal antidotes or panaceas came into existence. Since a theriac could oppose all poisons, it could antidote the poison of malaria.²⁴ As opium was an ingredient of most theriacs, later on all diaphoretic substances were considered antidotal.

The introduction of markedly aromatic substances such as camphor and cinnamon²⁵ to antidote poisons of infectious diseases, characterizes a slightly more advanced era, which also witnessed the use of the magic bezoar stone and other concretions from the gastrointestinal canals of animals. Magic isopathy, implying that every poison contains its own antidote, became more popular, as did amulets containing animal tissues. Slightly later amulets were prepared with arsenic and mercury²⁶ on the supposition that adaptation to the poison, habituation—to employ a modern term—occurred and the foreshadowing of modern immunology assumed clearer outlines. Replacement of universal antidotes by amulets containing single substances followed, supplemented in turn by the belief that arsenic, aconite, mercury amulets could be employed in certain diseases.²⁷

The 17th century witnessed employment of mercury in syphilis and the suggestion of the infectious origin of some diseases by Fracastoro,²⁸ the removal of some syndromes under the heading of special diseases, and the Paracelsian innovation of species of dis-

ease.²⁹ These ideas foreshadow the still more modern search for specifics, in that the suggestion of a living cause of disease naturally led to a search for "antiseptics" capable of killing the "vermiculi." The miasmatic theory of disease was altered to include the possibility of air contamination by small organisms. The time was ripe for a magically inclined Kircher, a Hauptmann, or van Leeuwenhoek, and an era follows with the development of pathologia animata when "worms" were found in the blood of patients by Castro, Borelli, and others. Lange³⁰ and Hauptmann³¹ laid the basis for the study of the contagious nature of infectious diseases and the further development of "internal antiseptis." Rivinus³² asserted that successful therapy of many infectious diseases could be attributed often to the unconscious use of an "anthelmintic."

The introduction of the quinine treatment of malaria initiated a new search for specifics supported by Sydenham and his followers.³³ The innovation of smallpox vaccination, long in vogue among the laity, re-emphasized the principle of prophylaxis, a long step from the use of the hair of the dog that bit the patient. Rapidly following are attempted vaccination against plague by Wezpremi³⁴ and Samoilowitz³⁵ and measles prophylaxis by Home.³⁶ These efforts fell into partial oblivion and the combination of accidents in smallpox vaccination and the derogatory attitude of many physicians, nearly undermined that procedure. Early in the last century Lux,³⁷ an adherent of the simile theory, attempted to extend the principle of using morbid products isopathically in disease. Hence it was a short step to the epochal work of Pasteur which found its full development in the discovery of diphtheria antitoxin.

According to unprejudiced medical historians, Neuburger,³⁸ for example, from a remote origin in magic influence of comets, incense purification, sympathy, amulets, etc., came the magnificent achievement of modern antitoxin therapy.

In conclusion: the unsupportable statement alleging identity of the magic and modern simile falls to the ground since they embody fundamentally different doctrines. One is a dogma based upon the arbitrary selection of some incidental external property as the sole means of determining the domain of drug activity. The other idea is diametrically opposed since its basic implication belies any selection founded on inference and relies solely upon experimentation. The question of possible unconscious stimulation by the magic simile is dismissed because of the impossibility of obtaining objective evidence. But if conceded for the purpose of discussion, then it has no real weight, since the same adverse criticism could be invoked against the most valid procedures in medicine. For these reasons

alone arguments against the simile on the grounds of identity or essential affiliation with the magic simile are to be depreciated as invalid and misleading.

The above remarks are directed chiefly at polemist who desire to lampoon the modern simile. With slightly altered emphasis they are equally applicable to a smaller group of opportunists, composed largely of adherents of the simile. In an ardent effort to fortify their belief by any evidence indicating great antiquity of their tenet, they permit themselves to be blinded by a superficial similarity of name and assist in the perpetuation of error.

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- ⁶ General rather than specific references will be most suggestive. Consult headings as brain, blood, menstrual blood, skin, faeces, sweat, sordes; various animals as bugs, snails, snakes, lizards; tissues as fat, teeth, bones, etc.
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- ²⁵ Marx: Origines Contagii, 1824.
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- ³⁶ Home: Medical Facts and Experiments, London, 266, 1759.
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THE HIPPOCRATIC SIMILE.—As Hippocrates advanced a doctrine of the simile, the formulation of all subsequent similes, particularly the foreshadowing of the modern, has been accredited to him. The unimportant priority question cannot be solved and may be dismissed with the observation that medical history reveals many parallels of the rhythmic recurrence of the same theory in slightly altered form and usually under a new name. This statement may recall Goethe's assertion that the truth is approached by a spiral path whose levels lie superimposed upon each other. For the present, discussion will be confined to the expressions of the simile in the Hippocratic writings.

The most frequently cited remarks occur in the book: "On the Places of Man".¹

“The pains (complaints) will be removed through the opposite of them, each according to its own characteristics. So warm corresponds to the warm constitution which has been made ill by cold; so correspond the others. Another type is the following: through the similar the disease develops and through the employment of the similar the disease is healed.

“So that which produces urinary tenesmus in the healthy, cures it in disease. Cough is provoked and healed through the same agent, just as in the case of urinary tenesmus. One other method: the fever from which an inflammation develops will be provoked and healed at one time, at another through the contrary of that from which it develops. If one bathes a patient with warm water and administers many drinks, then he will heal the disease through an excess of fluids; that which causes the swelling heals the existing fever. And when one gives a purgative or an emetic so will the disease be healed by that which produced it and provoked by that which heals it. If one gives much water to a man who is suffering from vomiting, so the material causing the vomiting will be removed by the vomiting. So the vomiting is stopped by an emetic. But one can also stop the vomiting if he withdraws from below that which is causing the vomiting as long as it remains in the body. So by two opposing ways health can be restored. If this held in all cases it would be easy, now according to the nature and cause of the disease to treat according to the contrarium and now according to the nature and origin of the disease through the similar.”

The inclusiveness of the Hippocratic viewpoint, which lacked dogmatic demand of exclusive devotion to one method or the other, is repeated in the following: “One must learn that one pain is released by another and then if something presses down from above, one must release it from below,”² which urges equal justification of the simile and contrarium in appropriate fields. Some statements are startling when torn from their context: “diseases are cured by the same which cause them.”³ The real meaning is: since diseases have natural causes, they are curable by material measures rather than by supplication to the gods. Some applications suggested belong to the magic simile: “in jaundice one gives the broth of the plover to drink.”⁴ Since the plover has yellow plumage the doctrine of signatures is suggested, the same obtaining for the use of red pomegranate juice for bleeding⁵ and elsewhere.⁶ Instances of possible dim foreshadowing of the modern simile are: garlic for a condition which it is alleged to induce,⁷ the purgative helleborus in cholera,⁸ cantharis as a diuretic.⁹ Applications of the “idem” as well as the “similimum” can be found.¹⁰

In an interesting brochure, Hugo Schulz¹¹ has discussed the long quotation given above. He remarks that the first Hippocratic statement in regard to treatment seemed obvious. Disease and health were opposed like good and bad, night and day, cold and warm, and diseases had disappeared in this way. Therefore the element of contrast was the decisive factor and thus the first of the Hippocratic rules originated: *contraria contrariis curantur*. Schulz adds that when the quotation is studied more closely, it will be noted that he has not spoken about disease at all, but merely the complaints produced or actually the disagreeable symptoms which accompany the disease. In the second part of the quotation it definitely states diseases; Schulz believed that the difference in expression meant that in the last instance one was concerned with something special, a direct relation between the disease and remedy. That this principle is widely applicable is seen in the two examples of cough and strangury. For therapy then, the other Hippocratic principle reads: *similia similibus curantur*.

More important than mere citations containing the thought of the simile is the very spirit of the Hippocratic writings. Perhaps no single thought has exerted a more profound influence upon medicine than the observation that the phenomena of disease are composed of two groups of events, the first composed of the direct effects of the injury, the second the healing reaction to the injury. The corollary to this proposition is that the direct effects are to be removed if possible, but the healing reaction is to be promoted, and this by imitation. Its importance is partly evidenced by the periodic recurrence of this Hippocratic physis under new names and in conjunction with new theories, but still the natural healing power: the *vis medicatrix natura*, the *archeus* of Paracelsus and Helmont, the *anima* of Stahl and others. (The above should not be interpreted that this is the only meaning of the "physis.")

The general viewpoint had been formulated by Heraclitus:¹² "Like a spider, sitting in the middle of a web, is aware as soon as a fly has destroyed some thread of the web, and therefore speeds to this area, as if it were concerned with the repair of the web, thus similarly the human soul, upon injury to any part of the body rushes quickly to that area, as if it had to be at that site of injury with which it is firmly connected and according to a definite relation." The most famous citation in the Hippocratic writings is in the book "On Epidemics," which states that "the physes are the physicians of disease." Also "the physis itself finds ways and means, not with conscious intent as with winking of the eyelids and as the tongue renders service and similar things. Because by itself, without education, without being taught it takes care of what is

necessary. Tears, moisture of the nose, sneezing, ear wax, saliva, expectoration, inspiration and expiration, yawning, coughing, swallowing, all in all, yet not in the same way. Urination, discharge of flatus, regurgitation, utilization of nutriment, respiration and in women what belongs to them and to the entire body, namely sweat, itching, stretching, and whatever else there may be."¹³ P*h*ysis here means the natural healing power or the physiologic power which rules the functions of the body. Similar thoughts are found in the markedly Heraclitic writing, "On Nutrition." The p*h*ysis is without instruction in everything¹⁴ and further: the p*h*ysis is sufficient in everything.¹⁵ The work on anatomy closes with the sentence: the rest has been added on by the p*h*ysis.¹⁶ The book "On Diet" reads: "p*h*ysis does this all by itself. If one sits and has complaints, one arises, if one walks and has complaints, then one rests, and other such things are properties of the p*h*ysis of medicine."¹⁷

The p*h*ysis is not able to accomplish everything. For example: "He (the physician) now should bring about the changes in such a manner that he himself takes on guidance. Partly he is supposed to change conditions existing, partly to leave them alone, if they work as and where they should. But partly he is supposed to alter them, especially if they are inadequate, especially those just about to start or those which have already begun."¹⁸ The physician must separate the useful and the harmful symptoms, bring about the former and prevent the latter.¹⁹ Symptoms are not always considered useful, nor the same symptom always regarded as one or the other. At one time it is the disease, at another, the means of healing. Coughing is healing or damaging,²⁰ skin eruptions may be the disease, or a useful phenomenon of the disease, a so-called apostasis.²¹

The p*h*ysis rules the physiologic processes and guides them into correct ways; it heals diseases; it is unconscious and instinct-like and unable to accomplish everything so that when incomplete, it should be supported by the physician.²² The subsequent development of these thoughts into the Aristotelian entelecheia with its vital influence upon all biology has been suggested elsewhere.²³

Many other attributes of the modern simile are found in the Hippocratic writings, but recital and discussion here would needlessly complicate matters. Suffice it to state that there is an appreciation of differences in effect from variation of dosage, altered response due to bodily conditions, an appreciation that symptoms represent the external perceptible phenomena of disease and do not constitute the disease itself. Koch²⁴ stresses: "Hippocratic diagnosis always involves the person . . . he rarely speaks of diseases, but always of people who have become ill." In short the abstrac-

tion of symptoms of disease from many patients is not the essential in Hippocratic pathology. At most it is a problem of a patient suffering from lobar pneumonia and not one of lobar pneumonia.

In conclusion it should be emphasized that the Hippocratic simile referred to the imitation of one outstanding symptom, whereas the modern simile takes cognizance of all the ascertainable phenomena. Some would emphasize this difference by calling the Hippocratic simile, the "superficial simile."

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THE GALENIC SIMILE.—Though some physicians in post-Hippocratic times explained their procedures as supporting the natural healing power, the importance of the simile steadily waned. Galen demands brief mention, not for his positive contributions on the simile, but to make contributions in the succeeding centuries more comprehensible. The simile is mentioned by name several times,¹

and he occasionally utilized the magic simile² and the doctrine of signatures.³ Frequently the word simile is employed in conjunction with digestion, in the sense that when food is eaten it becomes similar to the tissues already existing.⁴

The Galenic theory of disease is too well known to require detailed discussion. In general diseases were classified into cold, warm, dry and moist and medicinal agents assigned to similar categories, and to different degrees. For example, a remedy might be cold to the first degree and dry in the fourth. Since he employed a warm remedy for a cold disease, he proceeded on the basis of the contrarium.

But it is immediately evident that warm, cold, dry and moist are merely hypothetical properties and qualities assigned to diseases and remedies, and obviously his contrarium is purely theoretic and has little to do with so-called "allopathy." In so far as the simile is employed, it likewise is a theoretic simile.

The object of introducing Galen in this discussion may be stated as follows: Galenic doctrines prevailed in medicine for 1500 years. Medical literature in this period consisted largely of commentaries upon the Galenic writings and naturally mention the contrarium and the simile in the sense of the theoretic principles of Galen. An appreciation of his doctrine not merely serves to make scattered references to the simile in the Dark Ages of medicine more comprehensible, but also furnishes the key to understanding the polemics of Paracelsus against the contrarium and in favor of the simile.

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THE PARACELSIAN SIMILE.—As Paracelsus has already been presented as a staunch champion of the doctrine of signatures, the present opportunity may be utilized for a brief discussion of some related innovations.

"*Contraria contrariis curantur*, that is, heat dispels cold; that is false and has never been so with drugs."¹ "Not contrary by contrary; cold does not conquer heat, nor heat cold."² These statements are attacks upon the theoretic Galenic contrarium. The following citation was regarded as a precursor of the modern simile for a long time:

"What makes jaundice also heals jaundice. That is, good and

bad are in the same thing; out of the bad comes jaundice; but if the good separates, then it is the arcanum (remedy) against jaundice . . . because the drugs which would heal paralysis must come out of the same which cause it . . . so that arcana (healing powers) of minerals become understood, so that gold is the remedy for all diseases of those who seek after it. So also Saturnus has its arcanum which goes out of lead . . . what may be damaging in our hands, will also be changed through our hands into a drug."³ Inspection of the associated subject matter indicates that Paracelsus is concerned here with magic: every poison contains its own antidote. In the application of the modern simile great stress is placed upon the importance of conditions in the body which are regarded as co-responsible in determining drug action. A corollary to this assertion is the hypothesis that certain individuals are hypersusceptible to particular drugs and this elective action determines the so-called drug-constitution. Perhaps a foreshadowing of this conception may be found in the Paracelsian conception of "anatomic":

"Anatomic is an art by which you learn to recognize the form of everything; because you see nothing is without form, also diseases are not without form; but they are formed and therefore have a special anatomy, a special man so to speak. . . . Now when you hear this there is the further necessity that you know such shapes in the anatomy of herbs and plants and that you bring together the same anatomy of disease into order. The simile, according to which you should treat, gives understanding to healing."⁴

The idea of drug selection on the basis of the totality of the manifestations presented by the patient, as in the modern simile, in place of attempted augmentation of a single defensive mechanism, the superficial simile, is also advanced: "Also you must place anatomy on anatomy . . . now you have an agreement which does not deceive you."⁵ Due consideration for the totality of symptoms is particularly stressed in the following:

"Now the anatomy of this external man should be completely developed by the physician and indeed so completely that he cannot find a little hair on the head, nor a pore which he has not found ten times before. Because from this, out of the anatomy, the physician goes to the prescription, that limb to limb, arcanum to arcanum, disease will be placed to disease."⁶ The following is also suggestive: "Because arsenic heals arsenic, also realgar realgar, also heart heart, lung lung, spleen spleen; not spleen of a cow, not the brain of swine to the brain of man, but the brain that is, the external brain to man's internal brain."⁷

A relationship between drug and disease is also suggested:

"So when you encounter estioneum (lupus), cancer, so you

know that arsenicus lies on the same place which makes it. Now it is morbus arsenicalis, because it is so. Why does it happen that there is this philosophic distribution in a drug which any physician can learn? It occurs if that is its name, because that is a characteristic of a name. If you know arsenic in its nature, then you also know how to recognize arsenic in the body . . . as you know that, it shows the cure to you, that arsenic heals arsenic, anthrax anthrax, as poison heals poison . . . and heals the same anatomy, yes, the one to the other; that is philosophy. So now you know what arsenic is, so heal accordingly to the content of the anatomy, the arsenic with arsenic, as anatomy teaches you."⁸

A small dose is also advocated:

"Because drugs should be administered not with the weight but beyond the weight. Because who can weigh the beams of the sun, who can weigh the air? No one. But now in what way should drugs be administered? The drug should work in the body as a fire. . . . Can one find the weight of fire? No, one cannot weigh fire. Now a spark is without weight. Also the same is to be understood of the administration of drugs. . . ."⁹

The employment of the single remedy is also advocated:

"Because it is a despairing hope and belief to order so many simples in a prescription, because the poor people believe as long as there are so many, because of the number, if one does not help another may. Oh poor prescriptions! It is nothing else than that they forget that one filth spoils another."¹⁰

Perhaps the following citation is more definite: "Also understand that the power all lies in a simple and the same simplicia needs nothing else than alchemy . . . it lies in the extraction and not in the composition . . . what wise man is so simple and indeed so bad that he would put together what nature has separated, in this herb so much, in that so much, yet you, Mr. Doctor, command them to be put together."¹¹

Paracelsus owes not a little of his bad reputation to the fight conducted against the apothecaries. He stated: "Now in the apothecary shops there are no remedies, simply those cooked into each other as a soup of filth, the arcanum is drowned in this cooking and has no effect."¹²

Paracelsus also stressed the need for individualization of patients. He stated:

"But now of the drug effect, know that the nature of man is other and other (that is, different). Therefore in one much sweat is driven out, in the other not; he is not of the diaphoretic nature. Also in one type there is much vomiting, in the other not; because he is not of the vomiting type. Therefore it is an error when one

states that he makes a patient healthy by sweating or vomiting. They do not consider the variegated nature of man."¹³

As implied above, Paracelsus deemed it an advantage to describe patients according to a nomenclature of remedies. He states:

"A natural truthful physician speaks; that is morbus terpeninus, that is morbus sileris montani, that is morbus helleborinum, etc. And not that is phlegm, that is hoarseness, that is rheumatism, that is coryza. These names do not arise out of drugs, because with names equals are compared to equals, because out of the comparison comes the effect, that is, arcana open themselves in diseases. Because there is not simply one kind of colic but many types of colic and as many types as there are types of arcana in colic. From this follows colica zibetina, colica muscata, not colica ventosa, not colica fellis (bile), etc., nor according to another nomenclature than we describe."¹⁴

Paracelsus opposed palliation where cure is possible:

"Because things which are laxative or constricting are not arcana. Also what serves for excretion and defecation, that you know, but what concerns healing and arcana, you are all brother infants."¹⁵ Finally with re-emphasis upon the totality of symptoms Paracelsus may be dismissed: "Because out of the entire man comes health, not out of crumbling fragments, and that is never considered in colleges and has at all times merely patched, not warm to cold, constrictive to laxative, that is not a basis for a physician nor never has been."¹⁶

In recapitulation, the Paracelsian writings advance a simile, the small dose, the necessity for having drug pictures, the totality of the symptoms, the relationship of drug to disease, the single remedy, the individualization of the patient. All of these are attributes of the modern simile which, however, applies these thoughts on a quite different basis.

In the post-Paracelsian period the simile is often mentioned, usually in the sense of a magic simile. Typical of the group is Porta¹⁷ who attempted to apply the doctrine of signatures to the entire domain of botany. Indicative of his pure magic is the use of hairy plants in diseases of the hair, beautiful plants for improving beauty, gay plants, sad plants, etc. O. Croll¹⁸ likewise adopted the magic simile and Schroder¹⁹ presented related ideas; for example, the leaves of *Hepatica Triloba* look like the liver. Paracelsian astrology was elaborately developed by Carrichter²⁰ who arranged plants according to prevailing "constellations" and gathered drugs only during certain phases of the sun. The work of Thurneysser²¹ and Winckler²² follows the same trend. Severinus and Goelenius like-

wise are of the same stamp. A few writers of greater interest may be given brief consideration.

In recent years Fludd²³ has been mentioned occasionally.

"Do we not see that similar, whose nature is altered, is changed through putrefaction, and acts most destructively on that similar to it? So worms, dried after excretion from the body, if made into a powder, are given internally against worms. The sputum of tuberculosis after the necessary preparation heals against tuberculosis. The spleen of man is an antidote against swollen spleen. The bladder and kidney stone, heals and dissolves stones."

In this citation one perceives the tuberculin treatment of tuberculosis is definitely foreshadowed, yet reading merely a few paragraphs shows that Fludd is guided by magic in all his thinking. Valentine is also cited and his most relevant remark reads:

"Then equal must be expelled by equal and not opposite with opposite as heat with heat, cold with cold, prickling with prickling, because one heat draws another on itself, as the magnet does the iron. As prickling simplicia can dispel prickling diseases and poisonous minerals can heal against poisonous attacks and bring about health, when they are prepared."²⁴ The word "magnet" suggests that there is much magic in Valentine's writings, which also contain the doctrine of signatures and occasional flashes of the unconscious use of a more modern simile. More rarely the work of Rummel is mentioned:

"Out of what principio the disease arises, likewise out of the same principio, the cure must be instituted."²⁵ Rummel writes on the basis of signatures, sympathy, alchemy and astrology. Kircher²⁶ has been cited by Kobert²⁷ and more recently by Müller:²⁸ "poisons are healed mostly through their own antidotes." In regard to the simile at least he was oriented entirely by magic as this magic isopathy suggests.²⁹ Van Helmont is also quoted at times.³⁰ Usually he is activated by the doctrine of signatures and sympathy; still one place is worthy of quotation: "The stroke with the blood of a man who has recovered from the disease (zinzilla) acts well. Those who have recovered from the disease have a blood so balsamic that they are henceforth safe from this disease."

More attention must be given to the work of Alberti-La Bruguiere which has been recently cited by Müller.²⁸ The work is excellent in that it compiles most of the expressions of the simile up to the time of writing. Likewise it rejects the magic simile and some examples of the theoretic simile. In short it is a compilation of all earlier writers concerned with support of natural healing.³¹ As the work is now generally available,³² those interested may find it worth consulting but the only value of the compilation is the retention of

some expressions of the simile which otherwise might have been lost to medical history. However, Müller errs when he asserts that it is unknown to the homoeopathic profession since it is repeatedly mentioned in earlier homoeopathic writings.³³

No attention has been paid to the writings of Cardano,³⁴ Vidius,³⁵ Damascenus³⁶ and several others, since some are concerned with the Galenic simile, others with pure poetry or the magic simile. Sennert³⁷ is typical of the last group: "the similarity of the poison (arsenic) draws the plague poison on itself." Buxham's suggestion to employ antimony in smallpox is interesting in view of the fact that the drug produces an eruption similar to that of smallpox.³⁸ To these names may be added those who helped keep the simile alive by isopathic procedures; they are mentioned in the earlier section on the development of antitoxin therapy. Especially important are Lady Montague, the innovations of Wezpremi, Samoilowitz, Home, Munro, and Jenner.

Stahl has received unmerited fame. He wrote: "Entirely false and the reverse of what ought to be, is the rule in medicine to treat by oppositely acting remedies (*contraria contrariis*). On the contrary, I am convinced that diseases will yield to and be cured by remedies (*similia similibus*) that produce similar affections—burns by exposure to fire, frost bitten limbs by application of snow and ice water, inflammations and bruises by distilled spirits." The work quoted by Hahnemann³⁹ is that of Dippel who was a magician, hermetic physician, theologian, etc. Stahl based his opinion on magic though this does not imply that the ideas are without merit. Incidentally this Stahl was a Danish army physician and not the Stahl, immortal to medical history; this, too, has contributed to misunderstanding.

In a recent interesting historical study d'Orsay⁴⁰ has occasion to allude incidentally to the simile and he concludes that v. Haller and Linne ought to be credited with furnishing the stimulus to Hahnemann for the elaboration of his doctrine. The material submitted, however, clearly indicates that v. Haller and Linne are concerned here with a variety of the Galenic simile and serves to re-emphasize how frequently writers fail to penetrate the meaning of Hahnemann, a mistake presumably due to hasty scrutiny of his writings and the readiness with which traditional accounts are accepted. Much more logical precursors can be found in de Haën⁴¹ who wrote that solanum in large doses excites spasms, in smaller doses relieves them, or in Unzer⁴² who asserted that tobacco can remove the same diseases which it provokes. Inspection of the literature permits discovery of many isolated statements of the simile; in fact, occa-

sion will be taken soon to show that even Brown, though regarded as an enfant terrible by Hahnemann, mentions it.

If a predecessor must be found for Hahnemann, Stoerck (1731-1803) is the most logical candidate as Tischner⁴³ has proven. Stoerck made the highly significant statement: "If stramonium makes the healthy mentally sick through a confusion of the mind, why should one not determine whether it gives mental health in that it disturbs and alters the thoughts and sense in mental disease, and that if it gives health to those with spasms, to try and see if, on the other hand, they get spasms."⁴⁴ It will be observed that this is a program of investigation rather than a conclusion. More important, in the writer's opinion, is the fact proven later, that Stoerck was greatly interested and wrote considerably on a neglected phase of medicine which subsequently occupied a major portion of Hahnemann's time and energy. Direct connection is established through that fact that Quarin was Stoerck's pupil and Hahnemann's teacher and the Stoerck-Hahnemann association via Quarin is also suggested by Hahnemann's remark: "All that I am as a physician, I owe to Quarin."⁴⁵ The frequency with which Stoerck's name appears in Hahnemann's bibliographies may also indicate a source of stimulation.

The plan of presenting the modern simile by brief historical illumination was adopted in order to eliminate certain sources of confusion which obscure the problems actually involved. Hahnemann's simile, so-called homoeopathy, represents a focal point around which most of these traditional errors revolve. If Hahnemann had not advanced his simile, one might say, under unusual circumstances, his opponents would have had little occasion to belittle his ability either by endeavors to discover apparently phantastic parallels or by allegations of borrowing. On the other hand had his champions not been so ardent, zealous attempts to fortify their convictions by equally irrelevant recourse to medical history would have been recognized immediately as dubious expedients tending to cloud rather than clarify the situation. While it would be premature to attempt to evaluate the importance of Hahnemann's simile, it is essential, for purposes of record, to stress again the independence of the various similes. The most ancient is the magic simile which appears in various disguises of magic, sympathy, signatures, etc., yet it can be recognized by its major implication: some arbitrarily selected incidental external property of the substance is the sole index of its therapeutic utility; equally arbitrary selection of some single manifestation of the patient to represent the disease. This statement is not intended to imply that all practices originating in magic are unworthy of attention. In

the broadest sense a fact may be a composite statement of theories and perhaps each theory is a logical totality of facts. One might recall here the famous philosopher's stone and its relation to alchemy. At the time of alchemy the problem had a very deep meaning and innumerable workers exhausted their powers and health upon it. With the promulgation of the theory of unalterability of the atom, the question lost its meaning, indeed was regarded as foolish. At present, by virtue of Bohr's atom model, according to which gold differs from mercury merely by the absence of a single electron, again the question is acute and its solution is being prosecuted by the most modern methods of investigation. Such thoughts are extremely significant for medicine. The history of pharmacy and materia medica shows in a particularly convincing manner that many remedies, willingly employed by all physicians and therefore presumably productive of cures, are suddenly discarded and replaced by new medicaments, usually on no better evidence than a new theory which proves that the "apparent" action of the old drug rested upon erroneous conceptions, while the new drug is "good" precisely because of the new theory. With the decline of the old remedy the relevant literature and pertinent facts become enshrouded in oblivion. The facts upon which remedies were employed by the ancients are lost; the theories, long since exploded, steadily dwindle and soon become meaningless to those with a different world conception. The more fruitful theories tend to recur in altered form and under new names. For these reasons, although the theory of magic is waived aside with thoroughly modern disdain, remedies, procedures and ideas which arose from it are not necessarily repudiated.

With characteristic Grecian brevity Hippocrates formulated what may be legitimately regarded as the greatest therapeutic maxim as yet known: nature is the physician of disease and the Hippocratic law: if nature resists all is in vain. Depending upon unaided but still unparalleled keen observation, the Coic school came to regard certain phenomena of disease as endeavors at healing and urged their imitation, the Hippocratic simile. Their interest in prognosis, their unbiased observation, their disinclination to weave phantasies, and other traits symbolized in the name Hippocrates unmistakably differentiate this simile from the magic simile. That the subject is not extensively discussed by Hippocrates should cause no wonder, since the Hippocratic assertions mentioned above find no amplification at all. This simile has been named the superficial simile, not with the intention of minimizing its importance, but to stress the imitation of a single manifestation of the disease rather than to give due regard to the totality of phenomena. Perhaps the rarity

of Hippocratic prescriptions based upon the simile may be assigned to the readily understood inadequacy of pharmacologic data permitting its use.

The theoretic simile of Galen is so called because of the arbitrary assignment of qualities to both diseases and remedies. While the entire practice of Galen proceeds upon a contrarium basis, the frequency with which commentators discuss his "contraria" and "similia" rather than its relevancy necessitated its inclusion. The Paracelsian simile is a variant of simile magic but reference to it permitted the incorporation of a few citations whose pertinence will become obvious later. In the pre-Hahnemann era diligent investigation of the literature would probably reveal additional references to the simile, known or unknown to the writer, but their rediscovery and refurbishment would probably have no great significance since the existence of detached suggestions is presumed by everyone. For reasons already mentioned and subject to amplification later, Hahnemann's stimulus might have come indirectly through Stoerek's programmatic suggestion. However it is immediately apparent that Stoerek was not a necessary predecessor, for Hahnemann could have proceeded without knowledge of this work.

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SCHOOLS OF THOUGHT.—In a strict historical narrative Hahnemann's simile, so-called homoeopathy, ought to be treated next, but a brief digression on schools of thought may be interposed with benefit. While discussions intended to indicate the general significance of schools of thought have appeared frequently in recent years, the subject does not seem so familiar to physicians as to render further reference superfluous. More specifically homoeopathy as a school of thought is a topic upon which many people hold very definite opinions without considering it necessary to have any preparation nor to attach much importance to the views of those who have devoted themselves to the subject. This fact alone suggests that more space will be required to remove irrelevant accretions than has been allotted to previously discussed topics. It ought to be stated in advance that the following remarks are intended to orient the reader as to schools of thought in general, rather than to evaluate the possible merits of homoeopathic contentions.

Omitting entirely, for the present, influences motivated by non-intellectual factors, historians of science in general and of medicine in particular, are to some extent responsible for the cultivation and prevalence of the impression that we are necessarily nearer to truth

than our predecessors. The resultant general conviction is implied in a picture of science, wearied from exhausting struggles and previously misled by obstructing half truths, but now resting on a place of certainty. The failure to appreciate that similar convictions have obtained in every generation tends to give impetus to the suggestion that reformers serve to misdirect, while orthodoxy leads in the right direction (wherever that may be). Readers not infrequently gain the impression that current trends of thought represent doctrine, divergencies of opinion, dogma.

Most reformers have been dead sufficiently long for assimilation of their innovations; the comparatively recent death of Hahnemann and the incomplete digestion of his innovation perhaps assist in making comprehensible the hostility of some current criticism. Naturally this attitude is not peculiar to medicine, nor has it been directed solely against Hahnemann. If instances are needed to enforce the contention that orthodoxy may constitute a bar to scientific progress, the treatment of John Newlands by the chemists, Young and Ohm by the physicists may be recalled. Too often forgotten is the attitude, then and now, towards Harvey, Jenner, Semmelweiss, or the treatment given to Pasteur by the Parisian physicians. Paracelsus is an excellent case in point. Some medical histories still in vogue depict him as a charlatan, imposter, fraud, etc. Some very recent textbooks on the same subject reveal him as the one who freed medicine from 1500 years' imprisonment in the chains of Galenism, etc. This study is not concerned with Hahnemann; but it ought to be emphasized that the picture drawn in many current textbooks and histories is not necessarily detached and that the judgment pronounced by several living professional historians is, in no way, final. In fact some unprejudiced students of history, as Honnigmann and Diepgen, recently have suggested that the traditional attitude towards Hahnemann requires revision; perhaps as with Paracelsus standards are changing.

Schools of thought exist in every department of science; here one recalls the vitalists and mechanists in biology, the varieties of teleologists, etc. Schools of thought have always existed in medicine; the *Corpus Hippocraticum*, written around the school at Cos, stresses the defects of the co-existing school at Cnidos; nor should it be forgotten that the difference in opinion involves an issue which has not been solved up to the present.

Successively vying with each other are the dogmatic school with emphasis on humoral pathology, Erastistratos and his mechanistic school, the empirics, the methodists, the metasyncratic school of Themison, the pneumatists, the eclectic, and Galenism. Passing over to more modern eras, one encounters the revolutionary

Paracelsus, the school of iatro-chemistry and iatrophysics, the revolt from mechanism in Stahl's animism, the methodist school of Hoffmann, the neuro-pathology of Cullen, the stimulant school of Brown, the organotherapy of Rademacher, the nihilistic school of Vienna, the cellular school of Virchow. Naturally only a small fraction of the possible examples need be cited.

These schools represent revolts from traditional medicine and such progress as has been achieved may be safely attributed to the results of intelligent differences of opinion. The reformers likewise present certain mutual characteristics, for, with few exceptions, their individual doctrines have been advanced as the only viewpoint worthy of support. The Galenic modification of the humoral theory, Brown's stimulant theory and others possess this exclusive character. Few students, informed on the origin of some ideas in medicine, would care to deny that all these schools possessed a fruitful nucleus. A dissatisfaction with current teachings, a revolt against tradition in each case was followed by a (comprehensible) over-emphasis of the importance of the innovation by the reformer. The assimilation of the fruitful nucleus (when this occurs) gave decreasing occasion for the schools living in isolation, so that so-called official medicine may be legitimately regarded as a composite of such residues. Then the play begins anew. Often up to the moment of official adoption, then usually under the guise of a less disturbing terminology, the minority method was beyond the pale of rational medicine and its supporters deemed heretics, irregulars, and sectarian. While exceptions to the above situation may be found, the picture sketched above, recurs with striking frequency in the annals of medical history. To create an impression of greater urgency for the new, one finds fault with the old; reformers regale against prevailing systems and then announce their own.¹ Often these disagreements remain within the professional family, but instances are not unknown where extreme subjectivity prevailed, and the public was invited to witness the undignified spectacle of quarreling. However sufficient has been said to characterize the procedure of reform and to suggest the role played by schools of thought in the evolution of medicine. The intelligent reader will not, of course, interpret these remarks as an underappreciation of the value of conservatism based upon factual judgment nor of the inestimable value of honest criticism, regardless of how destructive it may seem. Perhaps a few high-lights from Bier's summary of the evolution of Virchow's thinking may save many words.

Even with the first volume of Virchow's Archives, Virchow fought against dominating systems as well as systems in general.²

Later he wrote that one condemns the parties of systems and recognizes only the empiric, the scientific school.³ At another time he stressed that progress in medicine has always been opposed by two chief handicaps: authorities and systems.⁴ After continuing in this vein for a number of years he introduced the solid and united system of cellular pathology. Like all systematists he emphasizes that his innovation is not a system, for he has introduced a "principle."⁵ He asks if any explanation is required for the fact that he was compelled to stress some facts almost to one-sidedness in order to develop the principle.⁶ But wherein his principle differs from a system is not clear since a principle is the guiding thought in a system. By "system" Virchow must have meant a priori speculation;⁷ otherwise his thoughts are contradictory and incomprehensible.

His opinion on systems apparently has undergone change when he remarks that thousands of individual facts can be compressed into a few solid rules and the material made comprehensible for the new generation.⁸ Again one may recall his statement that without a principle the worker can only proceed if engaged in detail investigation and the physician is in a bad situation if he is unable to correlate individual announcements with some principle.⁹

The failure to understand Virchow's sophistic refusal of systems and the inability to appreciate that he created a system has had its consequences. Since that time it has been popular to announce that one does not possess any system. One may recall the young Bier who once said: "I have only one principle and that is to have no principle." It almost seems as if the present era is one of individualism and it has actually been characterized as one of "mania for self expression."

Medicine is just in the process of recovering from the enthusiasm of the school of bacteriology which saw in bacteria the sole cause of infectious diseases. Immediately with the announcement of the syndrome of agranulocytic angina, a variety of "specific" bacteria were announced. But medicine is now entering the throes of the constitutional school of medicine which perceives in bacteria only one cause of infectious diseases and recognizes the constitution and disposition of the patient as equally important factors. Now a days some speak of the peculiar reaction of the hemopoietic system to a stimulus which results in agranulocytosis.

Although some may object to the word "school," there are three commonly known schools of chemotherapy. The largest group is still concerned with the task of finding exclusively parasitotropic remedies and aim at a "therapie sterilizans magna." A second group is searching for hypothetical substances which when dis-

covered will permit a substitutive therapy. The widespread interest and great progress in endocrinology reflects the activities of this group. A third group consider themselves above therapeutic problems and search for a relationship between the action of a drug and its chemical structure (and peculiarly enough, do not consider the body at all). The employment of the term "school" is particularly applicable in the field of abnormal psychology, for example, the schools of Freud, Jung and others. There are schools of causal therapy, of specific therapy, of alterative therapy, of electrotherapy, to mention but a few. In this connection the electrotherapist of the last century was usually regarded as a charlatan; now there are official councils on the subject and the physician without such equipment is said to be inadequately prepared to treat patients.

Medical systems have always existed and exist today in an unprecedented number. The present differs from the past chiefly in that formerly principles covered very wide fields, now systems are special and often private. Perhaps this diversity of opinion is responsible for medical progress.

As mentioned above all systems tend to exaggerate their own importance. The new always attracts neophytes; scientists, looking for promising fields, often lend their aid; gradually the nucleus of "truth" is discovered and the chaff discarded although salient features may be neglected until chance rediscovery permits introduction. It is the opinion of the writer that "systems" are necessary to medical progress, but their value lies in their partial truths. Even the most severe critic would hardly care to deny that homoeopathy played an extremely valuable corrective role and practically everyone will admit the merit of its "negative" contribution. Here it seems opportune to examine a related question: namely, whether or not its founder and its recognized organizations presumed it to be an exclusive form of therapy, therefore a cult.

Hahnemann regarded as unacceptable for the homoeopathic procedure the so-called surgical diseases as well as those presenting an obvious, ascertainable or removable cause which he presumed the intelligent physician would remove like any other obstacle to recovery. Actually homoeopathic physicians have been somewhat unique as a school, in stating that homoeopathy is a supplement to "regular" medicine and not a substitute for it. The official definition of the American Institute of Homoeopathy, the official national organization in this country, has long been couched in unmistakable language: a homoeopathic physician is one who adds to his knowledge of general medicine, a special knowledge of homoeopathy. Moreover inspection of the curricula and practices of homoeopathic colleges reveals that this definition is not merely a figure of speech

and further that homoeopathic physicians, with rare exceptions found in any diversified group, regard the procedure as *a* method and not *the only* method in medicine. A physician who employs the homoeopathic procedure exclusively, unless he strictly limits himself to highly specialized practice, is appropriately denominated a cultist. But what appellation ought to be bestowed on those who know nothing and insist on knowing nothing about it? Bier once said: "people who live in glass houses should not throw stones."

It would be incorrect and far from the intention of the preceding remarks to imply that no occasion has ever been given by some of Hahnemann's followers which would justify the appellation of a medical sect. It is not the desire of the writer to disinter some unfortunate situations which gave rise to the opportunity, although allusion must be made to one important item. Before doing this, attention should be directed momentarily to the danger of a cult to science. For examination of this question the contrarium principle is admirably adapted.

The following remarks are directed at the contrarium of ancient medicine but an opportunity is afforded here to mention the modern contrarium rule. The magnificent development of surgery is due solely to application of the contrarium rule. Likewise two related achievements, asepsis and anaesthesia, may be traced only to this source. Many of the prophylactic measures of enormous importance to public health also arise from it; therapy by substitution in some of the deficiency diseases, in many endocrine syndromes, the treatment of intestinal and skin infestation are based largely upon the contrarium principle. Most so-called chemical and functional antidotes in poisoning arise from the contrarium. Had the contrarium rule merely given origin to the above procedures, not to say innumerable others, it would have been of incalculable value to humanity, and certainly requires no defense except when advocated as the exclusive and solely correct method in medicine. The omission of these subjects in the text is dictated by the nature of the study and not because their value is underestimated. However, it must not be overlooked that many physicians, consciously or unconsciously, proceed as if the contrarium represented the exclusively correct doctrine. Even more believe that a physician must follow the contrarium or the simile, and it is precisely this "either-or" attitude, absolutely impossible to justify scientifically, which constitutes a great obstacle to obtaining a correct attitude toward the simile. After this digression, a few words on the ancient contrarium:

The Hippocratic school of medicine took cognizance of both the simile and contrarium. It remained for the mathematically minded

Galen to focus all medicine on the contrarium principle, which became the exclusive method, and for the next 1500 years, medicine did not make a single noteworthy advance. Blinded by authority, students found the highest glory in agreeing with Galen and his theories. When observations did not coincide with Galenism, physicians refused to believe their senses, or they succeeded in forcing their views into its procrustean bed. Tischner stresses the relationship of such a medical situation to the magic world conception, that is, the consensus of opinion or concord of a mental community to their canon,¹⁰ and describes the Galenic writings as the Canon of medicine for that period.

With this the chief danger intrinsic in an exclusive system is disclosed, for, as Spengler points out, the sole strict scientific method which an unchanging Canon leaves for continuance is commentating.¹¹ The fact that the adoption of a Canon means suicide scientifically requires no further emphasis.

While the true import of the following remarks is easily susceptible to distortion and may be avidly grasped by those wishing to misunderstand, opportunity ought to be taken to stress an obvious, persistent and almost studied failure to differentiate between groups of "homoeopathic" physicians. While they seem to be unanimous on the justification of the simile principle, the "small" dose, the necessity for provings, the importance of individualization of patients, there exists and has always existed the most profound difference relative to the extent of application of the simile principle, the size of the dose, etc. When the development of homoeopathy is presented it will be noted that, even during Hahnemann's life, two groups of homoeopathic physicians were separated from each other. One group called themselves the representatives of pure homoeopathy or Hahnemannians because their ultimate authority in regard to homoeopathy is Hahnemann. Naturally within this group there were all shades of differences from those with moderate views up to those who have no hesitancy of rushing through portals into which their master hardly dared to gaze. The other group call themselves scientific homoeopathic physicians. They recognize Hahnemann as a brilliant innovator, but thoroughly appreciate his fallibility and have never hesitated to challenge his opinions. The modern conception of homoeopathy has been largely due to the efforts of this group, in so far as homoeopathic physicians are responsible for progress in this field. That some homoeopathic physicians regarded Hahnemann's writings as a canon is inescapable, first as a fact, second as inevitable with a diversified large group.

Tardy appreciation of the true significance of intra-homoeopathic groups has been responsible for the belated interest in

homoeopathy itself. As the occasion will not present itself again opportunity should be taken here to indicate a few other sources of confusion. Homoeopathy is concerned with the simile principle and its application to the treatment of disease. If this principle properly interpreted is untrue, the entire structure of homoeopathy automatically crumbles and further discussion would be unnecessary. Therefore it seems logical to direct most attention to the elucidation of this keystone. Evidence has been introduced to show that ideas of similars are recorded in various epochs. Naturally these different simile principles have been interpreted in the most diverse ways and in accordance with the opinions prevailing at the given period. It is also immediately apparent that the several interpretations are utterly irreconcilable with each other. Perhaps in a very broad way all this heterogeneous mass can be lumped together and denominated homoeopathy, but the result is not conducive to either clarity or accuracy.

Assuming the accuracy of the suggestion that many similes have existed, it is then apparent that Hahnemann's application is a special application, but one of many. The value of his particular contribution must be judged partly by the standard of knowledge available during his life and partly by substantiation or refutation in the time which followed. But it is essential not to identify the simile as a possible procedure in medicine with the particular application by Hahnemann.

There is another elementary source of confusion. Regardless of an estimate of Hahnemann's importance to medicine, it is generally agreed that his endeavors extended in many directions. With Pinel he was among the first (in Germany) to advocate the humane treatment of the insane. It is common knowledge that he was recognized as one of the foremost chemists of his time. While his studies in chemistry receive more attention later it may be noted here that he made an error in regard to the chemistry of borax. Obviously the merit of Hahnemann's homoeopathy cannot be weighed by the correctness of his observations on the treatment of mental patients. Nor by the same token should his homoeopathy be assessed on the basis of his error in chemistry. So it is elementary but frequently forgotten that sharp distinctions must be drawn between Hahnemann's scientific endeavors in unrelated fields, Hahnemann's homoeopathy and the simile. Furthermore the reader will subsequently discover that the life work of Hahnemann can be divided into two periods, the first ending in 1810, with the publication of the first edition of the *Organon*, perhaps even a little earlier with "The Medicine of Experience." This period of his life is characterized by reports of observations. The second period

of his life is characterized largely by attempts to explain these observations. Thus in the interest of determination of real merit "two" Hahnemanns should be considered.

Nearly 150 years have elapsed since Hahnemann's original interpretation of the simile. During this time medicine has undergone unprecedented evolution. Homoeopathy and the simile also have undergone equally remarkable transformation, and there exists at the present time what may be legitimately termed the modern conception of homoeopathy and the simile. It is just as confusing to call the homoeopathy of 1810 modern homoeopathy as it would be inaccurate to characterize modern medicine by the conceptions of the same period.

While these remarks may seem very pedantic, even the most cursory glance at the pertinent literature reveals how rarely the nucleus of homoeopathy is discussed either pro or con. Frequently the simile principle is regarded as unscientific because Hahnemann or some homoeopathic physician has made some statement incapable of support. The various simile principles, Hahnemann, Hahnemannian homoeopathy, various innovations called homoeopathy as electro-homoeopathy, various kinds of homoeopathic physicians have been placed in an indescribably heterogeneous conglomerate, and conclusions have been drawn from this subjective basis. Unless these sources of confusion are thoroughly and constantly appreciated, little progress will be made in the accurate conception of homoeopathy and the simile.

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HAHNEMANN.—A study concerned with thoughts and practices need not treat the individual responsible for them. Moreover a biography of Hahnemann is particularly unnecessary at this place since adequate discussions are now available.¹ On the other hand he cannot be totally dismissed because misinformation about him is very widespread. The general failure to examine the sources personally and contentment with hearsay often finds reflection in judgments on his innovations. Attention is directed here to some influences which might have affected his theories and occasion is taken to correct a few of the widely prevalent errors which have tended to color decisions on his homeopathy.

Christian Friedrich Samuel Hahnemann was born on April 10, 1755 at Meissen, Germany. As the parents were poor, early education was obtained at home, but later instruction was received at St. Afra in Meissen. A farewell speech at this school shows the twenty-year old student an optimistic teleologist, the theme being the purposeful formation of the hand.² The same year finds him entering college at Leipzig, paying his way by tutoring in languages and by earnings derived from translation of foreign medical works. Beyond supplying an index, the first of these translations is interesting only in respect to the foreword. It advocates a combination of physics and mathematics with physiologic and medical knowledge.³ His second,⁴ third,⁵ and fourth⁶ translations contain nothing of his own. At Leipzig the foundation was laid for his great knowledge of medical literature and outside of Platner, it is doubtful if the faculty seriously affected his medical viewpoints. Two years later Hahnemann journeyed to Vienna for clinical instruction which was inadequate in most German universities. There he studied under the previously mentioned Quarin who apparently was an excellent physician,⁷ more practitioner than investigator,⁸ but ultimately director of the famous Allgemeinen Krankenhauses. As Wolstein⁹ was also a pupil of Quarin, it is possible that Hahnemann's early scepticism about venesection could have been accentuated by this acquaintance. Late in 1777 Hahnemann left for Hermannstadt to become physician and librarian to Bruckenthal

and 1779 finds him in Erlangen where he received his medical degree. His doctoral thesis¹⁰ reveals nothing of interest save the possible therapeutic value of mesmerism. Since his Vienna sojourn was simultaneous with the fight over Mesmer,¹¹ this could have interested him in the procedure and might account for its inclusion in some editions of the *Organon*.

Hettstedt, his next location, was the site of origin for several minor papers. The first¹² is interesting in that he suggests physicians and attendants as one source of spread in epidemics. His suggestions in this field are quite noteworthy as micro-organisms were then unknown. Self-criticism is indicated by his statement that perhaps his mistreatment was responsible for the long duration of the disease. In the main the treatment was designed to conserve strength. Some attempts to utilize chemistry are also found therein. The second paper¹³ reveals his use of the therapeutic methods then in vogue, but the third¹⁴ relates successes by lay people in cases where his, the customary treatment, failed. Increased scepticism of current theories is expressed and finds greater emphasis in his fourth paper of this series.¹⁵

Nine months later he turned to Dessau where he added chemistry to his interests. Here he became engaged to marry and moved to Gommern in order to develop a practice more rapidly. His first major contribution¹⁶ on therapy was written here. The study indicates an adherence to humoral pathology but distrust of treatment based thereon; his great guide in therapy is to not weaken the body although little is found which emphasizes a natural healing power. He counsels taking suggestions from all sources, but not relinquishing treatment to laymen; a middle position between empiricism and science of the time is adopted. His independence is indicated by the following citation which also serves to indicate his willingness to deviate from tradition:

"It is this choice of a remedy and the manner of use which characterizes the true physician, who is sworn to no system, rejects nothing not investigated by himself, nor takes the word of another, and has the courage to think for himself and to treat accordingly" (p. 179).

Simplicity in therapy, great attention to general hygiene, detailed rather than general instruction of patients, the role of psychic factors in retarding or accelerating recovery, indicate the general trend of his advice. Composite drugs are employed, the posology is not unusual. Local treatment in a form which recalls modern antiseptics was advocated and surgery performed when indicated. The suggestion of employing carbon dioxide inhalations in the treatment of pulmonary tuberculosis could possibly have been

taken from Beddoes.¹⁷ Of interest in the light of his future thoughts is the necessity for considering a patient as a psychosomatic unit, as a totality, still with emphasis upon the individuality of each case. The work represents hippocraticism in the best sense of the word and was favorably received.¹⁸ The same village witnessed the appearance of an important translation of a chemistry.¹⁹

His next move was to Dresden where his critical attitude toward the status of medicine and the attitude of physicians found expression in his extensive work on arsenic.²⁰ At this place one finds real indications of Hahnemann's desire to leave medical practice and to enter the field of forensic medicine.²¹ By virtue of ability, friendship and association with Wagner, then directly in charge of this work at Dresden, Hahnemann hoped to secure a position after Wagner's death. This hope was not fulfilled and Hahnemann left medicine to devote his energies to chemistry and supported himself by translations.

He then moved to Lockwitz in order to reduce expenses. A later letter to Hufeland indicates cessation of medical activities was necessitated by his inability to treat his fellow men as long as the action of powerful drugs was unknown.²² A willingness to renounce a life work because conscience commands, indicates an idealism rare but not unknown in science. It may account for Hahnemann's poverty during subsequent years.

The arsenic work deserves brief mention at this point: the fourth chapter is interesting in the inclusion of subjective symptoms into the toxicologic picture. Incidentally his suggestions on storing of poisons, a poison registry, etc., subsequently became legally adopted. But particular attention must be directed to his insistence on fact and disavowal of theory: "For this reason I shall have little to say and consider nothing as probable which is not based on several concurring facts themselves" (p. 69). There is a refusal of hypothesis and theory is employed only in so far as it has practical use. The work was considered classical for its time.²³ Another paper from the Dresden period dealt with venereal diseases and their treatment.²⁴ At this time it is sufficient to say that Hahnemann announced a new mercury preparation for the treatment of syphilis which ultimately proved very useful.²⁵ The study was stimulating²⁶ and the substance became widely employed even though the method of preparation subsequently varied.²⁷

Hahnemann's activities as a chemist may be passed over for the present. Following his location at Lockwitz he moved to Leipzig and there began a wandering life which covers the next sixteen years during which he changed his location about twenty times. While some events during this period will be considered later at

greater length, a few merit attention here. The early period is characterized by a refusal of a professorship at Wilna,²⁸ presumably because Hahnemann imagined something similar would be forthcoming in Germany. In 1791 one finds him still interested in chemistry,²⁹ 1792 in psychiatry. In this same year he published a vitriolic attack against Lagusius, physician of King Leopold II. The royal patient had suffered from some abdominal disorder and since one venesection had failed to relieve him, three more were performed within twenty-four hours. The incident serves to indicate the abuse of venesection, but it is cited here to emphasize Hahnemann's intrepid and gruff manner of expressing his opinions. On the other hand in response to an attack³⁰ made against an error in statement, relative to preparation of soluble mercury, Hahnemann states³¹ it is easy to abuse praiseworthy men as his opponent has done. The same personal tone was also taken against Gren.³² Later he complained about these attacks³³ but the point demanding emphasis is that one may easily anticipate his tone when his life work is attacked, if one understands his reaction to adverse criticism on a comparatively trivial point. The statement that Hahnemann was a mystic³⁴ at this time is not supported by any evidence.

His arrival in Königsutter in 1797 evidences his more complete return to medical practice which was not without result. He began to prescribe self-prepared remedies with the result that he was forbidden to continue this practice since it interfered with the vested rights of apothecaries.³⁵ In this rambling account one might easily presume, as Hare³⁶ has done, that Hahnemann was a mere "itinerant physician." More accurate is the fact that in this year³⁷ he refused a professorship³⁸ in the University destined to become the famous University of Dorpat.³⁹ Failing to secure another position⁴⁰ he turned finally to Hamburg where he displayed interest in psychiatry. Several more changes in location followed, until he finally settled in Torgau where his idea destined to become known as homoeopathy matured.

The factors responsible for the continual change of location have not been determined. Hahnemann stated in general that it was not the concern of anyone but himself.⁴¹ The rebuff in forensic work, the unwillingness to compromise his views of treatment, a familial trait for wandering may all have played parts.

After the publication of his chief work, "The Organon," Hahnemann apparently felt the urge to disseminate the doctrine by personal teaching and moved to Leipzig after being advised against going to Göttingen.⁴² He was admitted to the faculty of the University of Leipzig⁴³ after payment of the usual fee and the delivery

of a dissertation.⁴⁴ There is little evidence of his success as a teacher, but students provided him with material for study of the effects of drugs on the healthy human. Beyond some works discussed later, the period is remarkable only for a debate conducted with Dzondi⁴⁵ on the treatment of burns. On the other side there was increasing evidence of more general interest in the subject of homoeopathy as may be seen in the remarks of Bischoff⁴⁶ and Puchelt.⁴⁷

This happy period of Hahnemann's life was brought to a dramatic close by the death of Prince Schwarzenburg. The famous war veteran had suffered from a stroke of apoplexy. Dissatisfied with the help given by his physicians he proceeded to Leipzig with a train of followers for the purpose of becoming Hahnemann's patient, since Hahnemann would not attend him elsewhere. Hahnemann's treatment was not followed and there is the strong suggestion that he withdrew from the case upon discovering a Dr. Saxl performing a venesection without his knowledge. However, in October of this year the Prince experienced a second stroke and the seventh anniversary of his victory over Napoleon found him conducted out of Leipzig in a funeral cortege.

Naturally the excitement was tremendous. Four months previously an attempt had been made to prevent Hahnemann from practicing in the Saxon kingdom. No decision was rendered in this case or, more accurately in order to permit the Prince to come to Leipzig, a decision read that prohibition from practice "did not come into question at the time."⁴⁸ The legal status of Hahnemann's self dispensing had been brought to the attention of the authorities in December 1819 by the apothecaries and he had been ordered to discontinue this practice, providing this opinion was sustained by a higher court. The decision was rendered against him after the death of the Prince. Again some years before Hahnemann had suggested the use of belladonna as a prophylactic in scarlet fever. At this time an epidemic of some disease with a miliary rash appeared in Leipzig and Hahnemann suggested that the belladonna advised in scarlet fever would probably prove useless in this miliary disease.⁴⁹ Shortly afterward a group of Leipzig physicians published an account of the value of belladonna in scarlet fever⁵⁰ but failed to mention Hahnemann as the originator, hinting that they had been induced to try the remedy at the suggestion of Berndt⁵¹ and others. To this Hahnemann replied they had remained silent about mentioning him.⁵² The net result was a movement to expel Hahnemann by force, and naturally a counter movement to prevent this. While Judge Lindner's decision permitted Hahnemann to remain, he left for Coethen where the reign-

ing Duke granted him the right of self dispensing. After remaining here fourteen years, Hahnemann remarried and left for Paris where he died July 2, 1843.

The above must suffice in order to fix the general dates and to sketch broadly some important events of his life. It is now necessary to fill in certain periods and certain subjects which are closely related to the theme under discussion, the simile.

At first a note on Hahnemann as a chemist, partly for the purpose of correcting certain mistakes in current literature, largely to indicate his independence and his investigative nature. The usual account of Amcke,⁵³ Haehl⁴¹ and Lippmann⁵⁴ suggests that Hahnemann was self taught although Tischner⁵⁵ has shown that Hahnemann twice speaks of Leonhardi as his teacher.⁵⁶ Moreover it is known that Hahnemann visited Leonhardi,⁵⁷ and Leonhardi was a student of Porner who was also Hahnemann's sponsor. The status of Hahnemann as a chemist must be left to authorities in this field; reference is made here only to certain medical aspects.⁵⁵ Perhaps of general interest is the determination of the concentration of sulphuric acid through specific gravity; more important was the introduction of hydrogen sulphide for the detection of arsenic poisoning²⁰ and the suggestion of the value of this reaction for the detection of metals;⁵⁸ more generally known is the Hahnemann wine test⁵⁹ which he subsequently made more exact.⁶⁰ Except rarely⁶¹ the origin of these tests is now forgotten. The previously mentioned soluble mercury received the compliments of pharmacologists;⁶² his method of preparation of wine vinegars was long employed.⁶³ More important to the present theme is an emphasis on the significance of crystallization for purity of preparations; the danger of heat in the preparation of plant extracts; the use of fresh plants in the manufacture of tinctures.

Since the work of Lavoisier had just placed chemistry in a position to become exact, it is not surprising that an investigator could easily go astray. The amazing thing is that Hahnemann's relatively unimportant errors should be repeated today and his contributions thereby overlooked. One error, the discovery of a new acid in black lead, has passed into oblivion.⁶⁴ The remaining bug-bear is the famous pneum incident, that is, the error committed when he believed he had discovered a new alkali salt (pneumalkali) in borax.

The situation may become clear by recalling that borax was known in 1784 "but we do not know what it is."⁶⁵ The famous Crell attempted to solve the borax riddle and failed in 1799.⁶⁶ The following year Hahnemann announced a new substance "alkali pneum"⁶⁷ as a peculiar fire resistant substance. There was immediate opposition to his statements by Klapproth, Karsten, and

Hernstadt.⁶⁸ Different from their factual discussion was an insulting, quite libelous attack by Trommsdorf.⁶⁹ Hahnemann admitted his error, stating that other chemists had made similar mistakes.⁷⁰ Scherer himself called Trommsdorf's attack inhumane and intolerant⁷¹ and then recalled Trommsdorf's own errors which remained unretracted after the mistake was pointed out. Objectively considered Hahnemann's character was in no way involved. He would hardly have been foolish enough to attempt to make money out of a scheme which could be immediately detected; moreover all money obtained was given to the poor by Hahnemann as soon as the mistake was discovered. In order to avoid misunderstanding it should be noted in passing that the practice of selling *chemical* discoveries was common then as now; however it is often forgotten that it was then common practice to sell medical discoveries and some famous physicians, revered by medicine, indulged in this practice.⁷² In Hahnemann's era a medical professor announced the discovery of a fever remedy⁷³ which would be sold to the profession,⁷⁴ and this was thought entirely proper.⁷⁵ That the professor received a yearly pension of five hundred dollars for the secret is interesting, particularly since the remedy was a mixture of sulphuric and hydrochloric acid. However Hahnemann's error was a minor one in chemistry from which no great reward could have been expected and most of his contemporaries readily understood the situation and acquitted him as honourable. Reich, the professor who exploited the government for a profit has been forgotten, but Hahnemann's mistake lives in current literature. A recent writer⁷⁶ stated that Haehl¹ made no mention of the pneum incident and that he must rectify the omission. His source is a polemic work⁷⁷ which hardly anyone would dare call objective⁷⁸ and even fewer critical. It is peculiar that he accuses Haehl of wilful silence; the fact is that Haehl considers the subject in both volumes (I, 69, II, 72, 73, 78, 79) and under three headings in the index. Moreover it is stated on good authority (Tischner) that this had been *previously* called to the attention of the author who has not as yet retracted his remarks. One sees how subjectivity still persists. To return to the original theme!

In his work on Chronic Diseases⁷⁹ Hahnemann states that prolonged trituration or prolonged shaking drugs were altered remarkably, previously inert substances became active, and substances previously insoluble became "soluble in water and alcohol."⁸⁰ Although this has been called an illusion, some recent work by Neugebauer⁸¹ tends to confirm this impression in that at the sixth decimal trituration, the material has become colloidal in part, the relation of crude to fine parts being determined by the amount of vehicle

(sugar) and the duration of the trituration. Madaus and Kühn,⁸² following Hahnemann's original method for sulphur⁸³ have shown at the third decimal trituration 54% of the sulphur is dispersed and not retained by thick filters (Schleicher and Schüll filter, Nr. 602). This has led to a statement that Hahnemann is the discoverer of the colloidal state of materials,⁸⁴ a statement that is too inclusive. However he did elaborate a special technic whereby substances thought to be insoluble became soluble by virtue of a colloidal state.

It has been alternately implied that Hahnemann did⁸⁵ and did not (Lippmann) write on the caustic alkalis. The incident in mind here still lives in the causticum controversy. Hahnemann described a method for making caustic tincture (*Tinctura acris sine kali*)⁸⁶ which modern investigators⁸⁷ also call an illusion since the distillate should yield nothing but distilled water. The most recent investigation in this field⁸⁸ indicates that the distillate is actually a weak solution of ammonia.⁸⁹ The point involved is not without importance, the one side contending that Hahnemann secured "drug" effects with distilled water and therefore his provings as well as implied results are mythical.

In conclusion it may be said that he has been called, one of the seven men who rendered the most service to pharmacy in the years just preceding 1795.⁹⁰ Lippmann, the well known historian of chemistry, states that Hahnemann does not possess absolute significance for the science of chemistry, but, relatively, significance without question: by "far outstanding any of his numerous and even chemical contemporaries." This must suffice for Hahnemann as a chemist.

Brief notice should be taken of certain other attributes of Hahnemann. His great devotion to detailed planning of regimens of life for his patients has been mentioned;¹⁶ individualization of patients was a keynote as early as 1792;³¹ detailed and advanced suggestions for control of epidemics were given by him; he belongs to the few physicians who believed in a *contagium vivum* as held later by Schonlein, Henle and Pasteur. This viewpoint is well emphasized in his discussion of cholera⁹² where he recommended camphor as an antiseptic in accordance with thoroughly modern views: "the only remedy which possesses the ability to kill through its fumes the finest animals of a low order and in this way is able to quickly kill the cholera miasm (which probably consists of a living nature of the man-murdering type, imperceptible to our senses, that hangs on the skin, the hair, etc., of men, on their clothing and so passes from man to man invisibly) are most rapidly killed and destroyed so that by it the sufferer will be in a position to be freed and restored from

the disease excited by him." In this same work is found the recommendation of heat sterilization of clothing.

Although Hahnemann's psychiatric practice was limited he urged,⁹³ in contrast to the prevailing practice, the humane treatment of the insane and hoped to establish a small hospital for their treatment.⁹⁴ When one appreciates the situation existing in hospitals for the insane as depicted by Kerner⁹⁵ and Westphal,⁹⁶ when the instruments of torture devised for the insane⁹⁷ are recalled, the importance and independence of these suggestions is realized. Whether the thoughts were entirely original with Hahnemann or whether he borrowed them from Pinel⁹⁸ who had just published his epoch making work is unknown, but at least Hahnemann introduced such ideas into Germany. Even opponents¹⁰ have conceded this honor to Hahnemann. Not without interest is Hahnemann's suggestion that so-called mental diseases are somatic in origin,⁹⁹ a viewpoint of many modern psychiatrists. No attempt will be made here to recite the attempts made to belittle Hahnemann's character. Outside of the pneum incident already mentioned there was the accusation by Brückmann¹⁰⁰ concerning Hahnemann's fees. Hahnemann's response¹⁰¹ is not all that could be desired but is comprehensible in view of the frequency with which he had been called a charlatan and his years of poverty. His views on fees are very sensible.¹

Hahnemann's position as a great physician can hardly be assailed, as will be seen as his doctrine is presented. Although anticipating the text, in order to dismiss the topic it may be said that Hahnemann laid the foundation for modern "reiz" therapy. He recognized the hypersensitivity of the diseased body. He knew the necessity for the completion of action before administration of a second dose in stimulus therapy. He introduced pharmaceutical procedures as the preparation of tinctures from fresh plants, appreciated the significance of the biphasic action of drugs, attacked polypharmacy and replaced it by a simple regimen, wrote an excellent work for pharmacists which was long standard,¹⁰² was a splendid chemist, an innovator of psychiatric reform. In listing these accomplishments the writer has omitted his chief innovation, the simile rule, the introduction of the decimal system into pharmacology, the use of milk sugar as a vehicle and devices to secure solubility and the colloidal state.¹⁰³

This picture of a highly endowed observer, an excellent linguist, a man harassed by years of want reveals the lights; naturally there were also shadows of sufficient depth to do almost irreparable harm to his doctrine. Contrasted with diligence and enormous working power is an appreciation of his superior mind, which early mani-

fested itself as self-consciousness and sensitivity. If Hahnemann had a depreciating attitude toward many of his contemporaries, the feeling was enhanced by the belated recognition of his doctrine and the disapproval of some aspects of it. Misunderstanding was soon converted into personal attack and an unhappy warfare was initiated whose echoes still resound. Although there are many historical parallels (Brown, Schelling, Schopenhauer) for unfriendly treatment by contemporaries, Hahnemann's sensitivity, indeed intolerance to criticism, played an important role in the controversy. Moreover the complexity of the problems with which Hahnemann worked led to vacillation, which served only to increase confusion. Opposite to this trait is his highly developed stubbornness which meant the failure to retract outworn ideas; thus contrasting opinions are found side by side in his works. His therapeutic optimism undoubtedly was frequently responsible for premature enunciation of a generalization. None of these unhappy traits are peculiar to Hahnemann; all are reflected in many judgments of his simile.

Before discussing his simile, allusion must be made to one other point. It is commonly alleged¹⁰⁴ that Hahnemann's work is founded on the doctrine of signatures but such a statement is made with seeming unawareness of Hahnemann's attitude toward this doctrine. It is unmistakably expressed in the following quotation¹⁰⁵ and others can be found which read similarly:¹⁰⁶

"How uninquiringly our writers on materia medica have adopted the statements proceeding from these impure sources is evident, among other things from this, that they enumerate among the virtues of crude medicines such as were originally derived from mere suppositions or superstitious forefathers, who had childlessly asserted certain medicinal substances to be remedies of certain diseases merely on account of some external resemblance of those medicines with something appreciable by the senses in those diseases (signature) or whose efficacy rested only on the authority of old women's tales, or was deduced from certain of their properties that had no essential connection with their fabulous medicinal powers. Thus the roots of *Orehis* and of *Saloop* merely because of their resemblance in shape to a pair of testes, the ancients perceived in this an augury of their utility in aiding sexual function, are still said to be analeptics and aphrodisiacs. *Hypericum* is still esteemed as a vulnerary, because the ancients stamped it with this character on account of the trifling circumstance that its yellow flowers when rubbed between the fingers, give out a blood red juice, which procured for it the name of John's blood. Whence do *chelidonium*, *berberis* bark and the *tumeric* derive the reputation they enjoy in our materia medica as remedies for jaundice, but

From this, that formerly it was imagined that the yellow milk of the first and the yellow color obtained from the last two was a sure sign (signature) that they must be useful in a yellow disease. And from whence does chelidonium in particular get its name and its fabled efficacy in dimness of vision if not from the old story that swallows restore the sight of their young by means of this plant. The tasteless Dragon's blood is said to be good for bleeding of the gums and hemorrhages. *Ranunculus ficaria* and *scrophularia nodosa* are said to be useful in piles, merely because the roots of these two vegetables present a knotty appearance similar to hemorrhoidal tumors. Madder obtained its reputation as an emmenagogue on account of its dark red colour; and because animals, when fed on it, have a dark red colour deposited in their bones, it is therefore celebrated in the *materia medica* as especially useful in diseases of the bones. *Saponaria* is still celebrated in our books as a valuable solvent and detergent medicine, because a decoction of its root when beaten up, forms a froth like soap, and it loses its frothing power, not like the latter by the addition of acid, but on the contrary by adding alkali to it. And does soap derive its reputation for dissolving obstructions and indurations in the body from any other source than the conceit, that as in household operations and chemical manipulations, it exercises a solvent property, so it must do the same in the living organism also?"

Thus on the only occasions affording Hahnemann the opportunity to speak on the doctrine of signatures he took an adverse position to the practice. One should be clear that the doctrine of signatures is not "homoeopathic" in origin nor propagation, but in so far as it had medical support this came largely from the then official medicine. One should also be clear that Hahnemann urged the careful testing of drugs, but his request for an experimentally founded *materia medica* was received largely with derision. Both Hahnemann and scientific homoeopathy have always repudiated the simile magic and the doctrine of signatures.

But it would be incorrect to assume that the fault lies entirely with the opponents of homoeopathy. Single homoeopathic physicians have fostered the idea of a connection between the homoeopathic simile and the doctrine of signatures. For example Schlegel pictures the relation between signatures and the action of drugs with considerable detail and with a speculative, indeed poetic phantasy. Thereby he entirely overlooks that once the action of a remedy is known, it is comparatively easy to select some arbitrary and fancied resemblance.

But thereby the situation is not exhausted. The details of some Paracelsian conceptions were recited above with the intention of

examining the question of whether or not Hahnemann borrowed from Paracelsus.

With this data in mind one may question whether Hahnemann borrowed from Paracelsus. A contemporary of Hahnemann and a bitter opponent of homoeopathy has stated that such borrowing occurred.¹⁰⁷ Much later a homoeopathic physician arrived at the same conclusion.¹⁰⁸ On the other hand the greatest authority on Paracelsus, Sudhoff,¹⁰⁹ stated that homoeopathy cannot legitimately base itself on Paracelsus. In general homoeopathic physicians at present do not believe that borrowing took place.¹¹⁰

To make a decision on the question is quite difficult but there is considerable presumptive evidence that no borrowing took place. Tischner¹¹¹ states the most powerful proof of all. By employing a group of quotations similar to those cited above, he stresses that these are all that can be found in the Paracelsian writings. As these notes are being written the Aschner edition of Paracelsus rests on the desk, four huge volumes containing several thousand pages. Yet the above is all that pertains to the "homoeopathic" problem. In other words knowing exactly what to look for, demands the most prolonged and tedious search in the dark symbolic writings of Paracelsus. Only a most careful search permits the above compilation since Paracelsus does not express his views in the form of a connected discourse anywhere in the works. Of less importance is the fact that Hahnemann would not have been inclined to study Paracelsus closely since they differed in mental orientation. Again Paracelsus was despised by the medicine of Hahnemann's time which did not invite detailed study. In Hahnemann's translation of Cullen, the word "notorious"¹¹² is used to describe him and furthermore Hahnemann's co-workers regarded Paracelsus as insane.¹¹³ When Schultz made the accusation of borrowing, Hahnemann replied that Paracelsus wrote "incomprehensible gibberish."¹¹⁴ As already implied Hahnemann exercised a most destructive critique on the Paracelsian doctrine of signatures, and their similes have nothing in common. For these reasons Hahnemann's denial of borrowing is probably correct. However the question is not important. Haehl adds that Hahnemann does not mention Paracelsus when he had no reason to conceal him.¹¹⁵

Finally it seems desirable to depict briefly the status of medicine at the time of Hahnemann in order to obtain a picture of the background on which his conceptions developed. The 16th century was a period of development of the inorganic natural sciences, and interest in these fields was reflected in medicine in the 17th by the development of the schools of iatrophysicists and iatrochemists. The first group, fortified by the discovery of circulation, endeavor-

ored to trace all manifestations of life to physical events. For example fever was due to increased friction on the vessel walls, consequent to the rapid pulse. The second group attempted to apply the still infantile chemistry at the bedside by explaining life "chemically."

In the 18th century three schools developed as the result of these one-sided endeavors. Stahl re-introduced vitalism by his doctrine of animism.¹¹⁶ As his work finds greater consideration elsewhere it will suffice to state here that according to Stahl a conscious rational soul governs the body, mechanism being subordinate to it. Health and the course of disease depended upon the soul; the manifestations of disease were healing endeavors conducted by the soul. Health was established through excitation and movements regulated by the soul; plethora was capable of causing abnormal movements. Consequently venesection found frequent employment therapeutically.

The second school, that of Hoffmann, was essentially mechanistic in nature and based upon conceptions of Leibniz. The carrier of life is ether and nerve ether plays a great role in bodily events. Life consists in circulation and the chief attribute of life is the ability to contract and relax; therefore spasm played an important part in his doctrine. Hoffmann did not routinely follow his doctrine, and depletion, particularly of the alimentary tract was the leading theme of his therapy. He deflated his own theory by ascribing purpose to the ether monads.

The third school, that of Boerhaave, was anatomic and mechanistic. For example inflammation was traced to a collection of blood cells which caused obstruction in various parts of the body. Moreover the shape of blood constituents could become altered and this angularity was made responsible for acridities. Later acidity was viewed more chemically than mechanically. It was later held amazing that a man of Boerhaave's astuteness could have elaborated such a purely arbitrary doctrine.¹¹⁷ More interesting since it was active in Hahnemann's time is the famous Stoll school which achieved great popularity. Most diseases arose from gastric impurities, especially the bile.¹¹⁸ Hecker considered it a brilliant advance.¹¹⁹ The Kampf doctrine¹²⁰ consisted in the allegation that diseases arose from a plugging of the portal vein and other large vessels by coagulated blood. Treatment consisted of enemas twice or three times daily and cases have been reported relieved of the "stoppage" only after the administration of 5,000 enemas.¹²¹ Another interesting school was the natural philosophic school of Schelling.¹²² A single quotation may reveal the general orientation: "contagion is the magnetic moment of the dynamic processes

reigning in the organism." Steffens¹²³ presented an amazing series of conjectures: "hunger is internal tension of assimilation under the mass opposed to the external, hence the feeling of hunger at the cardiac orifice of the stomach." Allusion is made elsewhere to the more rational ideas of Reil.¹²⁴

Passing over numerous other schools of the period, the so-called antiphlogistic medicine, the school of galvanic electricity, the school of animal magnetism, there remains the work of J. Brown.¹²⁵

v. Haller had investigated irritability which he limited to muscle, in that irritability pertained to those tissues contracting after a stimulus. Muscles were "irritabel," nerves were "sensibel." The stimulus became the basis of life: adequate stimuli produced health (temperature, moisture etc.): insufficient stimuli produced asthenic diseases; overstimulation produced sthenic disease. The determination of the presence of asthenic or sthenic disease sufficed for diagnosis, therefore pathology was unnecessary. The natural healing power was also denied.¹²⁶ Treatment proceeded entirely upon a contrarium basis in that asthenics were strengthened and the sthenics weakened. Brown does mention the simile however:¹²⁷

CCLII: The remedies that effect the cure of sthenic diathesis, are the powers, which, when their stimulant operation is excessive, produce that very diathesis; but which, in effecting a cure, act with much diminished force, as to produce less excitement than health requires, or to prove debilitating.

CCLIII: The powers which produce the same effect in the asthenic diathesis are those that, when their stimulus is too weak, produce that diathesis. In effecting a cure, they must be applied so as to produce higher excitement than is consistent with the state of health, or so as to stimulate."

This could have been suggestive to Hahnemann although it is not his simile. Brown's theory caused great excitement¹²⁸ because it was thought to be scientific, although even then it was recognized that the premises were, in all probability, false.¹²⁹ It was quite dead by the end of the first quarter of the 19th century,¹³⁰ although it continued to display a feeble existence in Roschlaub's excitation theory and Rasori's doctrine of "contrastimolo." Elsewhere allusion is made to Broussais and his "vampirism." However sufficient has been said to indicate the great unrest in medicine at this time and to recall some of the numerous systems which flourished. Among all these Hahnemann's alone remains.

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HAHNEMANN'S SIMILE.—While Hahnemann's discovery of the simile has usually been attributed to a genial intuitive flash, there is considerable presumptive evidence that it represented the fruit of prolonged, more or less conscious deliberation. The traditional story is peculiarly reminiscent of Galileo's observation of the hanging lamp or Voltaire's delightful tale of Newton's falling apple. These romantic stories lose some glamour, but gain in intrinsic probability, when it is recalled that Goethe's equally sudden "intuition" of the occipital bone as a modified vertebra came as the result of considerable, though partly unconscious, mental effort. However, traditionally Hahnemann is supposed to have tested his intuition of the simile by taking cinchona bark (used in the treatment of intermittent fever) whereby he produced fever in himself.

Before examining his simile it seems advisable to review briefly two problems raised by this assertion. In the first place it has been repeatedly urged that since cinchona does not produce fever, Hahnemann's observation is an error and consequently his simile is founded on a mistake. The statements of a few students of this subject will serve to clarify this situation. Lewin¹ writes: "This china fever, often discussed, debated, dismembered, indeed denied from a lack of knowledge, occurs fairly frequently . . . the self observation of Hahnemann who developed a cold fever similar to swamp fever after the ingestion of a large amount of china bark, on this account must be considered correct." Garms² pointed out that workmen exposed to bark dust in the manufacture of cinchona develop paroxysms of chill and fever resembling an intermittent fever which comes to an abrupt end in a violent fit. A temperature of 105 has been noted following the administration of a one grain dose of quinine.³ Tommaselli⁴ recorded a high temperature following the ingestion of quinine by a malarial patient and remarks that in malarial cases showing this idiosyncrasy there may be severe febrile reactions with hemoglobinuria after even comparatively

small doses. Goodman,⁵ Plehn,⁶ Karamiteas⁷ cite febrile reactions in latent malaria and Jacobson⁸ and Herrlich⁹ state that a malarial background is essential to a fever from quinine. In this connection it may be stated that Hahnemann had once suffered from an intermittent fever;¹⁰ furthermore a recurrence of this fever was successfully treated by cinchona.¹¹ If this fever should be proven to be non-malarial in origin it could be added that Plehn⁶ and Gudden¹² have shown that malaria is not essential to the production of quinine fever. Solis-Cohen states a "transient rise (in temperature) occurs in rare cases."¹³ In speaking of quinine idiosyncrasy Pouls-son mentions that skin eruptions caused by quinine "can be accompanied by fever."¹⁴ According to Cushny quinine fever has been over-emphasized but his triple mention of the existence suggests that it is not imaginary.¹⁵ Meyer-Gottlieb¹⁶ mention the "paradoxical" action of quinine which may raise the temperature in place of the expected lowering. Jansen¹⁷ and Friedmann¹⁸ made similar observations. Although workers differ on the manner in which quinine does produce fever in some people, there now seems to be general unanimity among those who have devoted serious attention to the problem that it is capable of producing it. Naturally these remarks merely serve to indicate that the "original" observation was not an error. While it is not stressed here it ought to be noted in passing that the simile could hardly be repudiated, if subsequent observation had proven the non-existence of the quinine fever. In this connection it may be recalled that Robert Mayer made himself immortal by discovery of the law of conservation of energy by virtue of conclusions based upon observations which have since been proven incorrect.

Allusion should also be made to prevailing opinions on the mechanism of action of quinine in malaria. According to Sydenham¹⁹ the cathartic property of the drug removed "the urgent febrile matter." Cullen, with whom Hahnemann disagreed, believed the action could be assigned to a "tonic" action of the bark²⁰ and this idea was prevalent well into the first half of the nineteenth century.²¹ Even in the last half of the century "intermittents" were attributed to obscure conditions of the central nervous system,²² and some vague action of quinine on this system was postulated to account for the beneficial results. Early Hahnemann had inclined towards humoral pathology,²³ while he remained sceptical in regard to the rationale of depleting cures. In a later paper a biologic attitude finds stronger expression:²⁴ the opinion "that mercury *as mercury* destroys the venereal poison by mere chemical contact" is denied. He regarded as erroneous the prevailing belief that healing was proportionate to the amount of mercury injected,

stating that "this is refuted by experience since the smallest amount of mercury can remove the most deeply enrooted syphilis, if it only excites a sufficiently strong mercurial fever."²⁵ This early attack on the principle of "much helps much" is incidental to the present point; the important implication is that Hahnemann contended that drugs occasioned reactions on the part of the body and this reaction (in the present instance) he regarded as fever. This leads directly to a second problem: what was regarded as fever at the time of Hahnemann?

Stahl²⁶ wrote as follows: "By fever one understands a distinct and fairly persistent disturbance of blood movement and in immediate consequence to it, an increase of the feeling of heat and coldness." Nothing is said here of an objective increase in temperature. In fact prominent textbooks of 1780²⁷ hardly mention the thermometer. One of Hahnemann's contemporaries²⁸ writing a monograph on fever does state that "in most cases the febrile heat is controlled by an actual increased production of animal warmth in a given period." Since this monograph can be legitimately regarded as the most modern and advanced expression on the subject, the inference seems warranted that, generally speaking, the medical profession had not then grasped the full significance of "increased production of animal warmth" and furthermore the impression conveyed by the word fever was different than the thought aroused by this word at present. For example Hahnemann is alleged to have discovered mercurial fever²⁹ and his detailed description is available.³⁰ Reference to this long description of "an exquisite case of very severe mercurial fever" fails to reveal any mention of "heat" as an objective or subjective manifestation of the syndrome. In short the traditional story of the discovery of the simile by Hahnemann implies a series of co-incidences: that Hahnemann elected to study cinchona, that he happened to have an idiosyncrasy to it, that it does produce fever although Hahnemann probably meant something else by the same word.

Now since he called syphilis a fever³¹ and since he regarded mercury as curative in syphilis by virtue of its febrigenic property, it seems reasonable to conclude that he was aware of the healing value of fever in "febrile" diseases long before the famous cinchona experiment. Allusion should be made to his suggestion of employing mercury in lymph adenopathies by virtue of mercury producing fever.³² The above suggestion of early foreshadowing of the simile is fortified by Hahnemann's denial of Cullen's explanation of the action of cinchona.³³

"Through purification of the most bitter and the most strongly astringent substances one can achieve a composition which in much

smaller doses possesses to a greater degree, both of the properties of the bark, still no specific for fever will ever be obtained. The author should have answered this. The principle of the bark, still lacking an explanation of its action, will not be easy to discover. However one considers the following: substances which excite a kind of fever (very strong coffee, pepper, arnica, ignatia bean, arsenic) extinguish types of intermittent fever. I made a trial for several days of taking twice daily, each time four drachms of good china; the feet, the tips of the fingers, etc., first became cold, I was tired and sleepy, then my heart began to palpitate, my pulse became hard and fast; an uncomfortable anxiety, a trembling (but without shivering), a lassitude through all the extremities, then throbbing in the head, redness of the cheeks, thirst, briefly all the symptoms otherwise common to intermittent fever appeared one after another, still without the characteristic chills. In short, the particularly characteristic symptoms usual to intermittents, the dullness of sense, the type of stiffness in all joints, but especially the dull unpleasant sensation which seemed to have its site in the periosteum of all the bones of the body, all appeared in me. Each time the paroxysms lasted two to three hours and recurred when I repeated the dose. I discontinued and became healthy."

Moreover in the same work (p. 110) he states: "Had he (Cullen) perceived the power of the bark to excite an artificial antagonistic fever, certainly he would not have adhered so firmly to his explanation . . ." Not without importance to Hahnemann's views on the existence of a natural healing power is the statement that cinchona might be harmful if the paroxysm represented an attempt of the body to unload the morbid material. This view, though not original, serves to stress that he did not deny the existence of natural healing. The statement continues (p. 115) that he has employed ipecacuanha, which excites fever, in order to cure intermittent fever. Accordingly there is more than suggestive evidence that he had employed several agents in intermittent fever by virtue of their alleged febrigenic property long before the famous trial with cinchona which may be regarded as a "crucial experiment" rather than an intuitive flash. Tischner³⁴ has advanced the plausible suggestion that Hahnemann had performed similar experiments with ipecac, arsenic, coffee, etc., so that the result but not the method of the cinchona experiment was new to Hahnemann. Beyond the treatment of fever by agents capable of producing it, nothing indicates immediate generalization of the thought, although he mentions that certain acids improve gastric weakness when this is characterized by the tendency to abnormal production of acids.³⁵ In the next year his position is unchanged;³⁶ in fact, five years elapse

before this occurred. Then homoeopathy was definitely launched, although still unchristened.

As fever therapy played a great role with Hahnemann, it may be well to remain with this example in searching for precedents in addition to those mentioned early in the study. Imitation of nature will be discussed later.

The thought of utilizing fever therapeutically occurred to several workers just before Hahnemann. Boerhaave stated that he would be a great physician if he could produce fever as easily as he could stop it.³⁷ Similar thoughts were enunciated by van Swieten.³⁸ Treating fever by fever is expressly mentioned by Bordeu:³⁹ "the physician should, if the forces of the patient and the degree and character of the disease permits, change chronic diseases into acute, inveterate into fresh, particular into general . . . the physician must cure patients by creating and exciting a crisis (in chronic diseases), either by producing an increase of the fever or other manifestations which appear in its place." He also mentions instances of cure by fever (p. 848). These citations indicate that the "defensive" nature of fever is not a discovery of Hahnemann and that Bordeu had, so to speak, reintroduced the Hippocratic simile. The reader should also note that the idea of converting chronic processes into acute diseases is also foreshadowed in the above citations. It seems reasonable to conclude that either as the result of suggestions in medical literature or from personal experiences, Hahnemann was led to determine whether or not drugs capable of evoking certain phenomena were useful in the treatment of similar states. An experiment with cinchona and possibly other agents yielded positive results, which, though subjected to adverse criticism, in the case of cinchona is now accepted as correct.

The first generalization of his thought reads as follows: "*One imitates nature which at times heals one chronic disease by adding another to it and employs in the (preferably chronic) disease that drug which is in a position to excite another artificial disease as similar to it as possible and it will be healed: similia similibus.*"⁴⁰

It should be emphasized at once that Hahnemann has no intention of making this an exclusive guide in therapy. On the contrary he specifically states: "*The first way, to remove or destroy the fundamental cause of the disease, is the most elevated it could follow.*" Hahnemann calls it the "royal road"; he does not question its value but the extent of its possible application. Accordingly Hahnemann recognized the so-called "causal therapy." The second road "*to bring about a one sided (or opposing) alteration*" he illustrates by the treatment of constipation with purgatives.

"In acute diseases, which, if we remove the obstacles to recovery

for but a few days, nature herself will generally conquer, or, if we cannot, succumb; in acute diseases, I repeat, this application of remedies is correct, to the purpose, and sufficient, as long as we do not possess the above mentioned philosopher's stone (causal therapy) or as long as we do not possess any rapidly acting specific which, for example, would extinguish the variolous infection even at its very commencement. In this case I would call such remedies temporary."

Although this citation shows quite conclusively that Hahnemann did not deny the natural healing power, its introduction here is intended to show that at this time Hahnemann regarded acute diseases a proper field for the application of contrarium therapy in the absence of causal therapy. In chronic disease, however, palliation often brought adverse results, "giving a few hours ease while the disease plants its roots still deeper."

Since the conviction is widespread that Hahnemann's suggestion was an exclusive doctrine it may be advisable to reiterate: "It is not necessary to say that every intelligent physician would first remove this (the maintaining cause) where it exists . . . extract from the cornea the foreign body that excites inflammation of the eye; loosen the over-tight bandage on a wounded limb that threatens to cause mortification, and apply a more suitable one, lay bare and put a ligature on the wounded artery that produces fainting; endeavor to promote the expulsion by vomiting of belladonna berries, etc., that may have been swallowed; extract foreign substances that may have gotten into the orifices of the body . . . ; crush the vesical calculus, open the imperforate anus of the new born, etc."¹¹ Hahnemann never lost his respect for surgery and always advocated the removal of exciting or maintaining causes where they could be found. However he regarded the field of antipathic treatment with increasing distrust: "It is only rarely that homoeopathic physicians can use the antipathic process in the treatment of chronic diseases. But it is something. As the homoeopathic physician does not desire party dissension but has only the desire to complete the efficiency of his art, he utilizes the little which is useful, though he may find it in some other field, even if it be the field of the enemy."¹² Oblivion to the fact that Hahnemann was first a physician and secondly a systematist might easily provoke error. The implication of this remark is not that a patient in the throes of agony should not be given morphine; the obvious and correct interpretation is that a cathartic is not a cure for chronic constipation, arrest of nasal secretion by atropine not a cure for a cold. The discussion naturally hinges on an interpretation of the word "cure." Morphine is not a cure for gall stones regardless of how valuable it may be for

relief of an attack of gall stone colic. Moreover in so far as medicine regarded the suppression of symptoms as cures, Hahnemann's urge to look beyond symptomatic relief was timely even if it gave occasion for misunderstanding. While his vitriolic attacks on "allopathy" could, in the heat of the debate, give the impression that he desired his method to be the exclusive mode of therapy, the fact remains that in his early and best years and by his scientifically minded followers, it was not and could not be the sole method of therapy.

Omitting for the present the complicated question "what is similar?" allusion should be made to the fact that Hahnemann relied quite exclusively upon symptomatic expressions for the indications for treatment.

"It may be granted that every disease must depend upon an alteration in the interior of the human organism; this disease can be conceived mentally only through its outward signs and all that these signs reveal; in no way can the disease itself be recognized."⁴³ "The invisible disease producing alteration in the interior and the visible alterations in the exterior (the sum of the symptoms) together make what one calls the disease, both are the disease itself."⁴⁴

These and similar statements have been used as the basis for the most devastating criticism applicable to Hahnemann's simile, outside of its exclusiveness. The traditional interpretation given reads as follows: by internal alterations Hahnemann means the anatomico-pathologic alterations inside the body which are to be contrasted with the external manifestations, the symptoms. The anatomic-pathological changes inside the body are called unknowable, therefore the simile has no need of pathology. Therefore homoeopathy remains with the symptoms expressed by the patient and has no need of science. Some Hahnemannian homoeopathic physicians following Kent have pursued methods which justify this interpretation, others have been surprised that Hahnemann should have made this statement,⁴⁵ and still others have implied that Hahnemann, here as elsewhere erred.⁴⁶

But the above interpretation is not the only analysis of possibilities; in fact, its acceptance leads to contradictions within the Hahnemannian doctrine itself. Another solution is offered given by Tischner:⁴⁷ "On the one side Hahnemann knew the external manifestations to which belong the externally visible symptoms and also the corporeally conceivable internal alterations of a pathologico-anatomic type, and on the other hand, the alterations of the vital force which he conceived as "internal (immaterial) alterations." The reader may consult the original for detailed discussions. It is sufficient to point out here that if this analysis is

correct, external, outwardly reflected, etc., mean the body, the material, the mechanical; internal means the immaterial, the psychic, the living, the vital. The organ is "external," "outer"; life, living, the inscrutable is the "inner," "internal," world.

Thus interpreted Hahnemann would have included all discoverable phenomena as indications for treatment, not merely the symptoms. To use modern examples, the blood pressure, the urine analysis, basal metabolic rate, would all become elements of the totality of the symptoms. There is much to justify this interpretation because Hahnemann actually speaks of visible alterations of the internal parts in contrast to the inward being of man.⁴⁸ Moreover he states that everything which can be seen, felt or heard form indications for the selection of the remedy.

Limitations of space prevent further analysis of this important subject which later gave occasion for adverse criticism. Obviously it is vital to the correct appreciation of the modern simile. Anatomico-pathologic factors are as important as "functional" symptoms in the application of the simile.

The response to a question asking why Hahnemann did not include such objective findings in his growing materia medica has been indicated in the discussion of fever; fever as an objective increase in body temperature was then not generally appreciated. To state the matter another way: Hufeland's famous work⁴⁹ of this period devotes just nine lines to the entire subject of cardiology; in it only two characteristics of the urine are mentioned: fiery and hot; urinalysis in the modern sense of the word was unknown, auscultation and percussion of the lungs and heart was then in the most rudimentary stage of development. In other words if Hahnemann was to remain on the basis of experience, nothing remained except the employment of symptoms, and here again for the most part the subjective symptoms. This situation obtained during the era of greatest development of his materia medica and resulted in over-emphasis upon the symptomatic and subjective phase. Although incidental, mention can be made of the fact that Hahnemann's followers soon emphasized the necessity of pathology. Hahnemannian materia medica, with its endless lists of symptoms was retained and contributed, as perhaps no other single factor, to misunderstanding the simile, to continued isolation of homoeopathy, and consequently to the implication of sectarianism. Hahnemann ought not to be discredited for omitting things not as yet known; naturally this does not excuse his followers.

Having indicated that Hahnemann's simile was presumed to be applicable only in those diseases in which the body was capable of making a response, and further that the totality of actual mani-

festations, subjective or objective, constituted the indications of the disease to be treated, a third point may be introduced.

"We need only know the diseases of the human body accurately in their essential characteristics and their accidental complications on the one side, and on the other side the pure effects of drugs, that is, the essential characteristics of the specific artificial diseases which they excite, together with the accidental symptoms caused by difference of dose, form, etc., and by choosing a remedy for a given natural disease that is capable of producing a very similar artificial disease we shall be able to cure the most obstinate diseases."⁴⁰

The repeated use of the word "essential" signifies something special. A mere comparison of symptoms in the sense of a mechanical counting, so-called "covering the symptoms," is eliminated by this. One does not give that remedy which has the "most" symptoms in common with the disease, but the remedy whose *evaluated* (essential) symptoms are as similar as possible. An example may save many words. A patient complains of vomiting and for the purpose of illustration a remedy also capable of producing vomiting is administered. It is quite probable that such a procedure would fail to produce a favorable response. If the patient had the symptom as the result of a brain tumor, giving a remedy which produced vomiting by irritation of the gastric mucosa would certainly do no good, regardless of the concurrence of a hundred incidental symptoms such as the absence of nausea, the absence of blood in the vomitus, etc. Without attempting to exhaust the meaning of the word "essential" as applied here, accurately interpreted, the correct use of the simile requires knowledge of all departments of medicine; otherwise evaluation is impossible. The emphasis here is not directed at the barrier created against domestic practice, to which an impetus could be given by a "symptom" comparison, but to an early appreciation of the necessity of utilizing the totality of a symptom, in addition to the totality of the symptoms. Naturally misunderstanding on this subject could lead to pointless amplification and further confusion as well as to the right direction.

However there is another aspect which ought not to be overlooked here, namely, Hahnemann was acquainted with biphasic actions of drugs:⁴⁰ "Most medicines have more than one kind of action. . . . The last is usually the exact opposite of the first state."

This subject finds discussion elsewhere and is mentioned here simply to indicate that since two different effects are possible, there is the problem of which will be used for the simile.

"If in a case of chronic disease a medicine be given whose direct primary action corresponds to the disease, the indirect secondary

action is sometimes exactly the state of the body to be brought about. . . .'⁴⁰

In other words the selection of the simile depends upon a correspondence of the direct primary action with the totality of the symptoms of the disease. One other rather obvious, but still generally unappreciated feature deserves mention:

"Dare I confess, that for many years I have never prescribed anything but a single medicine at a time and have never repeated the dose until the action of the former had ceased; a venesection alone, a purgative alone and never a second until I had a clear notion of the operation of the first."⁵⁰ Thus, the single remedy rather than multiple remedies became a feature of his simile practice. While this statement has occasioned adverse criticism in that he continued to use venesection after he had found the new method, actually the citation favors him because papers written in 1796⁵¹ and 1797⁵² indicate his practice was often unaffected by his new idea. The obvious inference is that unlike a phantastic system which springs complete from the mind of the originator, Hahnemann was working only slowly to clarity.

The problem as to how the simile effected cure, Hahnemann answers like a true Hippocratic physician:⁵³

"As this natural law of cure manifests itself in every pure experiment and every true observation in the world, the fact is consequently established; it matters little what may be the scientific explanation of how it takes place; and I do not attach much importance to attempts to explain it. But the following view seems to commend itself as the most probable one, as it is founded upon premises derived from experience."

In early work Hahnemann urged imitation of nature.⁴⁰ This is not a surprising utterance for the teleologically inclined Hahnemann nor does it possess anything original in this form. While the chief occupation of medicine at that time consisted in the alleged imitation of nature, unfortunately it took the guise of exhausting cures by depletion, excessive venesection, excitation of inflammation by vesicating plasters, moxa, setons and similar devices.

On the other hand Hahnemann states: "Just as if these imperfect and forced imitations were the same thing as what nature effects in the hidden recesses of vitality, by her own spontaneous efforts in the form of crises! Or as if such crises were the best possible method for overcoming the disease and were not rather proofs of the imperfections and therapeutic powerlessness of our unaided nature."⁵⁴

He uses surgery as a model in that it does not seek to imitate

nature: a surgeon removes a splinter with a single cut while nature would attempt the same by a tedious suppuration. A surgeon would release a strangulated intestine, nature cause gangrene. The import of these remarks is that the route, like that of surgery, should be direct. In this same paper he calls attention to the fact that it has always been a matter of greatest admiration to see how nature unassisted at times effects cures. Accordingly there is no denial of natural healing, but an emphasis on its value; attention is directed to the frequency with which nature fails to cure chronic diseases and furthermore that many alleged imitations are not real imitations.

In presenting an explanation for the simile the following maxims are employed: "When two abnormal general irritations act simultaneously on the body, if the two are dissimilar, the action of the one (weaker) stimulus will be suspended for some time by the other (stronger). When two irritations greatly resemble each other, the one (weaker) stimulus, together with its effects will be completely extinguished and annihilated by the analogous power of the (stronger) other." Similar viewpoints had been offered by Hufeland⁵⁵ who may be ultimately responsible for this explanation. To make this more comprehensible to the reader it may be said that the appearance of disease was considered conditional, that is, dependent for example upon lowered resistance. Drug effects, on the other hand, could appear in every one. Therefore drug stimuli were stronger than disease stimuli, the former abolishing the latter, providing they were similar.

In explanation of the second maxim Hahnemann states: "Therefore in order to be able to cure, we shall only require to oppose to the existing abnormal irritation of the disease an appropriate medicine, that is, another morbid power whose effect is very similar to that the disease displays . . . it is only by this property of producing in the healthy body, a series of morbid symptoms, that medicines can cure diseases, that is to say, remove and extinguish the morbid irritation by a suitable counterirritation."

To imply that the drug stimulus opposed the "disease" stimulus as two agents reacting in a test tube (the body) would be to completely misunderstand Hahnemann. The theory promulgated is that the response evoked by the drug stimulus serves to annihilate the disease, in other words the drug evokes reactions from the body directly, and this response acting indirectly, so to speak, extinguishes the disease. In the first case the body would be passive, in Hahnemann's explanation it would play the necessary role. The annihilation of the disease also depends, according to the maxim, upon the fact that the body can tolerate only one disease

at a time. Therefore the natural disease is destroyed. As the drug is eliminated the medicinal stimulus (disease) disappears and recovery ensues.

This explanation is maintained throughout his life although his vitalism later changed the wording. For example: "The vital force cannot sufficiently oppose the disease. By giving a remedy which resembles the disease, the instinctive vital force is compelled to increase its vital energy, until it becomes stronger than the disease which in turn is vanquished. Then by interruption of medication, health follows."⁵⁶

In this manner one can summarize the implications of Hahnemann's simile: one must carefully prove drugs on the healthy to determine their real effects and then evaluate their essential actions; one must study disease in its totality, rather than simply in respect to a single prominent symptom. The remedy capable of evoking a similar state in the healthy is given to a patient. This produces a counteraction of the body to the drug stimulus (which is greater than the disease stimulus) by which the disease is abolished by the augmented now sufficient defenses of the body. Since the drug and the disease concur in their totality, the latter is entirely extinguished by this positive or radical cure as Hahnemann frequently termed it. The use of the word defense above is naturally an anachronism but has been inserted to preserve the teleologic orientation of Hahnemann; perhaps to have said augmented vital force would have been less an interpolation.

This presentation of Hahnemann's simile still lacks one essential which is difficult to include without his doctrine of disease which is mentioned later. However it must receive some notice here since its omission would constitute a failure to include one of his most characteristic doctrines, namely individualization of the patient.

If Hahnemann's tendency to vitalism and its ultimate inclusion as an explanatory hypothesis is overlooked, then he elaborated his thesis by remaining within the realm of experience; indeed Hahnemann's contribution is readily comprehensible as an endeavor to remain within the bounds of experience; to build a materia medica on experiment; to indulge in no hypothesis of disease. To accomplish this purpose in both directions, adherence to symptomatology was compulsory. That he sinned against his own principles by introducing vitalistic explanations is of minor importance because this occurred much later and assumed importance only in the fifth edition of his *Organon*.

The 18th century not only elaborated many single facts but witnessed numerous endeavors to systematize these facts as exemplified by Linne's classification of plants in this period. Indeed it is often

forgotten that Linne even attempted to introduce a classification of diseases similar to his botanical scheme. Perusal of the literature of Hahnemann's time, and even much later will reveal a variety of nosologic efforts. At that time "dropsy" represented a disease; it was not a therapeutic problem of cardiac disease, nephritis, nephrosis, cirrhosis of the liver, etc. Treatments were designed as "cure of a name"; prominent symptoms, for example, "spasms," "rheumatism," "continued fever" were regarded as diseases and treatment applied. It is readily understood that Hahnemann would have been led into a maze of difficulties had he adopted a simile for "dropsy."

Anticipating the discovery of bacteriology by accepting a contagium vivum, he held that, except for infectious diseases, which probably arose from some fixed "miasm," diseases were non-recurring events in nature, and therefore require summarization under a name only for convenience. Since innumerable stimuli acted upon one body which was not identical with another body, it was arbitrary to form a disease species. He speaks of diseases being like the clouds to which one does not give individual names. This conception of disease closely approximates the Hippocratic, but thrusts the individual even more into the center of the picture. In other words the problem of pneumonia does not exist for Hahnemann; it is always the problem of a patient with pneumonia.

There is another obvious reason for Hahnemann adopting the policy of individualization; as his drug provings had yielded a series of individual symptoms there would be a necessity for the individualizing conception in order to apply these in cases of disease.

This attempt to present Hahnemann's simile as well as his other thoughts has been motivated by the desire to delineate accurately his conceptions and not to justify them. Likewise the following idea is offered as a suggestion whereby the individualizing conception may be more comprehensible, even if one does not agree with the premises.

"Almost every subject or event can be approached from two standpoints; either as a single case or as the occurrence of a general case, whether this general is a rule or a law or the like. In the case of generalization the single case is scarcely interesting as such but essentially as 'a case of,' as a confirmation of a rule or law, as a representative of a type. For example I can define a hill, a typical moraine hill, by which it is arranged, 'explained' and placed on the shelf. But I can also study the individual characteristics in it and demonstrate that the hill contains a prehistoric building ground which can be investigated in detail. A German

divinity may be buried therein and I can describe the transformation into a Christian pilgrimage chapel and moreover depict the important role which the hill played in a war. . . ."⁴⁶

Windelband has denominated the generalizing method as the nomothetic or law giving and has placed this in contrast to the idiographic which describes the individual. He designates the natural sciences as nomothetically oriented, while the historical sciences as idiographic. Naturally the differences are not complete and the idiographic method is often used in astronomy. Nevertheless modern medicine is chiefly guided by the nomothetic viewpoint and homoeopathy is chiefly idiographic.⁵⁷ In so far as Hahnemann's method remains on the plane of description of observations, it attains stability to the extent that the observations are correct. When general medicine attempts to "explain," whenever these explanations are premature, each newly discovered fact will cause a shifting of emphasis and a consequent appearance of progress that is more often change than advance. However, the essentially idiographic or descriptive viewpoint tends to account for the relative stability of Hahnemann's *materia medica* and doctrine in general through more than a century.

There remains one outstanding exception to this doctrine of individualization and this must be briefly presented before closing the section on the simile. Hahnemann thought the acute contagious diseases depended upon a *contagium vivum*. Therefore they formed an exception in that they resembled each other and could be named. In one particular instance he believed that he found a prophylactic agent for scarlet fever⁵⁸ which he announced in a booklet which could be purchased. No comment will be made here on the unfortunate method of announcing the discovery, and it must also suffice to say that the remedy recommended (belladonna) was administered in such extremely small doses that considerable ado was raised over the posology. However, attention should be focused here on the division between prophylactic and curative procedures; in fact, he then thought belladonna contra-indicated when the disease had developed.⁵⁹ Somewhat later this viewpoint became altered.⁶⁰ He believed that a remedy might be prophylactic as well as curative; and finally his opinion veered toward the original decision.⁶¹ In short there was a deviation of the rule of individualization in regard to prophylaxis, whereby one remedy might be employed to prevent the development of a given disease, for example, scarlet fever.

Since there will not be another occasion to discuss the belladonna incident, a few notes on this subject may be added here. Decisions varied on the actual merit of belladonna as a prophylactic agent in scarlet fever. Hufeland,⁶² Schenk,⁶³ Dusterberg,⁶⁴ Masius,⁶⁵ and

Hedenus⁶⁶ had favorable results. A few, Jani,⁶⁷ for example, at first favored, then doubted its utility; the remaining opposition requires no mention because their objections were based largely on theory and not on actual trial. Wesselhoeft⁶⁸ was unable to confirm the prophylactic value in an American study. Sprengel⁶⁹ commented upon the work by stating that it offered the best dietetic prescriptions known until then. Somewhat later a disease resembling scarlet fever appeared in Germany and Hahnemann doubted the efficacy of belladonna in these cases;⁷⁰ he suggested other remedies⁷¹ which were said to be of value.⁷² In spite of opinions to the contrary Hahnemann's views on the dissimilarity of the two diseases were upheld.⁷³

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HAHNEMANN'S PATHOLOGY.—Almost invariably therapeutic systems have been elaborated on the basis of some definite notions about the nature of disease, and conceptions of pathology have furnished the general outline into which therapeutic practices were thrust. On the other hand Hahnemann attempted to elaborate therapeutics primarily upon the basis of some ideas of drug action. With his chief interest in pharmacotherapy rather than in pathology, it is not particularly surprising that his numerous writings do not contain a connected account of pathology. While Hahnemann was originally quite unconcerned over possible explanations of his proposed simile, he perceived the psychologic value of presenting at least something in this direction, particularly when the demand became increasingly more insistent. To depreciate existing therapeutic practices successfully, it was essential to take some position regarding pathology since these practices reflected conceptions of pathology. To attempt to explain the *modus operandi* of the simile would likewise necessitate utilization of past or contemporary conceptions of pathology, so that remarks on this subject are not infrequent in his works. It would be interesting to review the doctrines repudiated by him as well as to recall those selected to support his contentions, but the value of such a reconstruction would be problematical because of its arbitrary nature. Here attention can be directed merely toward a few problems of a pathologic nature which find reflection in his simile. Again the inclusion of a section on pathology permits reference to his theory of chronic diseases and his attitude toward natural healing, irrelevant topics whose discussion is required by the frequency with which the psora theory and denial of natural healing is linked with homoeopathy.

Brief allusion to earlier important doctrines of pathology, still current in Hahnemann's time, may assist in temporally orienting the reader. Remnants of Galenic pathology still existed, at times thinly disguised, again hardly recognizable as in Hunterian hemopathology. Paracelsian pathology was equally speculative. However it involved the assumption of an internal physician, the

archeus, a natural healing power. Diseases were cured by reactions proceeding from the archeus which opposed disease. Van Helmont presumed an archeus influus which presided over the entire organism and an archeus insitus over each organ. Diseases arose from the first and treatment was directed at it, rather than the cause of the disease. Cartesian thinking brought Sylvius to an exclusively materialistic basis and modified Galenism. Only chemical and physical explanations were permitted in the elucidation of physiologic and pathologic events in the body and hypothetical "acridities" were made etiologically responsible for disease. Sydenham pathology is hippocratically oriented since nosology is regarded descriptively rather than as a refuge for speculative hypotheses. The ultimate causes of disease were imperceptible; disease was an endeavor of nature to remove the morbid material from the body. If this transpired rapidly and energetically the disease was acute, if not, chronic. Acute diseases arose from external influences, as changes in the air; chronic diseases originated from abnormalities of the humours, dietetic injuries being largely responsible. From a practical standpoint Boerhaave subordinated theory to experience; academically he subscribed to an elaborated theory of acridities. For Hoffmann, life was movement, death standstill, disease abnormal movement. The body was a hydraulic machine activated by nerve fluid, which governed the tone of the tissues. Stahl's animism is a modification of the Hippocratic "physis" and Paracelsian "archeus." The anima causes organ function and prevents tissue destruction; it attempts to restore normal tonus. The chief cause of disease is plethora.

Haller gave the first scientific conception of irritability of muscles and influenced the views of many of Hahnemann's contemporaries. For example Cullen traced health and disease to the nervous system; fever was due to spasm of the small arteries. Brown viewed life as conditioned by stimuli. Health was moderate irritability, disease increased (sthenic) or decreased (asthenic) irritability. Treatment consisted in heightening the irritability when it was low and reducing it when high. Somewhat earlier Gaub had suggested that disease was composed of two series of phenomena: the phenomena of damage and those of reaction to the damage. Morgagni attempted to place disease alterations on an anatomic basis, by showing that certain organ alterations resulted in certain symptomatic manifestations. If he had opened the way for a macroscopic pathologic anatomy, Rokitansky had not revealed its possibilities in Hahnemann's active period and Virchow, who was to lay a foundation for microscopic pathologic anatomy was still unborn. If Morgagni's work was unobserved, Auenbrugger, who had paved

the way for physical diagnosis, was disregarded. When Hahnemann's viewpoints on pathology were enunciated, Lacombe had not yet invented the stethoscope and Skoda was but a child. Borden, again rejecting mechanism, returned to the Hippocratic "physis" and laid the foundation for a neo-vitalism in which he is followed by Barthez and Bichat. Hufeland,¹ a contemporary of Hahnemann, considered disease to be the operation of the vital force reacting to the morbid stimulus.

The eighteenth century will long be known as the century of systems, most of which originated in highly fantastic hypotheses on the nature of disease. Classifications of disease resembling botanical arrangements thrived. Major schools subdivided into minor contending factions. Some changed their outward appearance; for example, Stahl's animism resolved into French vitalism. Hallerian physiology found subdivision in Cullen's school and the unique ideas of Brown. Schools of the Hoffmann type represent compromises. All these conceptions of pathology found reflection in therapy. No useful purpose would be served by dwelling on this topic and perhaps sufficient has been said to indicate the general status of pathology and therapy as well as the sources to which Hahnemann might refer. This aspect of the subject can be closed by citation of two writers who suggest the effect of pathologic doctrines on therapy.

Hecker² wrote: "Who counts the sacrifice, since Stahl's time, of the so generally prevailing venesection, the solvent methods, the untimely given purgative and emetic? Who reckons the damages of each unfortunately selected curative method which places opposite to the acridities, decompositions, etc., assumed failures of the humours? The delusion of obtained perfection has been the plague of medicine since antiquity. We should never conceal to ourselves that there are infinitely many things which we do not know. We still have no physiology. We do not know what disease is, nor how curative remedies act, nor how diseases are healed."

The older of the present generation will recall the noteworthy remarks of Samuels:³ "Long, long time, through three hundred years, in pathology and therapy, system followed system, always with another therapy. The eclectic system of Boerhaave, the animistic system of Stahl, the mechanico-dynamic system of Hoffmann, the antiphlogistic theory of Girtanner against the phlogistic theory of Priestley, the 'generalisirte chemismus,' the system of Brown, Roschlaub's excitation theory. . . . Practical medicine followed these systems. It was good fortune when such a system required less blood, when the endeavored therapeutic goal was sought to be obtained through less emetic, less nausea cures, clysters. Because

it could be something else. Even in 1797 Bouillaud urged venesection in many acute diseases, beat by beat, Broussais demanded several hundred leeches on the abdomen for his presumed cases of gastro-enteritis. . . ."

As previously indicated Hahnemann did not proceed from conceptions of pathology to therapy but from drug action to therapy. A general survey of possibilities of therapeutic methods suggested three general curative methods, exclusive of the royal method, causal therapy. An attempt has been made to employ words and definitions in the Hahnemannian sense rather than to indicate modern meanings.

The first he termed hetero- or allopathic. This may be defined as a cure by means of remedies which act upon some other part of the body than the diseased organ, system or part, whereby the healthy tissues are converted into sites of disease with the view of deriving the disease from the parts originally involved. In former times it had been noticed that patients with hypochondriasis at times lost their symptoms if furuncles developed or a patient with gastric spasm remained free from pain if and for as long a time as an eruption developed. So attempts had been made to "imitate nature" by producing derivations or revulsions of disease, naturally to less important parts of the body. It is unnecessary to relate the quite innumerable ways and means of applying this therapy summarized under the phrase *aliena alienis* and called allopathy by Hahnemann. From the above it ought to be clear what Hahnemann means when he calls this method crude, indirect, not designed actually to imitate nature to mention his more pleasant remarks. If brain inflammation is to be treated by laxatives, then the gastrointestinal tract is "less important," of less dignity, only in this particular case; therefore the method is arbitrary. Criticism was also directed at lack of knowledge as to where such derivations should be made in case they could be evoked. The ontologic nature of such a pathology requires no comment.

The second method Hahnemann terms enantio- or antipathic. This may be defined as a cure by remedies which should produce a state opposite to that existing and to remove it, but by an action directed at the diseased organ or system itself. The general guiding principle is *contraria contrariis*, its origin is Galenism, its result expressed pharmacologically in combinations of words with "anti-": antispasmodics, antiphlogistics, antifebrilia, antarthritica, antirheumatica, etc. The possibility of an antipathic method¹ is conceded when an outstanding symptom of disease finds an opposite in a remedy, for example, painlessness at the site of pain through opium, treatment of constipation by laxatives, of burns by cold,

etc. The objections can be summarized under the following heads: limited possibility of application, essentially designed to palliate rather than cure; its symptomatic nature, leading either to rapid alternation of remedies or to grotesque polypharmacy. Another possibility which found no mention in his early writings is isopathy, the treatment of same with same, *aequalia aequalibus*. Expectative methods and therapeutic nihilism as passive attitudes naturally were not listed under the positive rules. There remained the simile. Examination of the literature revealed a large number of instances in which drugs capable of producing certain "diseases" in the healthy cured similar diseases in patients, the so-called involuntary homoeopathy. In short by remaining with observation and experience, the matter was established as a fact. The future of medicine consisted in determining actions of the drugs when they were to be applied on the basis of the simile, and his simile could be applied without subscription to any particular doctrine of pathology.

However both before and after his enunciation of the simile, incidental expressions reflect his attitude toward pathology and it is proper to introduce here some topics which find emphasis in his simile.

The occasional use of the word "humours" in his early writings⁵ suggests an adoption of humoral pathology, although treatment based upon it was rejected. Later he speaks of humours on fewer occasions,⁶ and then expressions like "scrofulous disposition"⁷ are found under circumstances which would previously have called for "humours." Although he subsequently adopted solidar-pathology, it did not become the sole method of consideration as is shown by a citation from his translation of Cullen:⁸ "the impossibility of saying anything probable here is due to the author (Cullen) having an exuberant dependence on solidar pathology (if I may use this word) and his sworn hostility toward humoral pathology. In my opinion he has proceeded correctly in general so far as he perceives and establishes the condition of the solid parts as the chief cause of disease, still he errs if he would attempt to advocate them as the sole cause of all manifestations of disease . . . what prevents us from assuming that the solid parts play the first and proximate role in disease and health is that there are many remote and accessory roles in the animal economy which are obviously introduced by the fluids. Are not the solid parts the daughter of the fluid, how imperceptible is the transition of the last into the first, must not also the fluid parts concur in the development of certain diseases?" After the turn of the century Hahnemann enunciated the following ideas which may also serve to indicate the meaning of the words *similar* and *dissimilar* as applied to disease:⁹

"We observe a few diseases that always arise from one and the same cause, i.e., the miasmatic maladies: hydrophobia, the venereal disease, the plague of the Levant, yellow fever, smallpox, cowpox, measles and some others which bear upon them the distinctive mark of always remaining diseases of a peculiar character; and because they arise from a contagious principle that always remains the same, they also retain the same character and pursue the same course, excepting as regards some accidental concomitant circumstances, which however does not alter their essential character.

"Probably there are some other diseases which we cannot show to depend upon a peculiar miasm, as gout, marsh ague, and several other diseases, that occur here and there endemically, besides a few others, also arise from either a single unvarying cause, or from a confluence of several causes that are always the same, otherwise they would not produce diseases of such a specific kind and would not occur so frequently.

"These few diseases, at all events, those mentioned (the miasmatic) we may therefore term specific and when necessary bestow on them distinctive appellations. . . .

"All the other innumerable diseases exhibit such a difference in their phenomena that we may safely assert that they arise from a combination of several dissimilar causes (varying in number and differing in nature and intensity)."

Likewise Hahnemann recognized a number of other "extrinsic" factors of disease which Scheidegger¹⁰ enumerates as follows: "harmful exhalation from inanimate and organic substances, insufficient pure, free air, excess or defect of sunlight, deviations of electricity in the air, barometric changes, moisture of the air, improper clothing, insufficient or unsuitable food, alcohol, uncleanness of the body, excessive exertion, excessive excretions of single organs, deficient sleep, mental over-exertion, care, fear, rage, etc." In short: "no alteration without a cause. Diseases must have their exciting causes, though they may be concealed from us in the greater number of cases."⁹ In summary diseases have causes; some have fixed causes resulting in "similar" diseases which can be named; others result from such diversified causes, they must be considered individual or "dissimilar" diseases. In this group Hahnemann places dropsy, scrofula, marasmus, hypochondriasis, etc. This viewpoint closely approximates the Hippocratic conception of etiology.¹¹

His demand for observation in place of explanation in pathology is revealed in the following citation:¹²

"Yet, in spite of the uniform disappointment of these innumerable attempts, the physiologists and pathologists would still return

to the old heaven: not because they saw any likelihood of these hypotheses leading to useful discoveries in the art of healing, but because they placed the essence of the medical art and their own chief pride, in explaining much even of the inexplicable. They imagined it impossible to treat scientifically the abnormal states of the human body (diseases) without possessing a tangible idea of the fundamental laws of normal and abnormal conditions of the human frame."

He continues to criticize the use of hypothesis, explanations, demonstrations, conjectures, dogmas and systems whose consequences were then apparent. He objects to the incorporeal something which prevailed in Helmont's and Stahl systems, the Paracelsian microcosm and macrocosm, the systems based on astral influence, numerology; in short he fights against the "explanation" mania. He then continues to criticize adversely the humoral doctrine, iatromechanics and iatrochemistry, Brown and other one-sided doctrines. In this same paper one finds the thoroughly modern viewpoint of so-called "organization" for maintenance of the individual:

"But though all the component parts of the human frame are to be found in other parts of nature, they act together in their organic union, to the full development of life and the discharge of the other functions of man, in so peculiar and anomalous a manner (which can be defined only by the term vitality) that this peculiar (vital) reaction of the parts to one another and the external world cannot be judged of, or explained by any other rule than that which itself supplies; therefore by none of the known laws of mechanics, statics, chemistry, or physics. All those theories to which age after age has given birth, when brought in contact with simple experience, and tried by a simple test, have ever been found to be far-fetched and unfounded . . . (he continues in the vein that medicine has tried to explain everything) . . . All, therefore, that the physician can know regarding his subject matter, vital organization, and all that it concerns him to know, is summed up in that which the wisest among us, such as Haller, Blumenbach, Wrisberg, comprehended and taught under the term physiology and which we might designate the empirical knowledge of vitality, that is, what the appreciable phenomena which occur in the healthy human body and what their connection is; the inscrutable, how they occur, remaining entirely excluded."

His first publication on the simile is oriented from the viewpoint that all diseases must have as their cause a stimulus of a nature which can disturb the function and well-being of the organs, whereby all uncertain, unprovable assumptions are denied. A few

years later in an attempt to explain he proceeds to indulge in speculation and postulates as uncertain a group of diseases as had any of his predecessors and what was originally an unimportant explanation advanced to meet certain scientific demands, became all important and led him away from observation into a maze of speculation.

For example, in 1809 Hahnemann divided diseases into two types: those with simple ascertainable causes and diseases produced by immaterial dynamic causes. The first group are exemplified by a splinter in the finger, calculi, corrosive acid in the stomach, depressed fracture of the skull, etc. The treatment of these cases is removal of the cause by surgical or other measures. The second group, the dynamic, gradually attain increasing importance as the citation below will show. Once he had embarked on an explanation and once the path of vitalism was adopted, the position remained unaltered, except in so far as it seemed increasingly important to him. Naturally his views caused dissension among the general medical profession as well as among his followers, particularly his belief that all endeavors to find the cause of disease were useless, because they are not discoverable.

“They only fancied that they could discover the cause of disease; they did not discover it, however, as it is not perceptible and not discoverable. For so far the greatest number of diseases are of a dynamic (spiritual) origin, their cause is therefore not perceptible to the senses; so they exerted themselves to imagine one, and from a survey of the parts of the normal human body (anatomy) compared with the visible changes of the same internal parts in persons who had died of diseases (pathological anatomy), as also from what they could deduce from a comparison of the phenomena and functions in the healthy (physiology) with their endless alterations in the innumerable morbid states (pathology, semeiotics), to draw conclusions relative to the invisible process whereby changes which take place in the inward being of man in diseases are affected—a dim picture of the imagination, which theoretical medicine regarded as its *prima causi morbi*; and thus it was at one and the same time the proximate cause of the disease and the internal essence of the disease, the disease itself—although, as sound human reason teaches us, the cause of a thing or of an event, can never be at the same time, the thing or event itself.”¹³

These are objections to the prevailing doctrines to which allusion has already been made: spasm, weakness, paralysis, fever, inflammation, hardening, infraction, plethora, defect or excess of acid, carbon, etc., in the body fluids, increased or decreased arteriolarity. Hahnemann regarded these as conjectural. If now these are objec-

tionable, then he must proceed in a different way and he elected the conception of a dynamic (spiritual) influence of the morbid factor acting on the body, like the magnet on iron. Thus disease for Hahnemann becomes simply a "deviation of life in feeling and activity" and conditioned almost exclusively through dynamic influences. "It may be granted that every disease must depend upon an alteration in the interior; thus disease can be only mentally conceived through its outward signs and all that these signs reveal; in no way whatever can disease itself be recognized. . . . The invisible disease producing alteration in the interior and the visible alterations in the exterior (in the sum of the symptoms), together make what one calls disease, both are the disease itself. . . . The invisible disease producing change in the inward and the complex of outwardly perceptible symptoms are consequently determined by one another, reciprocally and inevitably, both together make up the disease in its entirety, that is, constitute a unity so that the latter must fall with the former, that they must exist together and disappear together, so that, whatsoever is able to call out a group of perceptible symptoms, must have caused in the body the corresponding inner morbid alterations (which are inseparable from the outward manifestations of the disease), otherwise the appearance of symptoms would be impossible—and consequently whatever removes permanently the entirety of outward appearances of the disease must simultaneously have removed the inward morbid change because the banishing of the former is inconceivable without disappearance of the latter."¹⁴ In the sixth edition of the *Organon* Hahnemann emphasizes that the vital force brings about diseases, postulates a causal relation between vital force and the manifestations of disease, making the vital force, the first, the important, the disease provoking factor.¹⁵ Restated the symptoms are the results of the disease or a mere expression of the derangement of the vital force.¹⁶ The further consideration of this aspect of his pathology may be postponed until his "dynamic" views are examined.

In the discussion of his simile attention was directed to his method of individualization of patients and naturally this implies an individuality of disease and therefore a conception of pathology. The discussion revolves around the word "specific"; indeed, it is often forgotten that homoeopathy was originally introduced as "specific" therapy, the two designations being employed well into the middle of the last century. In ancient medicine specific diseases were diseases of a very definite unchangeable character, whose forms could be different in individual cases. As the fundamental character of the disease was unchangeable, the same therapy could

be employed regardless of the particular form of the manifestations. So the conception of scrofula implied a specific therapeutic agent in iodine or perhaps cod liver oil. Syphilis, gout, etc., were specific diseases, whereby an equally specific therapy was implied. Hahnemann's meaning of specific is entirely different, in that he did not generalize specific diseases-specific remedies, but subordinated the general to the particular, in short specialized and individualized. The specific was not the general conception of ancient medicine, but something very special. Neither diseases nor remedies could be classified according to family, species, and type; all details of form and character are summarized in a conception of uttermost individuality. Consequently there is no specific "for a disease called so and so, with all of its extensions, deviations and incidentals," which in pathology tend to be disregarded so that the unalterable and unchangeable fragment of disease can be discovered. Therefore as many specifics exist as there are varying states of individual patients. Moreover the simile is not adapted to disease species or types but to the single instance of disease with all its peculiarities. A remedy is specific to that particular case of disease.

Hahnemann's viewpoint on this subject was misunderstood. For example Hufeland perceived homoeopathy as a "heuristic principle" for finding specifics in the usual sense, as cinchona in malaria, mercury in syphilis, sulphur in itch, etc. But Hahnemann had no idea of discovering such general specifics. This does not imply an essential contradiction with his early attempt to find a prophylactic for scarlet fever since specifics might be found for the pure disease when complications had not as yet occurred. So cinchona might be specific for uncomplicated malaria, mercury for uncomplicated syphilis, but there is the implied corollary that actually still other similes would be necessary since pure diseases were rare. He also spoke of determining the "specific tendency of action" of a drug when proven on the healthy—again a conception of individuality. It is momentarily confusing when he speaks of a remedy being specific for a disease, for example, drosera a specific in whooping cough, or sublimate of mercury in autumn dysentery. What he meant is specific for a case seen by him, and numerous examples could be introduced to prove that one remedy is a specific for typhus one year, another the next. Occasionally epidemic diseases revealed a great similarity of symptoms, so that a given remedy might be specific, but another year an epidemic might require another "specific" or group of specifics.

In order to eliminate the confusion caused by Hahnemann's word *specific*, Schrön advised the phrase "concrete specificity."¹⁷ Many

other meanings of the word existed, most of which cannot be discussed here although two common interpretations may be mentioned. Even much later than Hahnemann, "specific" meant that the action of the remedy could not be explained.¹⁸ Again "a remedy which produces alterations in health and disease particularly in an organ acts specifically on it."¹⁹

While it constitutes perhaps needless repetition it may be well to recapitulate the ideas presented in this section with particular attention to their relationship to his simile. First, a note on the pathologic conceptions available to him, and the ideas adopted.

In the first place they are fixed by previous and contemporary notions. He knew the Hohenheim conception of macrocosm and microcosm, even if the name Paracelsus is not found in his writings; he knew the physis of Hippocrates, the archeus of Paracelsus and v. Helmont, the anima of Stahl and his thinking was influenced by these theories. Likewise he knew humoral pathology and the systems of the iatrophysicists and iatrochemists; he expressed himself forcibly and favorably on the physiologic discoveries of Haller, Blumenbach and Wrisberg; he rejected positively Brown's theory but was evidently influenced by it; he turned against the influence of the natural philosophers. If Morgagni had opened the way for pathology, Rokitansky had not revealed the possibilities of gross anatomy, and in fact was not yet born when Hahnemann's early writings began. Macroscopic pathologic anatomy had yet to evolve and develop into microscopic anatomy in Virchow's hands.

Nosology was naturally primitive. However Hahnemann could remain within the realm of experience by a temporal classification of disease: acute and chronic. Among the acute there was a large group which could be attributed to diverse extrinsic factors. Particularly important was a large group due to several infectious agents, each of which gave rise to a peculiar syndrome, sufficiently characteristic to receive a name. The recognition of the exciting factor gave opportunity for a "causal" therapy in many instances or a prophylaxis by evasion (in epidemics). With innumerable other manifestations of disease, such as colic, fever, dropsy, vomiting, the associated phenomena were so variegated that diverse causes could be reasonably attributed to them. These became "dissimilar" diseases in contrast to the "similar" infectious and metabolic diseases. Here also he remains within the realm of experience, even if the nosology is primitive. His presumption of "causes" still remains a legitimate conjecture which requires no justification.

Life itself constitutes an unknowable. But the phenomena of life can be recognized and when they are abnormally disturbed find expression in the symptomatology of disease so that the totality of

the symptoms represents all that can be known of disease, without resorting to hypothesis. Drugs produce artificial diseases, and if these are identical in expression with a natural disease, it may be presumed that the same attributes of life are involved. Nature sometimes cures diseases in that a new damage provokes responses which simultaneously remove the old disease. Drugs also have "biphasic action," producing a series of phenomena (primary action) which are changed into directly opposite (indirect secondary) effects by the reaction of the body. Consequently if a drug produced primarily the same symptoms as the disease, the reaction aroused secondarily would tend to remove the natural disease. If the drug is not repeated, its stimulus would cease and the patient ought to recover. Again experience (medical literature) had shown if two diseases were similar in nature, the weaker was removed by the stronger. Since drugs always acted, whereas the appearance of disease was conditional, drug diseases were stronger than natural diseases. If diseases were unlike in their manifestations, the stronger suspended the weaker; in the case of drugs, the symptoms might be temporarily suspended, but would return with the cessation of the drug stimulus. However two dissimilar stimuli (diseases) could complicate each other under certain circumstances.

As time elapsed his viewpoint became more ontologic and increasing subscription to vitalism became more obvious. For example in 1806 he stated that every disease owed its origin to an unnatural stimulus of a special type (which is a material stimulus), only to substitute after a few years his hypothesis of the dynamic origin of disease, a theory which stands unrestricted in the sixth edition of his *Organon*. Attention should also be directed again to the fact that his method of drug provings gave him a series of symptoms so that either logical necessity or desire to remain free from hypothesis of pathology would compel him to adopt an equally individualistic viewpoint of specificity of disease. With these subjects dismissed for the present one may turn to his expressions on natural healing of disease.

Except for historical purposes the position of Hahnemann toward natural healing would seem to be of little interest. However the fact that he apparently denied its existence was highly responsible for the diffidence and antagonism with which his simile was regarded. It constituted another hindrance to interest in his contributions and became a source of contention and debate.

In the first place if Hahnemann had denied natural healing he would not have been the only physician of this period to do so. Hartmann²⁰ emphasizes: "There would be and are at present only a few physicians—among the most recent are to be counted Brown

and Broussais—who have refused the living organism the capacity to heal of and by itself, the diseases which involve it.” The attitude of Rowley constituted a complete repudiation of natural healing without making the least concession to defenses of the organism.²¹ It is unnecessary to amplify this list since it will be immediately shown that Hahnemann is not to be included. However one point is worthy of emphasis: the suggestion that Hahnemann began the idea of refutation of natural healing, or fought the battle alone, or even concurred with such views, has no confirmation in fact. Actually it would be utterly amazing for Hahnemann as a teleologist and vitalist to deny natural healing.

In his earliest medical writing this statement is found: “Let us follow the footsteps of Hippocrates, Aretaeus, Sydenham, Sarcene, Lautter, Clekhorn, Huxham and Degner and take nature and experience as our guides.”²²

An attitude is also expressed in 1784, two years later: “in wounds the powers of the body are still preponderant, so we need only remove the obstacles to healing and nature completes her work.”²³

His attitude is more sharply defined in 1789. While recognizing the natural healing power, he is not inclined to ascribe too much to it:²⁴

“72. Nature herself will usually establish a copious discharge of fluid, probably for the purpose of gradually washing away the firmly adherent gonorrhoeal poison and of rendering it innocuous by extreme dilution.

“73. This effort of nature is however often insufficient and difficult, at all events disgustingly tedious, since along with the increase in the secretion of urethral fluid, the gonorrhoeal poison is simultaneously reproduced and continues to exercise its specific irritation, until the seat of gonorrhoea grown accustomed to the irritation becomes at length insensible to it, whereupon the poison (from want of the objective specific irritant) diminishes and goes away completely, whilst the sensitiveness of the urethra vanishes and the discharge becomes mild or decreases.”

In his notes in Munro²⁵ he implies that results are often ascribed to remedies which in fact belong to nature. The first work on his new principle states:²⁶ “In acute disease, which, when we remove the obstructions to cure, even for only a few days, nature cures for the most part, or, if we cannot we succumb; in acute disease I say, if the application of remedies is proper, to the purpose, and sufficient. . . .” Again he criticizes Brown sharply because nothing was entrusted to the power of nature. “What a blasphemy of nature,” he adds.²⁷

To follow the trend a specimen of 1805 may be presented:²⁸

"I am therefore astonished that the art of medicine has so seldom raised itself above the servile imitation of these crude processes and that it has at almost all periods been believed that hardly anything better could be done for the cure of diseases than to copy these crises and to produce evacuations, in the form of sweat, diarrhoea, vomiting, diuresis, venesections, blisters or artificial sores. (This was and remained the most favorite method of treatment from the earliest times till now; and it was always fallen back upon when other modes of treatment founded on ingenious speculations disappointed the hopes they had raised.) Just as if these imperfect and forced imitations were the same thing as what nature effects in the hidden recesses of vitality by her own spontaneous efforts in the form of crises! Or as if such crises were the best possible method for overcoming disease and were not rather proofs of the (designed) imperfection and therapeutic powerlessness of our unaided nature!"

As pointed out above this is not a denial of natural healing, but a repudiation of methods which were alleged to imitate nature. Three years later, 1808, he states that the poor who cannot afford medicine recover sooner than the rich whose windows are filled with bottles.²⁹ In the early editions of the *Organon*³⁰ one finds: "in all ages patients who were actually, rapidly, permanently and visibly made healthy through drugs, not through some other great event, not through the self course of an acute disease, not through lapse of time, not through the gradual preponderance of the energy of the body, etc. . . ." All these reservations are admissions of the existence of a natural healing power of the body. Spurred on by critics who perceived in such statements a repudiation of natural healing he added:³¹ "they followed merely the rude instinctive example of nature in her inadequate endeavors at resistance, when directed against moderately acute infections. They only copied the sustaining power of life which, incapable of exercising reason if left to itself in diseases and resting entirely upon the organic laws of the body, acts alone according to these laws, without reason or deliberation. They followed crude nature, who cannot like a skillful surgeon heal a wound by first intention by co-adapting its gaping edges; who does not know how to adjust and replace the divergent ends of a fractured bone, notwithstanding her ability to furnish, often superabundantly osseous matter; who cannot tie a wounded artery, but exhausts all her energy in causing the wounded person to bleed to death; who does not know how to reduce a dislocated humerus, but on the contrary, prevents human art from accomplishing reduction by speedily producing a swelling around the

joint; who, in order to remove a splinter from the cornea destroys the whole eye by suppuration; who in spite of her display of energy reduces a strangulated inguinal hernia by nothing less than mortification of the intestines and death; and who by transporting morbid processes in dynamic diseases, often increases the misery of the sick. No, this unreasonable vital force receives into the body those chronic diseases (psora, syphilis, sycosis) the greatest tormentors of our earthly existence, the source of innumerable diseases, under which humanity groans for hundred, yes, thousands of years and unable even to palliate one of these, this same vital force is utterly incapable of removing such diseases from the organism of its own accord, but suffers them to rankle in the system, until death closes the eyes of the sufferer after a long time of sorrow . . . that noble innate power destined to govern life in the most perfect manner during health, equally present in all parts of the organism, in the sensitive as well as irritable fiber, that untiring mainspring of all normal, natural, bodily functions was never created for the purpose of aiding itself in diseases nor to exercise a healing art worthy of imitation."

In short Hahnemann denies the frequent sufficiency of nature and implies that chronicity of disease is an evidence of the inadequacy of natural healing power. The end of the quotation "worthy of imitation" means that he intends a more direct way than the healing crises. In other words there is no denial of natural healing, nor is the vital force inactive in disease, but it is imperfect and accomplishes its purpose only by devious routes, for example, the crises. Nor do these statements contradict the explanation given for the simile since "homoeopathy knows healing only from the counteraction of the vital force against the drug correctly chosen."³²

Even as an old man he still left something to nature,³³ for patients with acute diseases, and without allopathic interference, who "were left entirely to their unaided natural force, recovered on an average sooner and more certainly."

In these quotations on natural healing one point is frequently overlooked: "only chronic diseases are the crucial test of pure medicine because they do not of themselves go over into healing."³⁴ This citation serves to emphasize that in his later years Hahnemann was mainly concerned with chronic diseases in which natural healing was not particularly evident; however he still recognized natural healing in acute diseases.

Finally one may take a citation from the work on chronic diseases itself, where incidentally he presents his explanation of the simile: "the chronic diseases which spring from miasms, cannot be healed.

even by such sacrifices (as the loss of fluids, crises, etc., L.J.B.), nor can real health be restored by this force alone. But it is just as certain that even if this force is enabled by the true (homoeopathic) healing art, guided by human understanding, to overpower and overcome (to cure) not only the quickly transient but also the chronic diseases arising from miasms in a direct manner and without such sacrifices, without loss of body and life, nevertheless, it is always this power, the vital force which conquers . . . it is the vital force which removes the enemy, in case it is supported by drugs . . . only the homoeopathic medicine can give this superior power to the invalidated vital force. . . ."³⁵

In short nowhere has Hahnemann denied natural healing; in fact, he makes the vital force a necessary condition for healing. The fact that Hahnemann represents the vital force and the disease (ontologically) as two opposed natures and that these two attack each other, the stronger conquering, is not surprising for the age.

However the mere suggestion that homoeopathy denied natural healing immediately was denounced by the natural scientific homoeopathic physicians in the now famous Wolf Thesis.³⁶ "Hahnemann does not deny the natural healing power, but he describes its effects as not worthwhile of imitation and rarely efficient. This opinion is not held by most homoeopathic physicians." Incidentally this last quotation shows how homoeopathic physicians of the natural scientific group varied in opinion from Hahnemann even in 1836. Griesselich, one of the greatest homoeopathic physicians of that time wrote:³⁷ "Hahnemann has often been criticized for his denial of natural healing power. Formerly I became confused as have others when I read the Organon. But I have not found a denial in Hahnemann's discussions and it seems to me that the reformer has given occasion to misunderstanding." It is therefore surprising that a medical historian should write of Hahnemann: "this complete denial or much more shameless impudent scoffing of natural activity in the curative process forms an essential basis of the Hahnemannian doctrine."³⁸ Likewise the very readable Max Neuburger has misunderstood Hahnemann in his recent work.³⁹ If one attempts to determine the causes for this misunderstanding, the chief factor will be found in the use of sources from late in Hahnemann's life where expressions are not clear and provocative of confusion. There remains for discussion Hahnemann's theory of chronic diseases.

A connection between the homoeopathic simile and the psora theory has been so studiously cultivated by some writers that it is widely assumed that the simile is related inextricably with the itch origin of chronic diseases, and moreover that Hahnemann devised

the doctrine and the homoeopathic profession approved its implications and alone supported its contentions. The purpose of this section is to examine some of these assumptions. The admission of the irrelevance of the material organ necessitates the excuse that inclusion was demanded by virtue of alleged connection and to reveal another source of confusion.

Perhaps no subject had received more attention at the hands of Hahnemann than the fruitless endeavors to find the cause of disease and his ridicule of "tolle causum." In this respect he approaches Hippocrates⁴⁰ who once stated:

"All who on attempting to speak or to write on medicine, have assumed for themselves a postulate as a basis for their discussion—heat, cold, moisture, or anything else they may fancy—who narrow down the causal principle of diseases and of death among men, and make it the same in all cases, postulating one thing or two, all these blunder obviously in many of their statements. . . ." In regard to the treatment of chronic diseases Hahnemann stated, "its start was pleasing, the continuation less favorable, the outcome hopeless."⁴¹ His usual therapeutic optimism having received a marked setback, he sought a way to improve this unsatisfactory situation.

To the modern reader, too often forgetful of time, it should be recalled that bacteriology was then unknown, although Hahnemann was among the few who anticipated living causes of disease. As long as bacteriology was still unborn, the epidemic appearance of infectious diseases was a mystery and prevention difficult or impossible. Atmospheric conditions were usually deemed responsible and man was helpless in opposing nature. With syphilis it was presumed that contact was sufficient to transfer the disease, hence the name *contagious* disease. However even as late as 1831, when Hahnemann⁴² urged the contagious nature of cholera, there was considerable debate over this point. Such diseases were usually listed under "poisonings" in textbooks on medicine. Under the influence of Hunter's teachings syphilis and gonorrhoea were still regarded as one disease, incidentally another view which Hahnemann did not adopt in his later years.

In an endeavor to bring unity into the unending confusion Hahnemann traced all the chronic diseases prevalent in Europe to three chronic miasms: syphilis, sycosis, and psora. By syphilis he understood the same disease with which modern medicine deals; moreover his view of its importance as a source of illness fits very well with the modern conception and needs no discussion. By sycosis he understands gonorrhoea although the modern conception varies somewhat here. The disease was very prevalent during the war

(1809-14) and moreover was accompanied by fig warts on the skin in a great number of instances. As the rash of syphilis was the external expression of the disease, so the fig warts were the external expression of sycosis. That gonorrhoea may have systemic manifestations is likewise accepted by medicine. However, for the third cause, and indeed the most frequent and important, he adopts psora or "itch disease." By analogy with the venereal diseases, the disease is contagious and appears at the point of contact with the infected person. There is a period of incubation of 9-14 days. At the end of this time an external eruption appears, but by this time the disease has also developed in the interior of the body. The external eruption is an "external substitute" for the internal disease while nature is absorbing the disease internally. As long as the external eruption is present the internal development cannot make progress, the external phenomena representing a sort of safety valve. If the disease is not cured it may suddenly break out with the most diverse, serious, even fatal sequella.

His stated reason for selecting the itch is that he had been impressed, when taking case histories, by the frequency with which patients had suffered from scabies and even where a positive history was lacking, signs pointed to its previous even if unknown existence. By degrees he had become acquainted with the internal manifestations of this disease which he called psora, that is, internal itch disease. In short all the chronic diseases which did not arise from the two venereal diseases, syphilis and sycosis, were due to a third disease. This disease had innumerable internal manifestations and the scabies eruption was the local manifestation.

This psora is the most ancient, universal and destructive and most misunderstood of the chronic diseases according to Hahnemann. Its frequency is totally unappreciated since it forms seven-eighths of the chronic diseases and is misunderstood since physicians think they may treat it locally when it is already a systemic disease when the eruption has occurred. He then cites a long list of cases to illustrate the evil consequences of suppressing the local eruption. The disease is more serious as a contagion than either syphilis or sycosis, since it spares no one. At the time the eruption first appears, the disease can be cured most easily, and by internal remedies. The rash should never be suppressed by local treatment.

The basis for the suggestion that Hahnemann was reasoning by analogy is found in an earlier article.¹³ In 1816 in speaking of syphilis he stated: "all the physicians of the inhabitable globe . . . have bungled the venereal disease from its very commencement and have regarded the local removal of the chancre as the main point of the treatment of syphilis, and the simultaneous employment of

mercury as a mere accessory." He then cites the practice of smallpox inoculation and smallpox vaccination and describes the local manifestations. ". . . Neither of them appears before the internal infection and development of the disease is completed in the system. So it is with measles and other exanthematous diseases: namely the part whereon the infecting virus was first brought does not produce the eruption peculiar to the disease, before the entire organism has undergone a change and is completely infected." Then he cites that the removal of a bitten part does not prevent the development of hydrophobia, the same being true of anthrax and of itch. He adds that as long as the chancre remains, the in-dwelling venereal malady can never break out. It seems to be a plausible even if irrelevant suggestion that Hahnemann may be guided by his psoric views concerning syphilis. Similar opinions were held in regard to syccosis in that the systemic manifestations were numerous, etc.

It is of course obvious to anyone acquainted with medical history that Hahnemann's views on the danger of the suppression of a skin eruption are not original regardless whether they are erroneous or not. This view is repeatedly mentioned by Hippocrates who considered that eruptions appearing suddenly and covering a large part of the body were healing phenomena. Other eruptions were regarded as an apostasis, a local deposit of the disease, which required further coction before cure was established. Similar opinions were held as regards hemorrhoids, discharges from the body; in fact there are eras in medical history when many measures were withheld, for fear of disturbing the natural healing power. Naturally the reflective mind will discern the problem of the skin as an immunizing organ, whereby violent procedures applied to the skin might disturb the process.

Dudgeon has admirably summarized the implications of the psora theory of disease:⁴⁴

1. That seven-eighths of all chronic non-venereal diseases are the result of an infection with a skin disease that has been driven off by external treatment.

2. That this skin disease is identical with that which we call the itch, although it presents itself under many different forms.

3. That practically every chronic non-venereal disease is scabies or a degeneration of it.

4. That none of these seven-eighths of chronic diseases are curable without a certain set of remedies which were unknown or unused before Hahnemann and therefore no chronic diseases were cured before the announcement of this doctrine in 1828, and that they have been readily curable since that time.

5. That itch is curable with these internal remedies and that treatment with external remedies is fraught with danger.

The meaning and responsibility of Hahnemann in relation to the psora theory can be understood best by determining what had been considered psora prior to his time, what opinions were prevalent in his time. With this material one can determine whether or not he was responsible for the doctrine, whether or not he and his followers alone held such views, whether or not they have been repudiated.

There has been considerable debate on the question of whether or not scabies existed in Biblical times, and there is much to warrant the belief that it was then known. The confusion seems to arise from attempts to make the Greek word "lepra" the equivalent of the Hebrew word "zaraath." At present most medical historians are agreed that zaraath probably included all chronic non-contagious diseases of the skin which disfigured those affected by them. There is a strong Biblical evidence⁴⁵ of the existence of scabies since Naaman was cured of zaraath by washing seven times in the river Jordan. It is highly improbable that syphilis or leprosy could have been cured in this manner although scabies might, because the river Jordan contains sulphur.⁴⁶

In the 13th chapter of Leviticus reference is made to more severe skin diseases cured in three weeks and in the tenth "zaraath" is applied to ulcers and in many other places to scars. The word therefore covered many conditions.

Hippocrates⁴⁷ makes only incidental allusion to leprosy and psora. Galen⁴⁸ states that psora partakes of more of the nature of ulceration than leprosy and it is a disease inveterate to cure.⁴⁹ Oribasius⁵⁰ distinguishes leuce, alphas, melas, lepra and psora from each other, psora being the most superficial. Aetius⁵¹ differentiates psora in that the scales are furfuraceous in nature while in lepra the scales are like those of a fish. Actuarius⁵² differentiates psora from elephantia by the type of scales and the greater depth of the lesion in the latter. Nonnus⁵³ states that psora is more superficial than lepra and is also variously shaped. Alexander Aphrodisiensis places psora among the contagious diseases.⁵⁴ Celsus does not mention either lepra or psora⁵⁵ but his second species of impetigo is now regarded as psora. Scribonius Largus⁵⁶ gives numerous remedies for scabies. Scabies receives more mention from Octavius than does leprosy⁵⁷ and Serenus⁵⁸ offers some popular methods of cure. Vegetius,⁵⁹ Vergil⁶⁰ and others⁶¹ of his time mention a scabies of animals. The disease is also discussed by Isidorus⁶² and Justin.⁶³ Incidentally Horace and Cicero frequently use the word scabies in an ironic sense.

If one now turns to the Arabians he will find Serapion⁶⁴ differentiating psora and lepra by pruritus. Avicenna⁶⁵ treats the disease under impetigo excorticativa presumably but the matter is not clear. Ebn-Zohr⁶⁶ mentions a contagious disease attended by itching and even described an animal infesting the skin: "there is formed in their bodies, on the exterior, something called by the people Scab, and which exists between the skin. If the animal is removed there comes out of the various parts of it a small animal. . . ." In the matter of priority Aristotle⁶⁷ had said that the lice in question live in small vesicles which contain no pus. The disease is also mentioned by Haly-Abbas,⁶⁸ Alsharavius,⁶⁹ and Rhazes.⁷⁰ The latter believed the disease due to a salt diet, old wine and neglect of bathing. Psora is also described by Paulus Aegina⁷¹ who recommends systemic as well as local treatment.

Even if these early writers are not credited with a knowledge of the disease, a definite description is found in the work of St. Hildegard in the 12th century.⁷² In both the 56th and 110th chapters are very definite descriptions of the itch mites (suren or seurn). Two centuries later Guy de Chauliac⁷³ wrote a description of the lesion under the name "syrones," told where to look for it, and stated that it was contagious. He did not advise differentiation as all the skin diseases were varieties of the same disease, an opinion with which Lanfrancus⁷⁴ differed. Paracelsus spoke of syrones but refers to another disease.⁷⁵

Toward the end of the 16th century Ambrose Pare showed very definite knowledge of the disease (les cirons sont petits animaux). Ingrassias described the parts usually involved as well as the effects, and connected the bite of the itch mite with the phenomena. Scaliger⁷⁶ displayed very definite knowledge of the lesion in 1557 and Fallopius⁷⁷ mentions "animalia in substantia cutis" and Rondelt (1592) described the itch mite as forming the third genus of pediculi.

It should not be supposed that all writers were equally well informed on the subject. Mercurialis⁷⁸ follows some other writers in ascribing scabies to depraved humours. He supposes that the blood deposits fluids, "thick, mixed with bile, impure," etc., in the integument, and that these are retained and give rise to scabies.

Throughout the 17th and 18th centuries there are many writers whose works show an intimate acquaintance with acarus. Bonoma addressed a letter to Redi (who aroused much antagonism by his opposition to the doctrine of generatio aequivoca) describing a method of extracting the acarus with a needle. He likewise showed that it was a living organism and that it was invariably present if the search made was sufficient (1687). He and Castoni, an apoth-

ecary at Leghorn, also described eggs but were unable to make sexual differentiations. They concluded that the cause of the itch (scabies) was due to the presence of an animal incessantly biting in the skin, instead of attributing it to the melancholic juices of Galen, the acridities of Sylvius, the special fermentation of other writers or irritating salts in the liquor sanguinis.

However the connection between acarus and scabies was not universally accepted. Junker in 1718 attributed scabies to drinking birch bark water in excessive amounts, as well as to certain baths. Linnaeus placed the mites among the insects (1734) and later classified the itch mite as a variety of *Acarus Syro* (1746). Lorry held that itch was a morbus depuratorius, for when it is imprudently driven in, affections of the lungs or other viscera arise and on the other hand, various diseases (asthma, inflammation, febrile disturbances, febrile malimores) have been cured by wearing clothes taken from patients with scabies. For him the cause of scabies lies in acrimonia sanguinis, residing in the acid and saline serum.⁷⁹ This acrimonia sanguinis, although not volatile, had a volatile and contagious smell.

Schubert (1779) stated: "although I do not deny that worms really exist in the pustules of itch, yet their presence is no proof that they are the cause of the disease. It is quite probable that they are generated by the disease in some way or other."

One should note the date (1772) at which the great Selle⁸⁰ stated: "experience convinces me fully of the lack of basis on which rests the opinion that itch owes its origin to worms." In 1805 the immortal Hufeland was undecided about the itch: "it is very probable that they are more the effect than the cause of the itch pustule." He recognizes in addition to the true itch which disseminated by contact, also syphilitic, gouty, serofulous forms, so that itch was a much broader conception than at present. He adds:⁸¹ "a rapid suppression of the eruption effected through external agents can . . . bring about very disadvantageous disturbances in the functions of the internal organs which can underlie dangerous diseases."⁸² He also knew a psoric dyscrasia due to impure air and improper diet. The famous Kurt Sprengel left the question of the relation to itch mite to itch undecided in 1807.⁸²

In the following year Autenreith⁸³ published his theory of chronic diseases. He traces all kinds of internal diseases to itch, particularly to itch which has been driven in. Several cases of "itch tuberculosis" are cited and many other diseases are included. However he does not imply that every case of tuberculosis, every paralysis, nor every epilepsy is due to this cause. He prefers to treat itch externally but he warns against lack of caution and ad-

vises sharp agents because "a somewhat corroded itch pustule certainly gives no occasion for return of the itch poison." Itch ulcers are the invaluable remedies in otherwise incurable itch sequela. Itch tuberculosis is healed by nature only at the beginning, for subsequently other dreadful diseases develop, for example, paralysis of the lower extremities, epilepsy, etc. He perceives no difference in *crusta serpigiosa*, the common suppurating scab, small dry itch of the aged. He also assumes scabies *ferina* and leprosy spring from the same origin, "even if in rare cases still one can perceive a chain of ever milder diseases of the skin, from elephantiasis and *lepra graecorum*, down to contagious *tinea capitis*, the common hereditary scald-head, down to thick crusted herpes and finally to this type of small dry itch."⁸⁴ Schonlein⁸⁵ said many years after Hahnemann: in recent times the view has prevailed that itch is a local process and on this account is to be destroyed locally; still experience does not confirm this; "on this account the rapid dispelling of itch is always dangerous."

In 1812 Alibert invited Gales to search for the *Acarus* and in the same year Gales published his studies.⁸⁶ During the next 18 years the theory of *Acarus* was widely accepted as the etiologic factor in the disease. In 1825 Wenzel⁸⁷ published his work which is strikingly like Hahnemann's following three years later.

In the following year Raspail showed Lugol the organism in the presence of a large body of scientific men and the remainder of the history depicts the decline in the number of individuals who did not accept the itch mite theory of scabies. However even as late as 1863 Devergie, a non-homoeopathic physician, wrote that scabies may be a spontaneous disease.

From the facts recorded above it seems fair to draw the inference that: 1) Scabies had long been known to medicine. 2) The itch mite had long been recognized and described before Hahnemann. 3) That the subject received much attention during Hahnemann's later years. 4) That 20 years and 3 years previous to Hahnemann, there were publications by Autenreith and Wenzel which are remarkably similar to Hahnemann's later work.

There remains to note any observations made by Hahnemann earlier in this life in respect to this subject. The most important was reported by him when he was 37 years old (1792), although he discussed the subject a year earlier.

In the last publication⁸⁸ he urges: "if one permits a recently infected itch patient to wash with a well saturated liver of sulphur containing water, several times daily and impresses the linen in it, then the evil disappears in a few days and without the infection recurring again. But must it not come again when an acidity lies

at its basis? I have had this experience very often and presume among others a living material as the cause of the disease. All insects and worms will be killed through the vapor of liver of sulphur."

The next year he wrote:⁸⁹

"The itch itself does not consist of emanations of congenital or acquired acridities, of a salt or acid character of the blood, but it is derived from small living animals, insects or mites, which take up their abode in our bodies beneath the epidermis, grow there, and increase largely and by their irritation of creeping about cause an itching and owing to the afflux of humours thereby produced, give rise to a multitude of vesicles which on being rubbed, or when the thin watery fluid they contain has evaporated, become covered with scabs. This is not an opinion adopted in order to get rid of a difficulty but it is based on experience. August Hauptmann, Bonomo, Schwiebe and other trustworthy men have frequently investigated the matter at various seasons of the year, in individuals of different ages and sexes who have been laboring under the itch and have found these little animals in the skin itself, in the folds of the skin, but especially in the border surrounding the vesicles. They have extracted and examined them under the microscope, made drawings of them and observed how they lay their eggs, increase rapidly and enormously and have found that they can live several days out of the body."

The article then proceeds to describe the mode of infection and states the quickest and best remedy for this affection is flowers of sulphur, a teaspoonful every morning until the "perspiration and clothes smell strongly of sulphur." Another recommendation deals with sulphur ointment. The article is signed "B" and is immediately followed by an addendum:

"The cause of itch given above is the only true one, the only one founded on experience. These exceedingly small animals are a kind of mite. Wichmann has given a drawing of them, Dover, Legazi and others have observed them. Linnaeus thinks that the dry itch has a different variety of mite from that with attending moisture.

"The itch attacks most readily and most virulently persons in whom cutaneous transpiration is scanty or weakened, who lead a sedentary life; also delicate individuals who have been weakened by other diseases, such as a fever, etc., or by residence in impure air.

"The mode of treatment described above is also right, and successful except that the continued use of flowers of sulphur has a tendency to cause tenesmus and hemorrhoids. Only external anti-

scabious remedies are required, and in very weakly subjects, internally strengthening medicine as china, wine, and steel filings.

"Sulphur ointment has the common but unfounded reputation of driving itch back into the system. The prejudice will however be removed if instead of an ointment, we employ only a lotion which eradicates the itch mite in the skin in a few days. Take half an ounce of Hahnemann's chalk-like flowers of sulphur (every chemist knows how to prepare it with equal parts of oyster shells and sulphur heated to redness) and the same quantity of cream of tartar, put both into a glass bottle, pour two pounds of cold water on them and shake a few times. With the clear water that appears when the mixture settles, the patient is to wash himself three times a day on all spots affected with the itch. A recent case of itch under this treatment disappears without the least bad consequences in the course of six or seven days, a more severe case in fourteen days and the most obstinate in three weeks. This remedy has the advantage—that having a very penetrating odor—the itch mites in the skin and the clothes are killed by mere exhalation from the parts washed and then all danger of re-infection is avoided. In orphan asylums there is no remedy to be compared with it, because it protects beds, rooms and furniture by its strong smell, from becoming a harbour for the itch mites and thus eradicates in a short time in such houses these pests, otherwise so difficult to get rid of. This sulphur ointment can hardly effect these. Cleanliness, fresh air, and wholesome diet must be imperatively enjoined on the patient. Dr. Samuel Hahnemann."

He repeats much the same suggestions in 1795:⁹⁰ "Is not the itch a skin malady merely of contagion? Is not the contagion indeed small animals of a miasm. . . . If there are skin insects which bring this malady to pass, what can it harm when one kills them! . . . One has indeed all too freely ascribed results to the apparent dispelling of certain skin maladies whose actions were existing unhealed cachexia, etc." In the dispensatory⁹¹ he concurs with the itch mite theory. By 1801⁹² there is some change in opinion: "with the employment of these names (itch, syphilis, smallpox, intermittent fever—L.J.B.) not the least step is made toward closer recognition and just as little has been done for their suitable treatment. The miasms of diseases are so completely unknown to us according to their inner nature as the disease developing from them."

For Hahnemann to adopt the itch theory of chronic disease was not as illogical as is often implied. He had often, for example in 1801,⁹³ stressed the "fixed" diseases and the usefulness of designations for them. Often he designated a single remedy for them as mercury in syphilis, belladonna as a prophylactic in scarlet fever,

and much later thuja in sycosis. In 1805⁹⁴ he speaks of a few diseases which one can call peculiar and gives them special names where necessary. The same expression is employed in the *Organon*.⁹⁵ For this reason there is nothing inconsistent in his adoption of a conception for a chronic "fixed" miasm. On the other hand since psora presents innumerable types, he demands a diversified treatment, so that he did not become inconsistent in respect to individualization in treatment. However elaboration of these points is foreign to the text. The modern interpretation of Hahnemann's psora has been presented by Bier,⁹⁶ Gerlach,⁹⁷ Leeser,⁹⁸ for those interested in further studies. Mackenzie⁹⁹ has made an interesting attempt to substitute "focal infection" for the conception of psora.

There are several possible explanations which tend to account for Hahnemann's adoption of the psora theory. It has been called a vagary of his old age, an unacceptable explanation. Close examination of the doctrine fails to show wherein he made a single advance over the views of Autenreith and Wenzel, and it is agreed by those who appreciate the medical views of this period that neither the origin nor the development of the doctrine can be attributed to Hahnemann. The writer has long felt that Hahnemann appreciated that his system was lamentably weak from the standpoint of pathology. In attempting to bolster this phase he selected the doctrine of psora because it was then an important subject in medicine. Probably reasoning by analogy from syphilis, a subject which had concerned him all his medical career, he postulated the initial lesion and later systemic manifestations of psora; yet in all this he had been anticipated by Autenreith and Wenzel. Hahnemann was severely attacked for the psora theory, and to no small extent because writers believed he plagiarized the doctrine. The literature on this accusation has been summarized by Ameke.¹⁰⁰

It is often stated that the psora theory possesses merit in teaching that skin diseases may have systemic manifestations, that systemic diseases have skin lesions, that the skin is an immunizing organ, that eruptions should not be treated too violently, etc. But this is not a Hahnemannian innovation since this view was common in antiquity. Likewise the suggestion that this theory may have opened the door to constitutional theories of disease is not quite correct. Perhaps it assisted in keeping the door open, for this problem also is as old as the Hippocratic writings. Roth has admirably summed up the situation in regard to the psora:

"Hahnemann belonged to the last century. As a therapist he pursued the road he himself had constructed. We therefore must not be surprised that many of his ideas are not in accord or har-

mony with those of the present century of which he hardly took any notice in his advanced years. Single sounds of progress pierced his seclusion and caused a disharmony of theory which differs widely from the clear views that he held when in the full virginity of his powers.”

In conclusion it may be said that psora as a disease was known to antiquity and as a generalization represented a well known conception early in the 19th century. It was neither invented by nor peculiar to Hahnemann. While it is not inconsistent with the implications of his other doctrines, its real connection is remote, if one exists at all. As suggested above and as will be noted later, it was thoroughly repudiated by the scientifically inclined members of his school.

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THE HOMOEOPATHIC AGGRAVATION.—When one recalls that Hahnemann worked with plant and mineral drugs and with oral administration instead of powerful protein substances and the intravenous route, the observation of the so-called aggravation is a credit to his acuteness of observation. Apparently the earliest statement on this point is as follows:

“If in a case of chronic disease, a medicine be given whose primary action corresponds to the disease, the indirect secondary action is sometimes exactly the state of the body sought to be brought about; but sometimes (especially if a wrong dose has been given), there occurs a secondary action, a derangement for some hours, seldom days. Thus too large a dose of henbane is apt to cause great fearfulness in its secondary action.”¹¹

At this time the aggravation is not due to the similarity of the

primary action of the drug and the already existing symptoms, but to a secondary effect. However a few years later in the treatment of a woman complaining of abdominal colic, four grain powders of veratrum were prescribed, one such powder to be taken each day for four days.² Marked aggravation, then cure resulted. Here it is presumed that the aggravation was due to a similarity of the primary action and the symptoms of the patient.

This case is frequently cited in order to prove that Hahnemann diminished the dose because of the marked aggravation of symptoms from the customary doses, whereby the reduction represents an attempt to reduce the severity of the aggravation. It seems plausible that his theory of posology could have been intimately related to such observations. However, the following year (1798) finds him employing the customary doses of traditional medicine.

In the *Medicine of Experience*,³ his reasoning is in accord with the veratrum experience:

“If we have not only selected the right remedy, but also hit upon the proper dose, the remedy causes, within a few hours after the first dose has been taken, a kind of slight aggravation which the patient imagines to be an increase of his disease, but which is nothing more than the primary symptoms of the medicine which are superior in intensity to the disease and which ought to resemble the original malady so closely as to deceive the patient himself in the first hour, until the recovery which ensues after a few hours teaches him his mistake.”

In short the correctly selected remedy ought to produce a primary effect so similar to the existing symptomatology that an aggravation of symptoms results temporarily. In this same work he states that if this aggravation does not occur, the correct remedy was not superior to the disease, the drug should be repeated in another but smaller dose. He implies that the absence of the aggravation means the dose has been too small. He also differentiates this aggravation from a pseudo-aggravation consisting of the production of new symptoms and meaning that the wrong remedy has been selected.

The question is discussed in great detail in the *Organon*. The remedy which has the greatest similarity to the symptoms of the disease is most appropriate; if the disease is not of long duration it will be extinguished “without any considerable disturbance,” . . . the symptoms, similar to the disease and excited by the drug, overpower the natural disease and the other symptoms which are not applicable to the case are not called into play and the patient does not feel them since the dose was too small to produce symptoms in the unaffected parts of the body.⁵ But it is impossible to

fit the remedy so exactly that some new symptom, even though slight, will not appear, yet this is not felt by the patient and taken care of by the activity of the organism.⁶ But since the remedy is superior to the disease it must produce an aggravation because of its superiority and its similarity.⁷ This slight aggravation is a good prognostic sign in acute diseases.⁸ The smaller the dose the slighter the aggravation.⁹ But the dose cannot be made so small that it cannot produce a perceptible aggravation.¹⁰ In chronic cases the aggravation may not be apparent for several days.¹¹

Translated into more modern terminology these expressions might read: There is hypersensitivity to drugs in the diseased parts of the body. When the primary effect of the remedy is exerted on the diseased parts there is an aggravation. But since the parts uninvolved by the disease are not hypersensitive, the non-homoeopathic actions do not appear since the dose is below the threshold of their sensitivity. The remainder of the items seem to be assumptions adopted to fit Hahnemann's theories, because he goes on to state that it is impossible to reduce the dose so far that it is still not superior to the disease, that the aggravation still is perceptible, that it is impossible to fit the remedy so accurately that some other slight symptom will not appear.

As implied above he differentiates the homoeopathic aggravation from the false aggravation:

"Every aggravation by the production of new symptoms, when nothing untoward has occurred in the mental or physical regimen, invariably proves unsuitableness on the part of the medicine formerly given in the case of disease before us, but never indicates the dose has been too weak."¹²

If one now turns from this comparatively clear discussion of the aggravation problem to Hahnemann's work on small doses,¹³ one finds the aggravation is not from too large doses but from too powerful doses:

"If we wish, for example, to attenuate a drop of juice of sundew to the decillionth, but shake each of the bottles with 20 or more succussions from a powerful arm, in the hand of which the bottle is held, in that case this medicine, which I have discovered to be a specific remedy for the frightful epidemic of whooping cough, will have become so powerful in the fifteenth attenuation that a drop of it given in a teaspoonful of water would endanger the life of a child; whereas if each dilution bottle were shaken twice (with two strokes of the arm) . . ." it cures the child without the least danger. Naturally this is a purely hypothetical case.

Here one encounters a striking contradiction. Originally the

dose was reduced in order to lessen the severity of aggravation. One may assume that reduction was followed until no "considerable disturbance" was noted. Now one perceives through dilution and succussion there is an increase in power and unfolding of powers. Actually if Hahnemann's writings are searched, instances may be found wherein large doses were given without aggravation,¹⁴ and in many cases of involuntary homoeopathy reported by him, there is no evidence that aggravation occurred. Again Hahnemann reports cases in which a dilution was used with apparently satisfactory results without mentioning an aggravation, although the dose used was subsequently regarded as much too large.¹⁵

In conclusion the following summary seems justified. In his early years large doses of drugs were administered. If their primary action was identical with the symptoms of the patient, a resultant aggravation seems entirely probable. Reduction in dose would seem indicated to lessen the severity of the reaction. If drugs seemed to act even in extremely small amounts, one explanation could be offered in the postulation of some new property conferred by dilution and shaking.

Apparently Hahnemann regarded the simile as an effect principle. Having elicited the effects of drugs in the healthy, he presumed the same effect would necessarily be observed in the patient. It is immediately obvious that this conclusion is justified, in general, providing the dose is so large that other conditions of drug action are overcome. It seems entirely possible in view of a generally existing hypersusceptibility to drug influence in the sick, that such aggravation could have been observed from even relatively small doses. On the other hand there is no necessity for very small doses to act similarly to very large doses; in fact, an opposite effect may occur. But once Hahnemann adopted the viewpoint of a superiority of the artificial disease over the natural disease and applied the simile as an effect principle, consistency demands the assumption of an aggravation, and he is forced to the assumption of an aggravation from even the smallest doses. It is perhaps an injustice, but candor impels the writer to suggest at least the possibility that Hahnemann's remarks on aggravation, and particularly those of his later years, create an impression that his statements are derived from theory rather than actual observation. It ought to be added here that the subject of aggravation was the topic of considerable discussion. Although it anticipates the subject, it may be noted in passing that Griesselich encountered the homoeopathic aggravation chiefly among those who knew something about homoeopathic theory and who believed that such aggravations must occur;¹⁶ in fact, he produced them even with

unmedicated sugar of milk, others with pure water.¹⁷ In this way Hahnemann need not be accused of misrepresenting facts to fit his ideas, for he may have been the recipient of false information.

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HAHNEMANN'S CONCEPTION OF THE SINGLE REMEDY.—In his earliest writings, long before he became "homoeopathically" inclined, one notes many indications of the single remedy. As early as 1784 he wrote in favor of a simple treatment "in place of a farrago of contradictory prescriptions."¹ In 1791 he stated: "as long as we do not accustom ourselves to use simple remedies . . . our therapeutics will remain a combination of guesswork, truth and poetry."² In 1796: "the habit still prevails in medicine of mixing together several medicines in one prescription that I leave Oedipus himself to tell what was the exact action of a single ingredient of the hotch-potch."³

"Is it well to mingle many kinds of medicines together in one prescription, to order baths, clysters, venesections, blisters, fomentations and inunctions all at once, or one after the other in rapid succession, if we wish to bring the science of medicine to perfection, to make cures, and to ascertain for certain in every case what effect

the medicines employed produced in order to be able to use them with like, or even greater success in similar cases? . . . I have no hesitation in asserting that whenever two medicines are mingled together, they almost never produce each its own action on the system, but one almost always different from the action of both separately—an intermediate action, a neutral action,—if I may be allowed to borrow the expression from chemical language. The more complex our receipts, the more obscure will it be in medicine. That our prescriptions are composed of a smaller number than those of Amatus Lusitanus avails us just as little as it availed him that Andromachus framed still more complex prescriptions than he. Because the mixtures of both those worthies are more complicated than our own, does that render ours simple?"⁴

"But do you seriously believe that your hotch-potch will do what you assign to each of its ingredients, just as if they were things that did not mutually react on each other, or that would refrain from doing so on your command? Does it not occur to you that two dynamic agents given together can never effect that which both, given separately at different times, would do—that an intermediate action must ensue which could not have been foreseen beforehand—and that this must be still more the case when several are given together! Who could tell beforehand that opium given along with coffee would in most cases merely exert a strong diuretic action? Who could have predicted it of these two remedies? Will opium still stupefy if ipecacuanha be combined with it?"⁵

"Here we often see the ne plus ultra of the grossest empiricism; for each single symptom a particular remedy in the motley, mixed and repeated prescriptions; a sight which cannot fail to inspire the unprejudiced observer with feelings at once of pity and indignation."⁶

"With a few simple means, used singly one after the other, more frequently with one alone, we may restore to normal harmony the greatest derangements of the diseased body, we may change the most chronic, apparently incurable diseases (not infrequently in the shortest space of time) into health, whereas we may, by the employment of a heap of ill-selected and composite remedies, see the most insignificant maladies degenerate into the greatest most formidable and most incurable disease. . . . A single simple remedy is always calculated to produce the most beneficial effects without any additional means; provided the most appropriate be selected, and in the proper dose. It is never requisite to mix two of them together."⁷

"It is usual at this point, for want of anything else to say, to excuse one's self by saying, the several ingredients in a prescription

are to be chosen with reference to the various aspects of the (hypothetically assumed) inward condition of the body, or indeed of the symptoms.

“Just as if one single simple substance, if it were but rightly known might not conform to several, nay all of the aspects of the complaint,—as if all the numerous symptoms could be covered by a medley, whose ingredients, so unknown in their action, in combination counteract, and in an unforeseen manner vitiate and neutralize each other! . . . But the case is worse still and the proceeding more reprehensible when we consider the action of each, or, at any rate, of the most of these substances thus huddled together, is individually great and as yet unascertained.”⁸

There is little need to labor further on this Hahnemannian innovation of the single remedy. The preference is for simple remedies and then as far as possible single remedies. Naturally he appreciates this is an ideal which cannot be fully applied at the time, for in the first edition of the *Organon* he wrote:

“It is only in some cases of ancient chronic diseases and permanent symptoms, that two almost equally appropriate homoeopathic remedies may be applied in alternation.”⁹

In other words Hahnemann thinks the *materia medica* is not sufficiently well developed and that this makeshift may be applied in practice. By the fifth edition of the same work, he rejects this proposal on the basis that one cannot foretell what alterations the first remedy has effected and that the situation may easily be different than anticipated.¹⁰ As a matter of fact he rarely but still occasionally employed alternation of remedies.¹¹

A special procedure in connection with the alternation of remedies is the following suggestion:

“When for other reasons we may consider it requisite as far as we can calculate, to give 8-9-10 doses of tincture sulphuris it is more expedient in such a case to interpose after every second or third dose, a dose of another medicine, which in this case is next in point of homoeopathic suitability to sulphur (it is usually *hepar sulphuris*) and allow this to act 8, 9, 12; 14 days before again beginning the course of three doses of sulphur.”¹² In other words one may interpose a similar but different stimulus temporarily. A similar viewpoint is expressed in *Chronic Diseases*.¹³

Closely allied to the above is the problem of successive use of remedies; for example, Hahnemann states that *mercurius*, *belladonna*, and *iodine* form a good series. In other words in a given case which suggests the use of mercury, when the picture changes it is frequently to a situation in which *belladonna* is indicated and that here *belladonna* seems to act particularly well, etc. However

there is no implication that such a series will occur, but merely that it often is noted. With this brief discussion of the single remedy, two remedies at the same time, the succession of remedies, one may turn to the question of the necessity for giving more than one remedy at a time. In general it may be said that Hahnemann rarely found occasion to do so. But, and this is the chief point, Hahnemann noted that it is permissible to use other measures in conjunction with the homoeopathic method, for example, careful attention to the diet; moreover in the *Organon*, Hahnemann¹⁴ recommends the use of antipathic or palliative procedures in urgent cases where the danger to life is so imminent as to preclude the use of homoeopathic agents. Likewise he recognized the value of chemical and functional antidotes. In "Chronic Diseases" he suggests the use of electricity in paralysis,¹⁵ as well as hydrotherapy,¹⁶ although he subsequently retracted his statement in regard to electricity.

In recapitulation it may be said that Hahnemann advised and used the single remedy in a vast majority of cases, but recognized the necessity for variation from this procedure. He recognized adjuvant methods, particularly diet, but did not frequently employ other procedures than the general regime. This is again to be considered in relation to the type of case which he treated.

Thus Hahnemann objected to polypharmacy on the basis that the effects of two remedies could not be anticipated, particularly when the action of both were for the most part unknown. Further that if the drug was studied it is very possible that the effects are much more extensive than appreciated, so that one agent might act in several directions. Had Hahnemann made no other contribution to medicine than to compel medicine to turn away from polypharmacy, he would deserve to be listed among the Great. His endeavors in this field were more successful than in others.

The following remarks may be added in respect to another phase of this question. In the early days¹⁷ remedies were given externally as well as internally. His practice subsequently varied somewhat in regard to both.¹⁸ In the first edition of the *Organon* the medicine is not diluted by a vehicle (for internal administration) since this increases the volume. By the fourth edition of the *Organon* he is giving drugs by olfaction and by the fifth edition he prefers this to other methods. This practice also varied. In the later editions of the *Organon* he permitted but one olfaction, and still later he permitted several.¹⁹ In the latter parts of "Chronic Diseases" he has rejected the olfactory method entirely and is inclined to divided doses by mouth and dilution of the medicine with water, thus returning to his early practice.²⁰ In the early editions of the *Organon* he permitted larger quantities of the drug to be rubbed

into the abdominal wall when the drug could not be swallowed,²¹ but in the fifth edition he discards the process,²² and in *Chronic Diseases* he returns to the old endermic method.²³ A similar variation could be traced in respect to the local use of remedies varying from frequent use,²⁴ through subsequent decline,²⁵ to practical exclusion with rare exceptions.²⁶ At least this suffices to indicate the trend of his opinion.

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HAHNEMANN'S VIEWS ON REPETITION OF DRUGS.—In his early writings¹ one finds him employing the customary doses of drugs and likewise repeating them at the usual intervals of once or twice daily,² although he was conscious of the cumulative action of drugs. Not without interest and in contradistinction to his later practices he advised the remedy to be given in increasing doses rather than

diminishing. The following year (1798) in discussing fevers³ he states: "I gave it (St. Ignatius' bean) in large doses every 12 hours, to children from nine months to three years $1\frac{1}{2}$ - $2\frac{2}{3}$ grs. . . ." Three years later in discussing scarlet fever⁴ he implies that belladonna acts for three days: "and, as the peculiar action of the plant does not last above three days, I repeated the dose every 72 hours." This refers to the "prophylactic action." But though the remedy acts for three days, in treatment he employs it every three hours: "To accomplish this object I found it best in this case to administer one half the dose recommended above as prophylactic every three hours . . ." A few years later he arrived at a definite rule:⁵

"The repetition of the doses of a medicine is regulated by the duration of action of each medicine. If the remedy acts in a positive (curative) manner the amendment is still perceptible after the duration of its action has expired, and then another dose of the suitable remedy destroys the remainder of the disease. The good work will not be interrupted if the second dose is not given before the lapse of some hours after the cessation of the action of the remedy. . . . So far from the good effect being delayed by not repeating the dose until after the medicine has exhausted its action, the cure may on the contrary be frustrated by its too rapid repetition. . . ."

He adds that too frequent doses frequently result in cumulation and the production of too violent symptoms; further unless one awaits the expiration of the action of the first dose, he can hardly be in a position to know exactly what remedy is then indicated.

Incidentally he attempted to fix the duration of action of the various remedies and his early experiences suggested that some act for six hours, others for 48. Later he considered that drugs might act for days, weeks, or months.

By the first edition of the Organon the rule is altered. He had stated that the improvement of the patient might continue after the remedy had ceased to act. Whereas before, another remedy might be given at the expiration of action of the first, he now advises no repetition until the improvement ceases. As hinted above he now feels that the action persists for days instead of hours. If a medicine is repeated within this time, though it may have given relief with the first dose, it will now produce an aggravation.

To be thoroughly consistent, the second dose should not be given. The first dose might be regarded as causing considerable improvement with the result that the remaining fragment would be removed by some other remedy, since the symptom picture would be different. But Hahnemann here is apparently following observations, and second doses of the same remedy were undoubtedly given.

Obviously there is not any fixed necessity for assuming that the patient will need a new remedy with each dose of the medicine. The problem is complicated by the fact that Hahnemann's therapeutic suggestions are concerned more with his favorite subject, chronic diseases, rather than acute processes, although he often fails to state that he is discussing the former.

Up to the fourth edition of the *Organon* the rule remains unchanged: do not repeat until the good effect of the first dose is exhausted. However he adds the important note that in acute diseases the drugs usually exhaust themselves in a few hours, whereas in chronic diseases the effects may persist for weeks.⁶ The ideas again change in the 5th edition of the *Organon*:⁷

"Every perceptibly progressive and strikingly increasing amelioration in a transient (acute) or persistent (chronic) disease is a condition which, as long as it lasts, completely precludes every repetition of the administration of any medicine whatsoever, because all the good the medicine taken continues to effect is now hastening towards its completion. Every new dose of any medicine whatsoever, even if it be the one last administered, that has hitherto shown itself salutary, would in this case disturb the work of amelioration."

". . . sometimes accomplishes all the good the remedy in question is capable from its nature of performing in a given case in periods of forty, fifty, or a hundred days. This is, however, rarely the case; and besides, it must be a matter of great importance to the physician and patient were it possible to diminish this period . . . and this may be obtained under three conditions . . . and thirdly, if this minutest yet powerful dose of the best selected remedy be repeated at suitable intervals."⁸ An extremely long footnote follows explaining the change in ideas. In general it states that in acute diseases drugs may be repeated as often as every 4-24 hours, in chronic diseases every 7-14 days. One notes here that he is perfectly consistent in his advice of the short interval for acute diseases and the long interval in chronic diseases. He implies that the rule of exhaustion of effect holds for mild diseases and in children and young adults.

By 1828 he has gone back to the earlier rule:⁹ "if we do not allow the antipsoric medicines, be they ever so well selected, to fully exhaust their action, the whole cure will come to nothing." The same idea is repeated seven years later in the second edition of this work. There is a minor variation, in that repetition is permissible when the improvement ceases even though the action of the remedy is not exhausted.

In this case he would use the 30th (which was then his standard)

and the dose would be repeated in the 18th, 12th, or 6th. During the intervals he administered placeboes, that is, unmedicated sugar of milk.¹⁰

In 1837 he changes once more in that in acute diseases the medicine should be given every 2-6 hours and in chronic diseases, usually every day or at least on alternate days.¹¹

These perhaps bewildering changes of opinion may be summarized as follows. In the beginning medicines were given at the usual intervals; later no repetition until the effect was exhausted; frequent repetition in acute diseases, infrequent repetition in chronic diseases; later do not repeat in the same dose.

These changes can be partly appreciated by the different types of practice. For example he urges the long interval when his practice was largely chronic patients, the short interval when Germany was swept by cholera. Again his opinions change with his conceptions of disease and of dynamization. But this is hardly surprising in view of the complexity of the subject with which he was working. If one will reflect for a moment it will be recalled that interest in this field was revived only when the problem became all important in allergic diseases and it is only within the last ten years that it has again gained the attention of the medical world. In this way the varying opinion of Hahnemann can be appreciated more sympathetically.

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HAHNEMANN AND DRUG PROVING.—Donner¹ recently published the results of an investigation of the sources of Hahnemann's materia medica so that those interested in certain quantitative aspects of the subject will find ample information in that work.

Since the study yielded quite identical results with those of Hughes,² whose work is easily available, and with independent personally conducted research, it may be regarded as authentic in regard to the development of Hahnemann's work. It is sufficient to state that Hahnemann performed a gigantic task, a labor which has been unequalled in the history of pharmacology. Since a detailed review is available in the sources mentioned more attention may be devoted here to a critical evaluation of Hahnemann's work than to its quantity. However it may be well to call attention first to earlier suggestions in this field.

Ancient materia medica was derived from peculiar sources. Folk tradition, old women's herbs, knowledge based on odor and taste formed the chief sources. However this source is not to be considered superciliously as so many have done and continue to do. When one recalls that mercury, arsenic, cocaine, quinine, ergot, chalmogra oil, digitalis, the salicylates, to mention but a few, entered medicine through this door, folk opinions may be valued more highly than some pharmacologists tend to assess them.

Heraclitus of Tares was said to have proven a number of drugs but none of his works have survived. In succeeding centuries certain kings (Attalus and Mithridates) made experiments not with the idea of determining the effect of medicinal substances, but with the hope of finding antidotes which might make them immune.

In modern times Mattioli³ recorded two studies on condemned criminals for the purpose of testing antidotes. Aconite seems to have been the poison used. His studies are apparently the first intentional poisonings for scientific purposes.

Gesner⁴ seems to have been the first to make studies upon his own body, but the experiments were not written in a connected manner. He mentions a proving with "eupatorium aquaticum," one with helleborus⁵ and an interesting study with tobacco, then quite unknown.⁶ He mentions that a friend studied aconite.⁷ In all these studies one or at most two doses were taken for the production of an acute intoxication. The studies are historically interesting but quite useless for medical purposes. Sennert⁸ as well as others (Baglivi, Sydenham, Hoffmann) mentioned the desirability of such studies but performed no experiments.

Stoerek (1731-1803)⁹ was the first actually to make an attempt in this direction. He published the results of the first of these labors in 1761, the study dealing with plants already known to folk medicine, for example, conium. A few symptoms of irritation were found; the plant was employed in the customary manner.

Two years later the work appeared which contained the pre-

viously cited suggestive statement of Stoerek's simile.¹⁰ It contained provings of stramonium, hyoseyamus and aconite.

In another paper¹¹ colchicum was considered, but the above mentioned reasoning is not followed in the application of the drug. The next study¹² mentions the proving of two new plants, but nothing characteristic was found.

In 1769 he considered the use of *clematus erecta* and *dietamus albus*; these are clinical trials and not provings.¹³ His last work involved a proving of *pulsatilla*.¹⁴ Only one symptom was discovered, namely pain in the right eye which he had injured two years before. However, it is very remarkable that more than one half of the cases mentioned are those of ocular disease or individuals who had, among other complaints, also ocular symptoms. At this time duties with the Court and increasing devotion to medical education interrupted the studies which were never resumed by him.

His student Quarin did not make provings.¹⁵

In general the writings had little effect. Kratochwill, a student of Stoerek's opponent De Haën, made a study with colchicum,¹⁶ but as might be anticipated, the results were negative. Krapf¹⁷ studied *ranunculus* but obtained nothing more than vesicles on the skin. This is all that is found in the Vienna school.¹⁸

Outside of the Vienna school, Alexander is to be mentioned.¹⁹ He criticized the traditional *materia medica* and reported on camphor, castoreum, saffron, and saltpeter. The work on camphor was motivated by a desire to determine whether camphor was a cooling or heating remedy, in short, by the old Galenic theory. It shows the tendency of the time even though it is useless for medical therapy. Other members of the Edinburgh school who made studies are Griffin²⁰ and Whytt.²¹ Both studied camphor.

Among the physicians mentioned by Hahnemann as having perceived the necessity for proving drugs was the great Albrecht von Haller. Hahnemann said:²² "Not a single physician, so far as I know in the past 1500 years, came to this so natural, so unavoidably necessary, simple, pure proving of drugs on the state of man, in order to discover what state of disease each drug has the power to heal, until the great immortal Albrecht von Haller. Only he before me perceived the necessity of it."²³

Haller also stressed the traditional nature of the then existing *materia medica*. He noted that the ancients knew only of investigation by smell and taste. Further one could not be sure that the same plants were used by them. He suggested a complete record should be made of the symptoms observed and that different preparations of the plant be employed. Then with these facts one should try the drug in those diseases which seemed reasonably susceptible

to the drug. It is important to appreciate that v. Haller never made a proving.

There remains to be mentioned only Coste and Willemin.²⁴ They did not make provings on the healthy but tested drugs in disease in order to see whether French plants could be used as substitutes for plants then imported. Withering, of digitalis fame, employed only the ancient tasting and smelling. The plant was tried by him at the suggestion of folk medicine. A more extensive discussion of the history of drug proving can be found in the writer's translation of Tischner.²⁵

Hahnemann was the first to actually carry out experimentation on the healthy human to any extent for the purpose of determining the field of therapeutic activity. Animal experimentation was not available since methods were crude and misleading toxicological evidence was the chief fruit of industry in this direction. Moreover it must remain a conclusion by analogy until human experiments are performed. Other traditionally employed and defective methods were equally useless to one desiring to remain within the realm of pure experience. Again in the absence of instruments of precision, the reports could be given only in terms of symptoms. Finally the work is original in its "idiographic" orientation, in the description of each symptom which a remedy produced in a prover. While there was early criticism of the method of reporting the results²⁶ no other was available if the worker remained with observation and did not indulge in speculation.

When Hahnemann began provings cannot be determined from available evidence but the suggestion is strong that the work began in the '50s and '90s. The extent can be presumed from the existence of provings with 27 drugs in his first work²⁷ to 110 drugs in his last,²⁸ this figure excluding a dozen more which were performed under his supervision.²⁹

Hahnemann's first major objection to the traditional *materia medica* was made in 1798:³⁰

"Nothing remains for us but experiment on the human body. But what kind of experiment? Accidental or methodical. . . . The necessity of this has been perceived in all ages, but a false way was generally followed, inasmuch, as above stated, they were employed only empirically and capriciously in diseases. The reaction of the diseased organism, however, to an untested or imperfectly tested remedy, gives such intricate results that their appreciation is impossible for the most acute physician. . . . The true physician whose sole aim is to perfect his art can avail himself of no other information respecting medicines than, first: what is the pure action of each by itself on the human body. . . ."

In regard to the method:³¹ "one administers these medicines each singly and uncombined to healthy individuals with caution and carefully removing all accessory circumstances capable of exercising an influence, records them in precisely the order in which they occur and thus obtains the pure results of the form of the disease." In a supplementary remark he adds that the drug should be given to a temperate healthy person in a fairly strong dose and best in solution. When the action is exhausted more symptoms can be secured by a second dose. Weak doses should be employed on sensitive people. In the beginning fairly large doses were employed: the dose should be such as one tends to use in prescriptions against disease in ordinary practice.³² If nothing is produced the amount should be doubled each day. With the weak acting drugs, they may be repeated several times a day.³³

In Hahnemann's last writing³⁴ the subject is treated expressly but not as fully as one would like: "I gave drugs prepared by me for this purpose in higher and lower dynamization, in larger and smaller doses as it could be borne by each person without the individual becoming severely affected. Most symptoms which one finds and to which no name is attached were observed on myself or on members of my family. Usually the drug was taken dissolved in more or less water, once daily or several times or more infrequently, in order to discover the action of the drug in all respects. Thereby the chief fact remains that the prover remains free from dietary errors and changes in regimen, as far as possible healthy and eager for the investigation, awaiting the great truths, and scientific and honest in the strictest sense without the least expectation of material advancement, indeed not once honored in advance by becoming publicly known as provers. They consisted of friends well known to me, and usually the attendants of my lectures. Each would report the symptoms experienced to me daily or every 2-3 days, partly in order to determine whether he was experiencing something which was already known to him (in order to inclose this in brackets in printing as not fully dependent upon the drug) partly in order to compare the exact description of his sensations and perceptions with the written expressions and then to select perhaps definite expressions with his unprejudiced approval. All the existing important accessory circumstances in the symptoms were given at the same time; I have previously drawn the attention of each of these."

In addition to the above remarks the following may be added in regard to dosage. In one instance he reports³⁵ that his experience with *cina* depends upon three instances of poisoning in children who had received 6 and 40 grains. Since one appreciates that he

treated worm infestations with doses up to 60 grains,³⁶ it is probable that these were patients and that the doses were large. He reports that *coeculus* is so powerful that it must be diluted,³⁷ the exception suggesting that large doses were in vogue. These remarks are of interest to those who have believed that Hahnemann's provings were secured with great dilutions of drugs, a thought which Müller³⁸ denied more than a century ago. While denial is correct in general, it is not in detail. For example the suggestion is strong³⁹ that silver was proven in a dilute solution and incidentally in an epileptic. A later report on *carbo vegetabilis*⁴⁰ also indicates provings with dilute drugs. Likewise in 1829 one finds the following statement:⁴¹ "in recent times only small but still highly diluted and potentized drugs because their powers are developed most fully." In the next edition of this work the dose recommended for proving is the 30th dilution.⁴² As all these references save one are subsequent to Müller's explanation, he was correct in general for the time of writing. The work on chronic diseases states that at least one proving⁴³ was carried out with a high dilution.

In summary one may state that the evidence suggests that Hahnemann early used the customary doses and gradually lessened the amount of the drug. While his vitalistic views could have been increasingly responsible there is also a good reason for this procedure. If a drug is given in such large doses that it produces immediate excretion, the full picture of the action is not determined; only small doses will reveal the complete action.

Adverse criticisms to Hahnemann's *materia medica* may be either general or specific. In regard to the first there is the question of the real health of the prover. The idea of a "norm" or a perfectly healthy individual is debatable and has even been called a fiction.⁴⁴ Realization of this came late to Hahnemann who said: "since there is certainly no man who can be absolutely and perfectly sound."⁴⁵ Moreover such an idea contrasts sharply with his endeavor to determine somato-psychic constitutions, or better expressed, his reports should contain detailed reference to the type of prover whereas they are singularly silent on this point.

Hahnemann emphasized the sequence of the appearance of the symptoms⁴⁶ but practically speaking the sequence is rarely expressed in his writings. Hahnemann emphasized the necessity for determining the "essential" action, which became subjective and leaves the domain of pure experience.

Hahnemann stated:⁴⁷ "All the sufferings, accidents and changes of the health of the experimenter during the action of a medicine are derived purely from this medicine and must characteristically

belong to this remedy even though the person had observed similar manifestations in himself a considerable time previously." This too is debatable.

The mere statement by Hahnemann that such and such an effect is a secondary effect or after effect is inconclusive. More evidence on the subject would be welcome.

More important than these matters is the decision regarding the real effect and not the psychological effect of taking a drug. The writer has produced many subjective symptoms in provers who became frightened when only sugar of milk was administered.⁴⁸ Moreover it should be stated that Hahnemann's provings were unknowns, both in regard to the substance administered and the amount given.⁴⁹

The fact that such psychologic effects were included is evident from the following evidence, to which could be added the erotic symptoms of Stapf and the flatulent symptoms of Gersdorf. The situation is more serious with Langhammar who was not only deformed⁵⁰ but apparently highly neurotic if not actually suffering from an actual psychosis. Roth⁵¹ has made a careful analysis of the Langhammar symptoms and has shown that there is a curious similarity under all drugs. A personal investigation revealed that this is particularly true of the sexual symptoms. The fact that Langhammar contributed more than 1000 symptoms is not as important as the knowledge that about 100 are printed in bold-faced type to emphasize their importance. Those interested in pursuing this type of study may begin by comparing the psychosexual symptoms of Langhammar listed under *Angustura*, *Argentum*, *Arsenic*, *Aurum*, *Belladonna*, *Bismuth*, *Calcarea acetica*, *Cicuta virosa*, *Cina*, *Cocculus*, *Colocynthus*, *Cyclamen*, *Digitalis*, *Drosera*, *Guaiacum*, *Helleborus*, *Hyoseyamus*, *Ipecacuanha*, *Magnus polus arcticus*, *Manganum aceticum*, *Menyanthes*, *Mercurius*, *Muriatic acid*, *Oleander*, *Phosphoricum*, *Ruta*, *Sambucus*, *Spigelia*, *Spongia*, *Stannum*.

In citations from the literature Hahnemann was extremely careless and included many symptoms from patients,⁵² from patients taking two drugs at a time, etc. Roth states, for example, that most of the symptoms of *Aconite* are impure and Dudgeon⁵³ places 6/7 of them in this category. Langheinz selected at random 134 symptoms from opium and found that 112 did not meet Hahnemann's own requirements. This must suffice to show that Hahnemann's *materia medica* is not necessarily pure. Knowledge of the living conditions in Coethen and appreciation of the fact that the 30th dilution was a standard dose for Hahnemann at this time, yields the strong presumption that all of Hahnemann's provings

late in his life are actually observations on patients. Even in single instances (magnesia muriaticum and natrium carbonicum) where larger amounts of drugs were employed (6-12 centesimal dilution) the evidence is quite strong that patients were employed.

Many other objections could be cited to acceptance of his materia medica at present but they will probably occur to the reader. The following appears to be a fair judgment. The early materia medica was a composite of provings on healthy individuals with large doses, then with smaller doses, then with high dilutions and very probably on patients. As a matter of fact this variation is largely to be anticipated. With large doses of a drug, nausea and vomiting or diarrhoea is a frequent sequel, whereby most of the drug is eliminated with the result that a toxicologic materia medica is obtained wherein all the drugs have practically the same effects. With smaller doses which do not excite marked symptoms or immediate excretion, more detailed pictures with entirely different phenomena can be developed. Thus any student desirous of knowing all the effects of a drug would vary the dose from the maximum tolerated to the minimum effective. However the inclusion of a patient's symptoms is absolutely not admissible on the basis of Hahnemann's own criterion, at least not without a definite statement as to the source of the symptom. To these objections must be added the fact that the reports of others are included, for example the work of Stoerek, Jörg, Alexander and others without full data as to the circumstances of production. Then too the work contained instances of accidental poisoning or intentional poisoning, either from scientific or criminal sources and finally from patients either from small doses of homoeopathic drugs given under Hahnemann's direction or large doses given by non-homoeopathic physicians who made reports in the literature. Naturally these last are also from patients. To summarize one finds increasing contamination of the materia medica called pura. Whereas the proving with cinchona was carried out with four drams of cinchona in two days, silver was later proven in the first decimal trituration and a few symptoms added from the 15th trituration. Finally in Chronic Diseases, Natrum muriaticum was proven in the 30th dilution, and he adds: "it is only with dilutions potentized up to this height that other medicines also display all their power to alter health when tested on the healthy."

Stripped of all non-essentials then, Hahnemann proposed a method of proving drugs on the healthy human, introduced the method and expended a prodigious amount of labor on the subject. He proposed to place pharmacology as well as therapeutics on an experimental basis.

It should also be noted that Hahnemann cannot be made responsible for failing to include tests and procedures which were unknown in his time. He can be judged only upon two grounds, the validity of his proposal, the success obtained in application of the method. Naturally the beginning of everything is difficult; things must come into existence, mature and ripen. No science yet known to man sprang full grown from the head of its founder and consequently perfection cannot be expected in his *Materia Medica Pura*. Moreover it is worthy of note that Jörg, Boecker, Munch, Bachr, and Clarus all followed the procedure of Hahnemann so that contemporary students regarded it as the best then available.

A more definite evaluation can be postponed until the further evolution of the simile principle is presented, but it seems fitting to close this section with a few citations from the past which serve to show that a method founded on experience was needed and the want had long been expressed.

Girtanner,⁵⁴ a contemporary of Hahnemann, clearly reveals the conditions of his time in the statement: "Since medicine has no firm principle, since it makes little use of such, since it gives only little certain reliable experience, every physician has the right merely to follow his own opinion. Where there is no knowledge, where all simply believe, there one opinion is worth as much as another. In the thick Egyptian darkness of non-information in which the physician stumbles around, there is not the least ray of light present by which they may orient themselves."

A statement of Kobert can be introduced.⁵⁵ "So it occurred that behind the swing which anatomy, physiology and pathologic anatomy took in the 17th and 18th centuries, that drug therapy remained behind, not only deplorably, but also more corruptly. The birth of a pharmacotherapy must begin with a complete discard of all drugs in general. . . ." The previously cited remarks of Samuels may also be recalled in this connection.

One other topic deserves passing mention here, namely, the preparation of drugs used in provings and in treatment. Allusion has been made elsewhere to Hahnemann's preference for water bath preparation of plant drugs rather than the direct use of fire. Likewise he opposed the preparation of drugs by fermentation.⁵⁶ In 1805²⁸ Hahnemann employed fresh plant juices dried in the sun and subsequently suspended in alcohol, a device of great antiquity. With some plants (drosera) he employed the dried leaves. However even earlier⁵⁷ he suggested the addition of alcohol to the fresh plant juice to prevent decomposition. Although this was not unknown, the use of *fresh* plant tinctures is an important innovation. Later⁵⁸ it became his favorite method of preparation and was employed

wherever feasible. That it was an innovation may be seen in the report of Bucholz⁵⁹ who subsequently reported it as something new.

With the turn of the century Hahnemann became increasingly influenced by his dynamic views and accordingly drugs were employed in a more dilute form.⁶⁰ The dilutions were then prepared by strong shaking. Several years later he emphasized the use of a new flask for each dilution.⁶¹ In general each dilution was prepared from one part of the drug in ninety-nine parts of the vehicle (dilute alcohol).

In regard to the inorganic drugs, the insoluble were at first proven in the form of a soluble compound. Later in life he employed sugar of milk as a trituration vehicle for gold and silver.⁶² At first he was undecided whether the material merely became finely divided or oxidized; later he believed they became soluble.⁶³ With mercury he originally employed his soluble mercury and other compounds, but later used a trituration of metallic mercury.⁶⁴ A dilution method by globules was also reported.⁶⁵

The opinion on the amount of shaking varied; at first a few then later many succussions. His assertion that a drug could become potentized merely by shaking is not without importance.⁶⁶ Presumably some of his "high potencies" were not actual dilutions of high degree but merely drugs prepared by prolonged shaking.

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HAHNEMANN AND DYNAMISM.—This subject will be presented briefly since the pathologic implications have been discussed, the remarks at this place being concerned with connecting dynamism and posology.

In his first essay on the discovery of a new principle, there is no allusion to any change in posology so that it may be presumed he was following traditional medicine. In 1801 he continued to elaborate the principle with the usual doses save that now drugs are routinely given singly. In the oft-mentioned study of scarlet fever the dose is mentioned twice: the dose of opium is reduced in order to assure intimate mixture of the opium with the alcohol used as a vehicle, as well as with the water in which the medicine is subsequently suspended. The object is to ensure good mixture and at the same time to reduce the power of the dose. The belladonna prescribed is also diluted 1 to 200 or 400 and is shaken. The object of dilution is again reduction of the power. Yet he adds:

“It is scarcely credible how much this and every other medicine loses in power, if we allow it simply to be licked up unmixed with anything in a spoon or give it only with sugar, or administer it without stirring it up well in the vehicle. It is only by stirring, which is brisk and long continued, that the medicine obtains the largest number of points of contact for the fiber, thereby alone it becomes powerful.”

This idea of increase of power by further division of the drug naturally met with opposition by those physicians who felt that the power could only be increased by adding more of the drug. Hahnemann's reply was the paper on the power of small doses. Here he explains the difference in action between a hard dry belladonna pill, most of which is not absorbed, and the same amount when it is thoroughly subdivided. At the same time he refers to an important subject, namely, the increased susceptibility of the sick patient to medicinal influences. The latter possibility had been foreshadowed many years before when he mentioned the relatively small doses of mercury necessary to cure syphilis and even more, in the “Medicine of Experience,” where he notes that remarkably small amounts of drugs are superior in power over diseases and that there is hypersusceptibility in disease. But in all these discussions there is no mention of increase of power by trituration or succussion. The dose may have been lessened for any of the following reasons: to lessen the aggravation when the primary symptoms of the drug and disease were alike; because of observations of increased solubility of the preparations, presumably the result of the mechanical processes employed; his trouble with the apothecaries. Probably all played a part.

Even with the first edition of the Organon, nothing is said of dynamization in the sense of the above discussion. Here he merely states that the dose should be small but sufficient to overcome the disease and that it is impossible to fix the limits of dose because drugs vary in strength. The words describing the process are diminution, subdivision, and attenuation. Nothing is said about how far he dilutes the drugs. On the contrary he states that divided doses have more effect than the total amount administered in one dose. In this connection he adds that a drop of medicine well diluted and shaken will have a greater effect than eight drops given at one time. Thus he is contradictory: early he advises the drug in water. Then in order to make the dose small he advises against this practice, then again he gives the drug in water in order to increase the power. He then proceeds by an arithmetical scale to show the effects of diluted medicine. One drop of a 1:10 dilution does not have 10 times the effect of 1:100, but only twice as much. One notes here also there is reduction in power by dilution, only that it does not proceed in a direct proportion; on the other hand he soon postulates an increase of power by dilution. Naturally all these assumptions are pure speculation since the effect of a dose is determined by the susceptibility of the object which must continually vary. However, it is not inconceivable that many drugs will be as active in disease as they would be in ten times that amount in health.

These ideas in general continue up to 1833 in the Organon. But in the previously mentioned paper on small doses¹ written in 1827, Hahnemann states in reply to the statement that his medicine is much like one drop of medicine in Lake Geneva, that the analogy does not hold because by the peculiar methods of homœopathic pharmacy, hitherto unknown powers are liberated, that is, the dynamic powers of the medicines. Thus medicines now become increased in power by trituration and succussion, so that one must be careful not to shake the medicine too much!

“The homœopathic attenuations so far from being diminutions of the medicinal powers of a grain or a drop of the crude drug . . . are exactly an exaltation of the medicinal powers, a real spiritualization of the dynamic property.”

Thus what was originally a method to insure mixing and solution with the vehicle now attains great importance. He even advises not carrying the medicine too much since shaking will increase its power. He considers dilution a necessary preliminary to succussion; otherwise the dynamic powers are not released. Whereas he had previously shaken the drugs twice, he now believes that each dilution cannot be potentized too much although he lays down the

rule of ten successions for each dilution. Now one finds medicines from the 60-300th "potency" act more penetratingly but for a shorter time.²

Since the subject is further discussed under the heading "the further development of the dilution problem," attention should be directed here briefly to a few problems concerning the word *dynamic* in the writings of Hahnemann.³

If one proceeds from the standpoint of empiric dualism, then there are two series of phenomena which need not and cannot be traced to each other. The one is called psychic and the other physical. The psychic is known in man and is also applied to a lesser extent to animals and plants. These individualities are considered "totalities" of a purposeful type. If aim or purposefulness exists in the inorganic world, it is considered to be another type.⁴ Of the many possible objections to these statements which are introduced merely for the purpose of discussing dynamism, nothing will be said here. Discussion of attempts to make thinking a secretion of the brain, to limit "psychic" to the nerve cells, to interpret "psychic" in terms of the physical would all lead too far. But the fact remains that as long as one does not proceed metaphysically, he can pursue these questions by different means: the mechanistic by the natural sciences as chemistry and physics, the psychic by philosophy and its associated science, psychology.

So far as is known the "psychic" is always bound to organic material. Yet this need not make them identical. To bridge this gap several words were used by earlier writers. For example Paracelsus called all events not mechanically comprehensible "magnetic." In a similar sense the words "feinstofflich" and "dynamisch" were employed, although the first word was also applied to such theories as are embraced in "telepathy" and other aspects of occultism and anthroposophism.

Thus Hahnemann often employed the word "dynamisch" to cover such events as were not comprehensible by crude mechanistic thinking. In these cases the conception very nearly approaches the modern expressions "biologic effects" and "functional." In his first use of the word,⁵ dynamic means the contrast to crude mechanical forces as pressure, thrust, etc.

In the example previously cited in reference to the hard pill he states: "it is utterly different with the solution, indeed with a profound solution. Be this as thin as one wills, in its passage through the stomach, it contacts many more points of living fibers and since the drugs act not atomically but purely dynamically, they exert far more marked effects than a million times more (remaining inactive) parts of the drug contained in the compact pill."⁶

In this case the word is employed in contrast to "atomically"; that is, here the material plays no role, but only the "power" (Kraft) or energy. If the analysis is carried farther it will be discovered that the words "virtuell," "geistartig," "dynamic" are often used interchangeably. In the Organon these words are constantly employed as well as in the "Geist der homöopathischen Heillehre."⁷

In the sixth edition of the Organon, Hahnemann has expressly considered the word dynamic⁸ and relates some events which he considers "dynamic," for example, the rotation of the moon around the earth and the relation of tides to the moon. These are events which do not occur through material tools or mechanical means but "are without perceptible connection between cause and effect being discoverable."

Passing to the subject of medicine he speaks of the dynamic action of morbid influences as well as the dynamic power of drugs on the vital principle and compares these to the power of the magnet on fragments of iron. "It draws it on itself and acts as on a fragment of iron . . . by means of immaterial, imperceptible, spirit-like, proper power, that is, dynamic."

The word contagious (austeckung) is applied in the same sense: "as a child with small pox or measles gives them dynamically (in an invisible way) to healthy children near him but not in contact with him . . . as the magnet affects the needle. . . ." Similarly when he refers to drugs, there is the express mention of "without participation of material parts of the drug substance." The example employed in this connection is first the nausea and vomiting provoked by a disgusting scene. Without examining the subject in detail one perceives that Hahnemann speaks of various events as dynamic or spirit-like or "virtuell" or imperceptible or immaterial, these words being synonymous, in short, events which one cannot understand as effected by crude or classical mechanics. In another group of expressions in which magnetism and the like are employed, he is using the word in the sense of energetics. It would lead too far to cite the places where the word implies an energetic world conception and where it implies a spiritualistic world conception.

Another aspect of the question needs mention. Too often it is forgotten that these are expressions of Hahnemann's time and too often it is suggested that Hahnemann is uttering these suggestions as something new. Identical views on "dynamism" can be found in the writings of Stahl⁹ or for that matter Hufeland.¹⁰ Something quite related can be found in the modern scientific conceptions, as in the "psychoids" of Driesch. But enough has been said to indi-

cate that those who speak most of Hahnemann's dynamism, high potencies, etc., often realize but little of his real intention. Perhaps the word even means for the most part "the manifestations evoked in the higher animal life, the irritability, the sensibility" to employ the words of one of Hahnemann's contemporaries¹¹ or again Vogt's meaning when he states that it is a word used to fill out the gaps in our defective knowledge of chemistry.¹²

The chief point involved is that the high potency question revolves around these "dynamic" notions of Hahnemann. Whereas the subject is examined from a physico-chemical standpoint later, here it may be said that Hahnemann's conception of "powers" released from drugs actually does not make them comprehensible. Just as will be shown later that mankind in general and high potentists in particular fool themselves with the word "infinite" and that just as the divisibility of matter as given by the Lohschmidt number is finite, so it could be shown that as far as physical research has investigated the problem, energy is not infinitely divisible. There is no more basis for the "dynamic" conception of the high potency than there is for the "physico-chemical."

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HAHNEMANN AND HIS POSOLOGY.—The general trend of Hahnemann's views on this subject has been mentioned in broad outlines. It is necessary here to give a few more details, but still to avoid a detailed chronology.¹

In early writings² he employed the traditional amounts of drugs, giving powdered antimony in doses of 50 grains and jalap root in doses of 70 grains. On the other hand he suggested a method of

treating syphilis with small amounts of mercury, moreover with a compound not supposed to produce mercurialism.³ It may be presumed that this referred to one disease and one remedy. In all probability it did not represent a general viewpoint since the doses given in the translations of Munro and Cullen are, perhaps, even larger than ordinary for the period. With the announcement of his new principle,⁴ the dose should just produce the artificial drug disease and should not exceed in severity the manifestations of the natural disease. A little later he gave four grains of arnica to a four-year-old child and increased to nine grains; doses of 17 grains of nux vomica, 10 of ledum are also mentioned and 1/6 grain of arsenic was regarded as a "somewhat strong dose." An incident is recorded where a patient of his took four powders of four grains each of veratrum at a time.⁵ The next year a dose of 40 grains of camphor is mentioned for an adult and in other cases equally large doses of different drugs for children. For example one finds 1/3 gr. of hysoeyamus extract for a child,⁶ indeed: "at the correct place the most active drug even in considerable doses brings about only good, not damaging results."⁷ About the same time one notes a decline in the dose⁸ and expressions stating that the good effects are seen from "a hundredth or even thousandth part" of the dose,⁹ an opinion which was decidedly emphasized in his next work.¹⁰ By 1801¹¹ he is employing only one drop of arnica tincture and a short time later is using millionths of a grain of belladonna for the prophylaxis of scarlet fever.¹² By 1805¹³ he speaks of hundredths, thousandths, and millionth parts of a grain, a little later of quintillionth¹⁴ and by 1809¹⁵ mentions nux vomica in the 18th decimal dilution and arsenic in the 36th. The first edition of the Organon is singularly silent on dose except for "smallest doses."¹⁶ By 1814 he is employing bryonia in the 30th dilution; by 1816 doses are definitely stated for each drug,¹⁷ and range from the tincture to the thirtieth centesimal dilution; likewise variations of the amount of single remedies for different cases is advised. This situation holds up to 1822¹⁸ although the preponderant doses range from the 12th-30th centesimal dilution. In 1825¹⁹ the tendency is for still greater dilution in comparison to earlier announcements. Essentially the same holds for 1826²⁰ and 1827.²¹ In 1828²² while larger doses are occasionally mentioned, for example five grains of sulphur, the general tendency is to higher dilutions, and the same is true of 1829.²³ However the tendency of the more zealous of the followers to go even higher necessitated a rebuke:²⁴ "I do not approve of your potentizing the medicines higher (than to XII and XXII); there must be a limit to the thing; it cannot go on to infinity. But by laying it down as a general rule that all homoeopathic remedies

be diluted and potentized up to thirty, we have a uniform mode of procedure in the treatment of all homocopathists and when they describe a cure we can repeat it as they and we operate with the same tools." In 1830²⁵ and 1833²⁶ when dose is mentioned it is the 30th centesimal dilution. However in cholera he advised camphor in large doses. The designation of the 30th dilution as the most generally used²⁷ does not mean he employed it exclusively. One soon finds him advising it, followed by a lower dilution.²⁸ Case histories reveal that he actually employed the lower dilutions in these years²⁹ and his own medicine case, found after his death, revealed bottles of the 2-30th dilutions.³⁰

The administration of medicines by olfaction, usually considered as first advanced in 1832,³¹ was described in 1818³² and again in 1821³³ and elsewhere.³⁴

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HAHNEMANN'S SELECTION OF THE REMEDY.—Brief amplification of this subject seems desirable in order that some related points may be noted. In an early work¹ his examples of involuntary homoeopathy deal with a single symptom or at most a few symptoms presented by patients and alleged to be counterfeited by drugs. In the precursor to the *Organon*² the selection of the remedy receives greater consideration and there is an emphasis upon a careful history of the illness and thorough inspection of the patient.

Later it is stated: "the sum of all the symptoms in each individual case of disease must be the sole indication, the sole guide to direct us in the choice of a curative agent."³ The use of the word "sole" gave rise to many debates revolving about the point of what Hahnemann would have included under symptoms. Even at that time it was stated that homoeopathy might remove the symptoms but that the disease would remain, or again if nothing else was demanded except the symptoms, homoeopathy would be the grave of science.⁴ In regard to this criticism it has been shown that Hahnemann would include "pathology"; moreover⁵ the exciting causes were deemed important, the moral and intellectual character, the occupation, the social and domestic relations, age, sexual power, etc., were all given consideration. As already stated the total phenomena, subjective and objective, are regarded as true indications in place of such hypotheses as excesses or thickening of the blood, etc. In addition to the fact that the remedy should produce the greatest similarity to the disease,⁶ he added that all the symptoms were not of equal importance⁷; in other words, a symptom like headache was too general, too poorly defined to be of value. Right-sided, supraorbital headache, aggravated by pressure over the frontal sinus would be deemed important. In other words a foundation is laid for the totality of a symptom as well as the totality of the symptoms. Directions were also given for determining peculiar symptoms, that is symptoms which individualize the patient.⁸ Incidentally of interest is the suggestion that the symptoms manifested between the paroxysms of malaria are more

characteristic than those of the attack.⁹ In acute cases where individual disease names were applicable, the characteristics of the epidemic were regarded as important so that he is guided likewise by etiology or at least "genus epidemicus." This is evidenced particularly in his work on cholera.¹⁰ Likewise there are quite definite suggestions that etiology as well as symptomatology are important.¹¹ With chronic disease he demands a most detailed search for the individual features of the disease.¹²

Corresponding to the primitive status of physical diagnosis, the subjective symptoms received most emphasis, but he inquires as to the pulse, the reaction of the pupils, condition of the skin, etc.¹³ Even anatomic diagnosis is considered in some instances, as a supuration of the lung, but usually this is considered as insufficiently definitive when used alone. Thus Hahnemann would apply his simile on the basis of the etiology, pathology, symptomatology, and would not use it at all by virtue of some prognostic indications. Unfortunately his doctrine came at a time when symptomatology was practically the sole method of diagnosis, so that other aspects did not receive the attention merited. Lastly it should be mentioned that various types of indications seem to be inferred in some instances, for example, etiologic indications in *nux vomica* and *arnica*, constitutional indications in *pulsatilla*, etc.

In addition a final word should be said on his views of primary and secondary actions of drugs. His chief expressions on this point are the following:

In his early essay¹ he states: "most substances have more than one action; the first a direct action which gradually changes into the second (which I call the indirect secondary action). The latter is generally a state exactly opposite to the former. In this way most vegetable substances act. . . . If in a case of chronic disease, a medicine is given whose direct primary action corresponds to the disease, the indirect secondary action is sometimes exactly the state of body sought to be brought about; but sometimes, (especially when a wrong dose has been given) there occurs in the secondary action, a derangement for some hours, seldom days." A similar statement is found in his study on coffee.¹⁴

In the precursor to the *Organon* the subject receives even greater attention.² Here it stresses that the phenomena and symptoms which occur in the first place may be termed a positive disease, which is followed by the exact opposite or negative symptoms which constitute the secondary action. In the fifth edition of the *Organon*¹⁵ several aphorisms are devoted to the topic:

"Every drug, like every other influence affecting vitality, alters the harmony of the vital force more or less, and produces a certain

change in the state of health of the body for a longer or shorter space of time. This is called the primary effect. Although a product of the drug and vital force, it is probably chiefly due to the action of the drug. Our vital force by means of its energy, endeavors to oppose this effect; the resulting conservative reaction is an automatic activity of the vital force and is called the after effect or counter effect.''

In the next aphorism he calls the after effect, the curative effect.¹⁶ Up to this point the discussion is very clear. The body receives passively an influence acting upon it. The alterations produced are chiefly due to the drug; they represent damage. Following this there is an active reaction upon the part of the vital force which is conservative and tends to restore health. Thus a drug is given whose primary effects correspond to the symptoms present. Since a small dose is used, the additional damage is slight, but the healing reaction which follows not only serves to abolish the drug damage but also other injuries which may exist. One notes¹⁷ his emphasis that only sufficient after-effect should be produced in order to prevent this reaction from becoming excessive and causing further damage to the patient. In this sense Hahnemann's views find close accord with those of Gaub and Virchow whose opinions are mentioned later. In place of the above described curative secondary effect, there may be the somewhat similar counter-effect. If a constipated person is given a large dose of a cathartic, that is, a substance whose primary effect is opposite to the symptom presented, the direct effect will be expressed as a purgative action, but the secondary effect will be the opposite, that is, increased constipation. To this extent counter-effects and curative effects are differentiated. In provings only primary effects are developed.¹⁸

In the early writings the word "alternating" action is used at times. Here it usually means that a drug may have primary and secondary effects. Later his opinion changed: "some drugs are known to produce certain effects, which, in regard to minor features, appear to be counterparts of other symptoms that may have appeared before, as well as after the former. But notwithstanding this difference, these contrary symptoms are not to be regarded as actual after-effects or counter-effects of the vital force; because they merely indicate an alternation or fluctuation (*wechselzustand*) of the various stages of the primary effect on which account they are called alternating effects (*wechselwirkung*).¹⁹ Likewise, in the later writings, one finds less emphasis upon the differentiation of the two actions and the implication that all symptoms are available for therapeutic use.

Finally a single note on Hahnemann's attitude toward isopathy introduced by Lux.²⁰ This question is closely related to the problem of specificity since isopathy approaches one form of specificity in the modern sense.

"The antipsoric medicines treated in the following volumes contain among them no so-called isopathic remedies, because their pure effects—even those of potentized itch matter are far from being adequately proved, so that a sure homoeopathic employment of them may be made, I say homoeopathic, for idem it is not, even though we give prepared itch matter to the same patient that we took it from, because if it is able to do him good, it can only do so in the potentized state, seeing that the crude itch matter, which he has already in him, is an idem without any action upon him. The process of developing the potency alters and modifies it, just as gold leaf in the human body, is ever more and more modified and altered at every stage of its dynamization. . . . Isopathic and aequale are erroneous expressions which if they express anything can only mean similitum because they are certainly not the same."²¹

The same attitude is taken in the *Organon*²² but he adds there: "Moreover in this way undoubtedly certain diseases peculiar to animals may give us remedies and medicinal potencies for very similar important human diseases and thereby happily enlarge our stock of homoeopathic remedies. But to use a human morbific matter (for example a psorin taken from itch in man, human itch or the evil resulting from it) for healing—this is remote. Nothing can result from this but trouble and aggravation of disease."

Thus Hahnemann's only objections are that the substance is unproven and, more important that the substance is altered by virtue of preparation; therefore, it is the "similar" rather than the "same." Hahnemann was a staunch adherent of vaccination for smallpox; and more accurately than v. Behring, Hahnemann perceived that it was homoeopathic rather than isopathic. The problem which Hahnemann raised, a subject on which his views are clearer than most physicians at present, is naturally a difficult one. The differences between homoeopathy and isopathy are so small that what one may call isopathic, another will call with equal right, homocopathic.

That Hahnemann's prophetic words actually anticipated the future may be seen in the remarks of v. Behring:²³

"The scientific principles of this new tuberculin therapy are yet to be established, just as the principles of my antitoxin serum therapy remain to be explained, notwithstanding the assertion by many authors that the therapeutic action of my diphtheria and tetanus antitoxins are clearly understood since the promulgation of

Ehrlich's side chain theory. For speculative minds the new curative substance will undoubtedly become a most interesting object of scientific investigation, but I do not believe that medicine will profit much by it. In spite of all scientific speculations and experiments regarding smallpox vaccination, Jenner's discovery remained an erratic block in medicine, until biochemically thinking Pasteur, devoid of all classroom knowledge, traced the origin of this therapeutic block to a principle which cannot be better characterized than by Hahnemann's word: 'homoeopathic.'

"Indeed what else causes the epidemiological immunity in sheep vaccinated against anthrax, than the influence previously exerted by a virus similar in character to that of a fatal anthrax virus? And by what technical term could we more appropriately speak of this influence, exerted by a similar virus than by Hahnemann's word: 'homoeopathy.'

"I am touching here upon a subject anathematized till very recently by medical pedantry; but if I am to present these problems by historical illumination, dogmatic imprecations must not deter me. They must deter me no more now than they did 13 years ago when I demonstrated before the Berlin Physiologic Society, the immunizing action of my tetanus antitoxin in infinitesimal dilution. On this occasion I also spoke of the production of the serum by treating the animals with a poison which acted better, the more it was diluted, and a clinician who is still living, remonstrated with me, saying that such a remark ought not to be made publicly since it was grist for the mill of homoeopathy."

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SUMMARY OF HAHNEMANN AND HIS HOMOEOPATHY.—While it is difficult to summarize the spirit of Hahnemann and his homoeopathy without doing injustice to the subject, the following general suggestions are offered. Müller¹ has criticized Bier² because the latter states that according to the reader's position one finds greatness or foolishness in Hahnemann's innovations. However Bier's viewpoint is correct. If the reader appreciates Hahnemann's recommendations in the field of chemistry, his ideas on public health measures and control of epidemics, the use of disinfectants and heat as a sterilizing agent, his rediscovery of the simile, his method of proving drugs, his observation of the aggravation with comparatively weak substances in place of the foreign proteins of today, his attempt to direct attention to minimum effective doses rather than maximum tolerated doses in order to utilize phase effects, his pharmaceutical innovations in regard to increasing drug surface, solubility, etc., his awareness of the difference in the therapeutic management of acute and chronic diseases—to mention but a few items—there can be but little doubt of the greatness of the man. On the contrary if one chooses to note his theory of dynamization, his acceptance of the psora doctrine, the use of high potencies, etc., Hahnemann has been associated with much foolishness.

The great need of homoeopathy of the Hahnemann type is a study of Hahnemann in relation to his time and with full appreciation of the human element in his work. He has been regarded as a god or devil, worshipped or hated; sincere attempts to understand him are exceedingly rare. Some of these real attempts have been mentioned elsewhere, and it is expected that Tischnier's work³ will fill in the great defect now existing.

The best attempt in this direction outside of those mentioned in the introduction is the frequently forgotten study of a great student of Hahnemann, Dudgeon. Though time has altered many of Dudgeon's interpretations, his critical study of Hahnemann is the best in English, although Haehl's study is more recent, larger and technically more exact. Certainly no correct appreciation of Hahnemann can be obtained without knowledge of the works made available by these writers.

There has been but little endeavor to consider Hahnemann in the light of his own time. Until the conceptions prevailing in therapy, materia medica, pathology and nosology in 1800 are grasped, one cannot appreciate Hahnemann as he was, but only Hahnemann as one thinks he was. A corollary to this suggestion is the problem of considering Hahnemann at 44 or Hahnemann at 85. There is also the problem of whether one shall consider only his observations and principles founded on these observations, or his explanations and speculations which entrapped him in a net of phantasy.

It anticipates the discussion somewhat to state that Hahnemann made valued innovations, but at the same time exhibited many weaknesses. Repeatedly one notes how he vacillated in his opinions and practices and the conclusion might be reached that he had a vacillating character. Yet most of the problems he attacked still remain unsolved; many he suggested are still untouched. For example, it is only within the last few years that any attention has been directed to the matter of the interval between repetition of doses. How naive are the opinions of present day medicine on this subject! On what fragmentary evidence is the request "to take every three hours" actually based, to mention only the most elementary example. In short one can conclude that Hahnemann was eternally changing his mind or that new observations in candor compelled him to alter his opinion. As Bier has implied only a fool is so positive that he need never change his opinion. If Hahnemann's ideas frequently look ridiculous in the light of present day knowledge, then one must not forget that "the daring horseman is the only one thrown from the horse."

Reduced to essentials the noteworthy innovations of Hahnemann's homoeopathy are as follows:

1. The basis of science is experiment and experience (observation) and not speculation.
2. The basis of the materia medica must be the effects actually observed in the healthy after drugs have been given singly and alone and in various doses.
3. The healthy human individual should be used for this purpose supplemented by experimentation on animals. On the basis of this knowledge one may proceed at the bedside.
4. There are various ways to cure. The royal road is the removal of the cause. This principle is more difficult to apply and less frequently available than is presumed.
5. The simile principle is not applicable to so-called surgical diseases and those with an ascertainable, removable exciting or maintaining cause.

6. Remedies applied on a contrarium basis are largely palliative in type.

7. Many remedies thought to be applied on a contrarium basis really rest on the simile principle.

8. The simile principle is widely available in curative medicine.

9. It is employed when the symptoms of the disease and the primary action of the remedy correspond.

10. The result is a temporary aggravation in the condition.

11. To avoid too severe aggravation the dose should be small.

12. The totality of the symptoms and not the name of the disease guides the choice of the remedy.

13. The remedy is to be given singly and alone since its effects in combination with other substances have not been determined.

14. The more acute the disease the larger the dose and more frequent the repetition. Chronic diseases in which there is marked sensitivity to drug stimuli should be treated by smaller doses and at longer intervals.

15. Drug action is increased by solubility of the preparation and increased drug surface through trituration.

Some of his weaknesses and possible reasons therefore are:

1. An appreciation of the natural healing power of disease early in his career, but insufficient esteem for its importance throughout the latter part of his life. The best explanation is his interest in chronic diseases where natural healing naturally is not well evidenced.

2. Intolerance to criticism, great aptitude for skillful polemics, stubbornness. Among other answers a partial explanation is found in the belated appreciation of his work. This almost inevitably happens to those who seek to reform. He would have found excellent parallels in the life of Paracelsus, Harvey, Jenner, Vesalius, or, to employ an anachronism, Semmelweiss.

3. In the latter half of his life, he fell into the same snares as beset the paths of his predecessors and contemporaries.

4. The small dose became the infinitesimal and then proceeded beyond the bounds of science.

5. The observations on trituration and solubility and the effectiveness of the small dose are translated into the doctrines of dynamization of remedies, release of new powers, the "potency" doctrine and succussion.

6. The sane views on infectious diseases are replaced by dynamism and a doctrine elaborated by crude analogy.

7. The leading pathologic dogma of his time was accepted in an attempt to introduce pathologic conceptions into a doctrine which had become hyperdynamic.

Other valuable innovations as well as mistakes could be cited but there is little need to extend the list. Thus a man who startled his contemporaries by his discoveries in chemistry, who emphasized drug proving on the normal, who demanded individualization to an extent never before appreciated in medicine, who was so acute an observer as to record aggravations from relatively weak vegetable drugs, who foresaw the biphasic action of drugs now so much in vogue in pharmacology, who revolutionized pharmaceutical technique, who approached the colloidal particle, who recognized the diversity of therapeutic problems, who first studied the "interval" in medicine, who appreciated bacteria as the cause of disease at a time when this was quite unknown in medicine, who foresaw the necessity for alteration of the etiologic agent in isopathic therapy, such a man belongs among the great in medicine. Still his career ended in a maze of speculative doctrines such as dynamization, ultra-dilution, psora and others which are at total variance with his early work.

Most medical historians up to the present have elected to write only the history of the closing picture. Perhaps Hahnemann has not been dead sufficiently long to be appreciated.

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THE SUBSEQUENT DEVELOPMENT OF HOMOEOPATHY.—To trace the subsequent development of homoeopathy adequately would require a large volume if one delved into the development in each country. Even by the middle of the 19th century there was a large literature, many journals, clinics, hospitals, societies, pharmacies, and its representatives were found in almost every country in the world.¹ For these reasons the discussion is restricted to the evolution in Germany, the scene of its birth.

Medicine, in general, underwent considerable modification. The old "pathologic" school which opposed Hahnemann gradually passed into oblivion, although evidences of it were obvious in the middle of the century. Their errors and excesses were partly responsible for the development of the nihilistic school represented by Skoda, Bock, and others. Their practice consisted largely in expectancy, dietary measures, and at times symptomatic palliation. Great as the academic value of their work was, it soon became evi-

dent that the diagnosis of a widened bronchus, an altered heart sound, a change in the fat content of the liver, while scientifically meritorious, hardly met the practical requirements of everyday life. The most exact opinion that a child was dying of oedema of the glottis hardly consoled the parents, nor did an attitude of expectancy or a prescription of a demulcent serve to increase lay confidence in medicine. Again disbelief in the therapeutic properties of remedies led to belief in their harmlessness, and the so-called school of "Indifferenten" developed. Here a few remedies were regarded as universal agents.

Still a fourth movement is personified in Wunderlich,² who objected to the consideration of therapy as a mere adjunct to pathology, and regarded the attitude of complacent expectancy as lamentable. As a representative of the physiologic school he perceived an opportunity in the practice of shortening disease if unable to heal it, of relieving if unable to cure. Apparently the fact that a school of therapy founded on *usus ex morbis* was hardly a physiologic school, escaped his attention. Guided by views of the necessity for investigation, aimed at localizing disease, a therapy of sweat cures, emetics, purgatives, vesicants, narcotics, moxa developed, or therapy lapsed into a resigned level of expective symptomatic therapy for disease which could not be directly attacked. Still another movement is evident in the school of Rademacher, which took over some thoughts from Paracelsus, others from Hahnemann. He relied on "experience, analogy, and logical hypothesis,"³ so that his therapy was founded more on instinct than anything else.

Attention should also be directed momentarily toward the chief problems raised in the controversy between homoeopathic and non-homoeopathic physicians. The brief enumeration of these reproaches directed against homoeopathy will save many words in the narration of the subsequent development of homoeopathy.

1. Hahnemann denied the healing power of Nature. In the previous section it has been shown that his expressions on this subject did lead to confusion. Regardless of whether Hahnemann did or did not value natural healing power, his associates perceived the *modus operandi* of the simile in the stimulation of this power. This was officially announced in the Wolf Thesis which represented the opinion of organized homoeopathy of the time. Another attempt to remove this source of confusion was made by Rau⁴ whose entire work is based on the view of imitating the natural healing force. For example the title of section 92 in that work is "the curative efforts of nature ought to be assisted, not arrested." The subject finds discussion subsequently but it may be said in advance that

organized homoeopathy did not deny the existence of a nature healing power, but attempted to assist it.

2. Hahnemann's ridicule of "tolle causam" and his emphasis on the symptom complex as the source of indications for treatment were considered equivalent to neglect of the basic cause of the disease. As this has been discussed there is no necessity for repetition here. Nevertheless attempts were made to define more clearly the conception of symptom complex (Rau), the characteristics of it (M. Müller, Mosthaff, Watzke), the history of development of a disease (Wolf), the relationship to physiology and pathology (Schrön), the importance of etiology, semeiotics, and diagnosis (Griesselich) to the practice of homoeopathy. Whatever misunderstanding Hahnemann may have occasioned was rectified by the natural scientific group.

3. Hahnemann's unfortunate adoption of the psora theory and his promulgation of antipsoric remedies led to the general conviction that this subject was identified with homoeopathy. Its elements of truth are to be found in ancient thoughts on "latent dyscrasias," "inner qualities." The rejection of the psora by the scientific school of homoeopathic physicians was immediate, but without regard for the origin of the theory or the repudiation by homoeopathic physicians, it remained and remains a constant source of attack on homoeopathy.

4. The older Hahnemann presented a doctrine which at best is hyperdynamic. If Hahnemann stated: "disease and healing develop only through dynamic influences,"⁵ this was rejected by the homoeopathic physicians who sought to minimize hyperdynamism by investigations in physiology, chemistry, physics, pathologic anatomy.⁶

5. The conclusion of the action of a medicinal action on the healthy as applying to the action in illness was designated as deceptive. This objection has limited validity and even today one may advocate with propriety that the morbid symptoms which drugs produce in the healthy are the indications by which their field of curative action may be recognized. To be sure this should be supplemented by provings of drugs in disease, a field which still remains untilled by the homoeopathic physician.

6. The explanations advanced for the principle *similia similibus* were shown to be wrong. In the time which was to come, this was found not to constitute a real objection for what single living process has been fully explained up to the present time? However, and this is important, the homoeopathic group (Müller, Kretschmar, Purkinje, Werber, Watzke⁷) urged that these explanations should be considered merely an attempt to discuss the simile more

accurately and to support it more firmly rather than to regard them as having ultimate validity. But failure to appreciate this led to confusion between the simile as a matter of experience and the attempt to explain the experience; when explanations were found false the simile was subjected to further opprobrium.

7. Since the so-called homoeopathic aggravation was supposed to occur and since Hahnemann held it necessary, further injury might be produced. More exact observation and reports by Rummel, Kurtz, Schrön, Schneider, Trinks, Goullon, G. Schmid and others revealed that the so-called homoeopathic aggravation was partly a phantasy of Hahnemann, partly a misunderstanding of the course of the disease, partly conditioned by the drugs, but was in no way necessary for the homoeopathic cure.

8. The potency theory of Hahnemann was considered ridiculous and except in the field of increased solubility of drugs by dilution and increased surface by trituration, it was generally conceded that Hahnemann erred decidedly here. But this was also urged by the scientific group of homoeopathic physicians; in fact, Ran stated: "potentisation by dilution is nonsense" (i.e. p. 238).

9. It was held that it was impossible to prove drugs on healthy people with small doses. The provings with so-called high potencies were properly rejected; on the contrary lower dilutions of drugs (small doses) did and do produce symptoms. The question is impossible to argue; it must be settled by experiment. This is discussed later.

10. Hahnemann attempted to separate so-called primary and secondary actions in order to gain insight into the development of the drug disease. Many homoeopathic physicians (Trinks, Piper, Hering) warned that thereby the totality of drug action might be lost.

11. Single and avoidable defects in the provings of Hahnemann, particularly in respect to objective symptoms and chemico-anatomic findings, were proven. This objection is valid but it can be assigned to the embryonic state of the method rather than the method itself.

12. The advice of Hahnemann relative to certain "one-sided" diseases which could not be completely covered by homoeopathic remedies was regarded as incompleteness of homoeopathic therapy. This argument is valid to the extent that homoeopathy could not possibly be the exclusively correct method.

13. The advice of Hahnemann against the repetition of drugs and the suggestion of healing by a single dose contained an unsuspected truth, particularly in respect to the problem of repetition. Without destroying this genial observation, the problem of interval was changed (Aegidi, Hartlaub, Wolf) and the dose theory altered

as well (Kurtz, Veith, Schmid, Trinks, Schrön, Vohsemeyer, and particularly by Griesselich).

But of all these things medicine remained uninformed. To it homoeopathy was a closed book in which Hahnemann had written all the chapters.

A few other common arguments of the day may be noted in passing. The most frequent was: "the homoeopathic procedure is pure empiricism in the bad sense of the word." This finds its source in the "practical" nature of homoeopathy, in contradistinction to the theoretical systems of Brown and others. As a matter of fact the homoeopathic group took over the advances of physical diagnosis and pathology as Arnold wished and attempted to determine actions of drugs on single parts of the body; for example, the action of ammonium chloride on mucous membranes, urea on the kidney, phosphorus on the spinal cord, the action of sulphur and opium⁸ on the urine and blood, on the excretions;⁹ the newer type of work may be seen in Reil's proving of oxalic acid,¹⁰ Miguel's work on sulphuric acid,¹¹ etc. It should not be forgotten that each of the five existing schools called the others irrational.

Attacks on the practical aspects of homoeopathy were also not lacking. The most frequent was "the results of homoeopathy are not actual drug effects, but represent natural healing." This led to development of clinical observations¹² and statistics, which tended to show that actual drug effects were secured. Gradually this argument shifted to one still employed: "the results of homoeopathy are to be ascribed to the strict dietary schemas." There can be no doubt that Hahnemann introduced marked changes in dietetics. Many modern writers do not fully appreciate that the old "dieta" referred to the general management of the case and not simply to the food intake. The argument that small doses could not act, as well as the fact that homoeopathic physicians had recourse to other measures found frequent repetition.

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GERMAN DEVELOPMENT.—The year of 1835 is generally regarded as the time when German homoeopathy ceased to be under the exclusive influence of Hahnemann. More accurately the development of a new movement began with the studies of Moritz Müller whose work appeared in the so-called Stapf's Archiv (Archiv f. hom. Heilk.¹). Although Hahnemann's "potentization" doctrine drove many sympathetic physicians out of the so-called homoeopathic ranks, Müller attracted many workers by his own influence.

While Hahnemann was at Coethen, Hartlaub simplified the materia medica,² Gross,³ Rau,⁴ Bergmann,⁵ Caspari⁶ wrote monographs. The appearance of Heinroth's attack⁷ was followed by Gross's answer⁸ and numerous other replies. Schwiekert's treatise on materia medica⁹ was thought the most important. Caspari's book for lay practice¹⁰ forms the beginning of a series of books of this kind which have grown in volume. Rummel's criticism of homoeopathy is a precursor of later and more definite criticism.¹¹

The publication of the psora doctrine by Hahnemann completed the division of the two groups of homoeopathic physicians.

Wolf and Rau declared the psora theory entirely hypothetical, and Griesselich stated that Hahnemann intended merely to recognize and correct some of the errors in his hyperdynamic system and under the term embraced what others designated dyscrasia, acidity, cachexia, etc. Griesselich also states that it is an important concession of Hahnemann that the symptoms are not the sole indication for the remedy. The psora theory lost ground and furnished an opening wedge for the constitutional theory. The first homoeopathic pharmacopoeia had been published earlier and was republished in 1828. By 1833 a clinical homoeopathic journal had been published, Stapf gathered all of Hahnemann's writings¹² and the first lay journal for homoeopathy was published.¹³ The works of Ruckert¹⁴ and Weber¹⁵ became the leading textbooks until the appearance of Jahr's works. Like Müller in Leipzig Roth became teacher of homoeopathy at the University of Munich. In 1832 Boeninghausen had published his repertory which is still employed by many who use that method of prescribing. Hausen, who was not a homoeopath, assaulted "allopathy"¹⁶ and Simon¹⁷ published his crude assaults which led to the development of a journal against homoeopathy.¹⁸

The reorganization of the homoeopathic profession was effected in 1831 (Hahnemann withdrew from it) and in 1832 Hahnemann published his attack on Müller¹⁹ which alienated many more physicians from Hahnemann. By this time a homoeopathic hospital was in existence. The fight for control was a bitter one but ended in partial reconciliation of the two groups. At the truce meeting Hahnemann required a pledge of unconditional observance of the simile, avoidance of antipathic measures if possible, rejection of heroic methods as blood letting, purging, etc., avoidance of all "stimulating" remedies.

If Hahnemann had removed Müller, the best homoeopathist of the time, another objector, Griesselich, had arisen. His sketches are still worth reading.²⁰ He recognized the spirit of the simile, the advancement of physiologic experiments with drugs, while dynamism, psora, and potentization he regarded as secondary and not important. He stated that homoeopathy would appear as a caricature until its physicians corrected the want of sober unprejudiced observations and abandoned their credulity. His journal²¹ is excellent and is discussed elsewhere. Also belonging to this period is Hartmann whose journal²² and book²³ became the source of Bachr's great work, perhaps the most neglected work on homoeopathy.

By 1835 Hahnemann had fully relinquished dictatorship of the homoeopathic ranks. Homoeopathy then changed so much that one of Hahnemann's staunchest adherents stated: "homoeopathy is no longer the same as when established by Hahnemann nor as given by him later. The time has passed when every one who takes an interest in it, must accept it as infallible and take Hahnemann's word as the gospel; and while formerly the reports of accomplishments of homoeopathists, for reasons before stated, were only supplements of Hahnemann's dictates, those of a later date are not infrequently in direct opposition to the teachings of the Organon. Parties have formed; the one still adheres firmly to Hahnemann's dogmas, the other raises its voice against most of them and threatens their downfall" (Hartlaub).

In 1837 the Wolf-Rummel theses appeared as the platform of the natural scientific group. A summary of these eighteen theses may be given as follows:²⁴

1. Strict acknowledgement of *similia similibus curantur*.
2. In order to apply this law of cure correctly it is necessary to study carefully the materia medica for years. It cannot be applied by an individual without medical training.
3. The homoeopathic method does not consist in the mere comparison of symptoms, nor does it favor empiricism and lack of

general medical education; on the other hand it accepts those parts of the "old school" which are known to be useful.

4. The scientifically educated homoeopathic physician comprehends the pathologic conditions under the totality of symptoms.

5. The homoeopathic law of cure not only demands that there be a similarity of the symptoms but also a similarity of the disease and the comparison of the former is only an expedient to recognize the latter. The homoeopathic physician therefore makes sure that the existing similarity exists between the natural and medicinal disease as regards character, nature, and site.

6. The homoeopathic physician must know the meaning, the importance and the cause of the several symptoms, in order to judge which he may safely ignore and which he must consider to be the peculiar feature of the disease.

7. Homoeopathy gratefully acknowledges the facts of pathologic anatomy, etc., that the "old school" has discovered in many forms of disease but considers the dynamic features more important in that they are more susceptible to treatment.

8. It is not the business of the homoeopathist to remove simply the present complex of symptoms, but to abolish permanently the totality of both the subjective and objective symptoms of the disease.

9. If the material substratum of a complex of symptoms is recognizable, it influences the choice of a remedy but does not serve as the only indication.

10. Homoeopathy always considers the totality of symptoms and not merely single annoying and secondary ones. Therefore it is not simply a symptomatic treatment in the bad sense of the word.

11. The homoeopathic practitioner, just as much as those of the opposite school, requires all of the auxiliary sciences of medicines; none of them are unnecessary for him.

12. The psora theory of Hahnemann is only of conditional importance in practice as he put forth a great many antipsoric remedies and not a single one only.

13. The homoeopathic materia medica, though offering much assistance in making practical and reliable prescriptions is not perfect, but needs to be developed; and many reliable reprovings of the remedies should be made.

14. Any remedy is homoeopathic as soon as it occupies its relation to a certain disease according to the main principle of homoeopathy. Whether used in the thirtieth potency or diluted not at all, in grain, scruple or even larger doses. If Hahnemann later considered the dilution of remedies as absolutely augmenting their action, and unconditionally believed that when thus diluted they

are capable of affecting the healthy organism as well as the diseased, we must protest against it, and the more definitely on account of the attempt which has been made to draw practical conclusions from this theory, which must be considered entirely objectionable, that is, that the 30th potency is in all cases a sufficient and the most suitable dose.

15. The principle of allowing a remedy to act as long as improvement is perceptible is reasonable and practicable. However the duration of effect cannot be predicted; for the action of a remedy does not mean a steady and permanent effect of it, but a persisting of the vitality from the impulse given it by the remedy, for the restoration of health.

16. We consider palliatives as employed by the old school allowable when the dangerous effects of a disease must be instantly removed.

17. We oppose the views of Hahnemann that diseases can only be cured by the assistance of the art and not by the *vis medicatrix naturae*.

18. The writings of Hahnemann can no longer be considered as expressing the standpoint of homoeopathy today, either theoretically or practically; however great may be our veneration for his genius and for his discovery of the fundamental law of cure, we are not willing to subordinate our convictions to his authority or to humble ourselves for the derision and doubts of our opponents. Being convinced by the truth of the fundamental principle of homoeopathy, *similia similibus curantur*, we shall ardently endeavor to develop it, together with its genuine scientific elements: to use one remedy at a time; to enrich the knowledge of medicinal agents by provings on the healthy human organism; to give the system a rational basis; to add other practical rules which have been approved by experience and to test everything that has been added for the demonstration of certain theories which have no connection with the principles of homoeopathy.

These eighteen principles are largely those of Griesselich, Schrön and Wolf. Rummel, Hartmann, and Müller took perhaps a slightly more moderate position. Others predicted that the adoption of this platform (which was unanimously adopted) would mean the downfall of homoeopathy.

One notes that 4 of the 18 theses mention dose. These theses marked the activation of the dose controversy in homoeopathy which still slumbers beneath the surface.

Most of the literature of the 1835-1840 period deals with the controversy between the "young progressives" and the "old Hahnemannians." Another debate was started by the isopathic

question which unfortunately was lost and the world was compelled to wait for the vaccine and serum era of the present time. Naturally the guise under which many so-called isopathic agents was introduced was the responsible factor in its defeat. Isopathy was introduced by Lux, consciously assisted by Hering and made ridiculous by Hermann.

The influence of the Wolf theses led to re-proving of drugs under the specific school of Griesselich, Koch, Arnold, and the Vienna Society. This period witnesses the work of Jahr²⁵ which was widely translated and re-edited. Unfortunately Jahr was an old type Hahnemannian who attempted to resuscitate several of Hahnemann's dogmas which had been abandoned. The popularity of the work was to no small degree responsible for homoeopathic conservatism and not a little misinformation. The works of Boeninghausen²⁶ represented even a more rigid adherence to Hahnemann. Their unfortunate translation likewise tended to retard progress. Noack's extensive studies belong to this period.

From time to time controversy with school medicine occurred; for example, the prize essay contest by the University of Göttingen for the best essay of proving the "Nullity of Homoeopathy." The contest was won by Harnisch.²⁷ Until 1850 there was little progress; pamphlet literature is abundant and usually worthless. Buchner, professor of physiologic materia medica at Munich (this was an alias for homoeopathy) published some interesting studies.²⁸

The death of Griesselich, whose works are considered later, perhaps was responsible for the stasis in homoeopathic literature. Griesselich led the scientific element in homoeopathy up to 1850. He was followed by C. Müller and Hirschel and Meyer. Under the direction of the first a plea was made to include objective phenomena (characteristics of the urine, etc.) in the provings. Hirschel's²⁹ works are a testimony to great endeavor to make homoeopathy scientific.³⁰ Space forbids a review of the Richter-Bock controversy³¹ and the Wunderlich³² attack. The best literature of this period (1850-1860) is by Arnold,³³ Schneider³⁴ and Kafka.³⁵

Many physicians were attracted to the homoeopathic ranks through the school of Rademacher (1772-1849). He represented a modified Paracelsian viewpoint.³⁶ The three primordial diseases of the whole organism are curable by the three universal remedies: natrium nitricum, cuprum and ferrum. The primordial diseases of single organs are curable by organ remedies, that is, certain remedies for each organ as pulmonary remedies, kidney remedies, etc. The two types of diseases may co-exist and demand both types of remedies. Organs may be successively involved and require consecutive remedies. With the exception of a universal and an organ

remedy, drugs should always be given singly. Diseases were named after remedies; for example, morbus cardui mariani was an organ-symptom-complex demanding *Carduus Marianus*. His theory of epidemic remedies, genus *epidemicus*, was important to homoeopathy; in other words he showed that in an epidemic patients exhibiting different symptoms were cured by the same remedies.

Overlooking, for the purpose of brevity, Rapp, Fischer, Bruckner, and Schaedler, who formed the school of organotherapy, the chief adherent was von Grauvogl³⁷ who introduced the so-called constitutions into homoeopathy. These constitutions (hydrogenoid, oxygenoid, and carbo-nitrogenous) led to the choice of certain remedies in constitutional diseases. This thought forms a liaison between Hahnemann's triad (syphilis, sycosis, and psora) and Rademacher's three primordial diseases (ferrum, nitrium, and cuprum diseases). Baehr's studies³⁸ represent the last great work of the German school up to 1865, an arbitrary point selected to end the study of the development.

Homoeopathy owes to Germany the development of the scientific trend in homoeopathy, the best literature, the most careful re-provings and the best critical literature on the subject.

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THE RECEPTION OF HAHNEMANN'S WORK.—It may be of interest to note the immediate reception of Hahnemann's work. The attitude of Hufeland is considered separately.

Hecker¹ denied the value of the simile because Hahnemann recommended poisons in treatment and because he paid too much attention to symptoms. Another reviewer,² however, believed that sharpness of criticism toward Hahnemann had caused the suppression of original ideas to the detriment of science. Fischer³ approved drug provings and the adjustment of doses to the body. Sprengel⁴ believed that Hahnemann's method was essentially one of counter-irritation and that it confirmed older experiences in this field. The

use of one or two remedies was considered over-simplification;⁵ others stated that while it is clear and natural, one can go too far in this direction.⁶ Wichmann⁷ stated that if he took prescriptions less than a foot long to the apothecary, he would be regarded as an idiot. This is suggestive of the reception. Hahnemann's plan to thoroughly study remedies whereby a special relationship to the kind of disease present might be found, and, when symptoms similar to those of special cases (and with similar tissue involvement) were present, to treat by means of a single remedy rather than a remedy for each symptom plus correctives and modifiers for each of the ingredients, was largely misunderstood.

The same variance of opinion met the work on scarlet fever. One⁸ states he had good results; another without personal experience recommended that Hahnemann be pensioned to prevent further reports.⁹ Hufeland correctly stated that much of the result might be attributed to a special preparation which Hahnemann employed.¹⁰

The early collection of provings met with favorable criticism¹¹ but the *Medicine of Experience* received violent criticism.¹² Up to this time Hahnemann had not replied to his critics, but at this time he proceeded to do so.¹³

With the first edition of the *Organon* the split with the medical profession became more marked. Hecker's attack¹⁴ exposed some weaknesses of Hahnemann whereby the entire doctrine tended to be rejected; a few rational criticisms appeared,¹⁵ and Hecker's diatribe was so virulent that his colleagues took him to task.¹⁶ Schenk's note¹⁷ stated that Hahnemann's explanation for the small dose in scarlet fever was that no heat was employed in the preparation of the belladonna. Kranzfelder's unfavorable criticism¹⁸ had little weight and was disregarded by both groups. Hahnemann's publication on *veratrum* received generally favorable comments.¹⁹ Hahnemann's reply to Hecker was written under the name of Hahnemann's son.²⁰

By 1813 Hahnemann showed that homoeopathy had gained many followers²¹ and Clarus of the University of Leipzig advised the suppression of lectures by force.²² The death of Prince Schwarzenberg and the implication that it was caused by failure to bleed, although Hahnemann had relinquished the case weeks before,²³ resulted in Hahnemann's departure for Coethen.

By 1822 the first homoeopathic journal was founded²⁴ and Jorg published his attack on the *Organon* and made provings.²⁵ This year witnesses Groh's attack,²⁶ soon followed by the Meisener works.²⁷ The most important attacks are mentioned in the foot-
notes²⁸ since it is impossible to discuss them here.

Sufficient has been said to imply that the cleft widened in spite of Hufeland's endeavors to hold the two groups together. In recent years, especially the last quarter of a century, there has been an increasing tendency of the two schools of thought to re-unite. Unfortunately it has progressed only slowly, but the present indications suggest that this may be effected in the near future.

These notes are included merely to hint how heated the debate became as well as to suggest how the factors underlying the isolation of homoeopathy led to a complete misunderstanding. Reference to such topics as Homoeopathy, objections to, criticisms of, controversies over, in the Catalogue of the Surgeon General's Library which contains an extensive but very incomplete list, will emphasize the situation more clearly than a prolonged discussion.

The exclusion of homoeopathic literature from the general domain of medicine was followed by a more effective policy of silence, for example, about the Arndt-Schulz rule which is discussed elsewhere. In short the usual channels of inter-communication were closed: medicine was uninformed or erroneously instructed about events transpiring within the so-called homoeopathic school; on the other hand, homoeopathy, bereft of the powerful co-ordinating influence of the allied sciences, was compelled to travel alone and lost not only the sobering effect of calm, impersonal, factual criticism, but also decades during which its energies were exhausted in the establishment of institutions and legal battles. In order to avoid any possibility of a recrudescence of this lamentable chapter, no allusion has been made to the American situation at all and with rare exceptions no reference has been made to the era between 1870 and 1925.

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In Austria, outside of the work of Bischoff, there is the vulgar and hostile work of Grogmann (*Animadversiones in Homöopathen, Ueber das Heilungs-princip der Homöopathie*); see also the antagonistic report of Schinko: *Das Hahnemannsche System*, etc.

HUFELAND AND HOMOEOPATHY.—Medical history is agreed that Hufeland was the greatest figure in German Medicine during Hahnemann's time. It is advisable to determine his position, not only because he gave suggestions which influenced German medicine, in fact, all medicine in the time that was to come, but also to make even clearer how acute thinkers misunderstood Hahnemann's ideas.

Strauss¹ in his speech on Hufeland as a physician states:

"Moreover it may be counted as an honor to him that he appeared against the extension of homoeopathy with the power of his authoritative position." This seems a peculiar statement, when Hahnemann's papers, some thirteen in number, appeared in Hufeland's *Journal*. In the same symposium v. Hansemann spoke. Elsewhere he had written:² "It is pitiful that one possesses no means of controlling doctors who become homoeopaths or other charlatans in order to gain approbation." In the symposium v. Hansemann urged "freedom of science" but neglected to state that his quotation and topic was taken from Hufeland's papers on homoeopathy. Only a few remarks from Hufeland's contributions can be introduced here.

"The great experiment which humanity has attempted on itself for thousands of years—called medicine—is not as yet finished, and indeed like all earthly things will never be brought to perfection." "There are undeniable variations in constitutions of disease and its character, so that at one time one, at another time another healing method is more suitable."

"The subject (homoeopathy) is all the more important when the originator is a man to whom we cannot deny our respect. And that is the case with Hahnemann, for no one will deny, at least those who did not become acquainted with him yesterday, for the author of this publication has been united with him through friendly and literary relations for more than thirty years and has valued him each time as one of our most distinctive, enlightened and original physicians. It is only necessary to recall that medicine owes to him the discovery of the wine test and soluble mercury, according to

my opinion the most active preparation of mercury, the prophylactic against scarlet fever and many other thoughts. . . .”

“Unbiased factual representation and factual proving is our aim.” “It has stood firmly in medicine until now that the single true and basic cure of a disease was a causal cure, that is, one founded which was based on the discovery and removal of the cause.” “How many patients have already come to grief through the mere (treatment of the) name of a disease, pleuritis, phrenitis?” “But it is not always possible to employ this type of cure. . . .” “Cases are of three types: either the remote causes cannot be found or they cannot be removed or the action of the proximate cause on the organism has become enrooted for so long a time that they have become independent and continue even after the removal of the remote cause.” “In all these cases there is nothing left for the physician than to direct the cure against the proximate cause (the disease itself). “If the fever continues after the removal of the remote cause, so we direct our cure against the fever itself and give specifics as china and other agents.” “This differentiates itself from homoeopathy in not excluding causal cure, in not stressing the single and general in its general principles, in its compatibility with derivation and stimulation. Often new diseases cure old ones.” “It should be clear from this that homoeopathy is in no way new: Only making it general and the elevation to the sole and basic principle of medicine is new.” “It will also remain always very meritorious and must be considered as a progress in medicine that through homoeopathy this part of the specific cure works accurately and will bring firmer principles.” “Only against the elevation of the same to a sole and general principle do we protest and ask that it always be subordinated to the causal indication.” “Now follows the choice of the remedy . . . so in the middle of the last century narcotics were used . . . against insanity because one saw insanity produced in healthy people through them. . . . The healing effect of an agent in a similar disease, in a similar system of the organism, gives us the right to employ it in a similar disease, in a similarly diseased system. . . . Consequently the principle of homoeopathy is not new. . . .” “It is certainly very well taught that effects of drugs are to be determined in the healthy state.” “The increase of activity through increased points of contact, through solution in fluids, or through long continued trituration, above all is worth observing.”

According to Hufeland the advantages of homoeopathy are:

1. It will require study of semeiotics and symptomatology.
2. It will persuade physicians that the healing agent should not be worse than the disease.

3. It should lead back to simplicity in prescribing.
4. It should and has led to more exact provings of drugs.
5. It will give dietetics its right place.
6. It will induce more careful preparation of drugs.
7. It will never do positive damage.
8. It will give the organism more time for rest and undisturbed self help.
9. The cost of cure is extraordinarily decreased.

According to Hufeland the disadvantages are:

1. It can easily lead to a pure symptomatic type of cure and suppress the causal medical treatment.
2. If prevailing, it would have a disastrous effect on the basic sciences.
3. It could bring about a dangerous neglect.
4. It would interfere with apothecaries.
5. It robs the physician of dependence on the healing power of nature.

But as Hufeland adds: "Time will tell."

In Hufeland's foreword to Rummel's article (Rummel was a homoeopathic physician) he states: "it pleases me very much that the meritorious writer is absolutely in agreement with me in the basic idea represented by him, namely that the homoeopathic method is nothing else than a supplement and a complement to our existing specific method against disease itself. . . ."

It is interesting that Hufeland as well as the homoeopathic profession did not accept Hahnemann's implication of an exclusive method. Likewise Hufeland, differing from many moderns, saw the value of provings on the healthy. Moreover, Hufeland recognizes that an agent whose proving on the healthy shows it is specifically effective at the site which is affected by the disease, brings about an alteration which here permits the removal of the existing abnormality. Also he regarded the principles of homoeopathic pharmacy as praiseworthy.

In his second paper (1830) he states: "The first thing that determined me to write was that I found it incorrect and unworthy of science to treat the new doctrine with ridicule and persecution. . . . Most repulsive to me in science is suppression and despotism; here should rule only freedom of spirit, fundamental provings, basic refutation, opposing observation, restrictions to facts and not to personality."

"Prove all and hold fast to the good is and remains the first commandment of science. . . . Medicine is a science of experience, practice a continuous experiment . . . and the experiment is not concluded."

“Freedom of thinking, freedom of science, that is our highest palladium and it must so remain if we are to progress. No type of despotism, no sole ruling, no suppression of thought. Even the government should not be permitted to invade into scientific subjects, nor depress, or favor an opinion exclusively; both have, as experience teaches, done damage to the truth. Only proving through experience, discussion and counter-discussion, continuous free study, and time can and will surely in the end separate truth from falsity, the useful from the useless.”

“There are several ways to reach an end, especially in medicine.”

“Nothing is so detrimental to medicine in general as a public scandal, a public common degradation of one artist by another.” “Personal insult, biting contempt, never further truth but only brings out emotional excitement and bitterness in place of determination of the facts, and it becomes a personal fight.” “O, that I may comprehend, more and more how much we do not know, indeed I find in this the principal development of my knowledge; to recognize what I do not know.”

“Homoeopathy is to be positively denied as a general principle of all therapy. Indeed if it was taken as such in its first crude form it would be the grave of all science and mankind. . . .” “But homoeopathy is worthy of observation and is not to be repudiated but used as a special healing method and subordinated to the higher principle of rational medicine.” “. . . I am convinced by my own observations, that not seldom, and at times highly strikingly, after the use of other powerful healing methods have been in vain, it performs service.”

He goes on to state that the principle is not new,⁴ the determination of the diagnosis not new,⁵ the principle of finding the remedy not new.

“But it must also be remarked here that the idea of the psora as the soil of chronic disease is in no way a discovery of homoeopathy . . . but has been long known as such in medicine.” “One advantage on which homoeopathy can pride itself is that it does no positive damage, it never attacks the body excessively or destructively. Only sins of omission can be laid upon it, but none of commission.” “What one cannot accomplish with little, he cannot accomplish with much.”

He continues that homoeopathy does not take cognizance of natural healing power, that it is one-sided.

His conclusion is: “No homoeopathy, but indeed a homoeopathic method in rational medicine. No homoeopaths but indeed rather physicians who employ the homoeopathic method at the right time

and place." "The special and most beautiful task of homoeopathy remains: to find and seek for new specific agents."

Hufeland gradually worked his way to clarity on homoeopathy and natural healing and stated in his greatest work:⁶ "Even Hahnemann's homoeopathy, in spite of all apparent disregard for the natural healing power of nature, actually contributed to the support of physiatry, because does not his entire principle and effect rest upon the stimulation of the living power, in the alteration of the abnormal condition into the normal by specifics, that is, by such agents as have a characteristic relation to the sick organ or morbid condition? Also is it not often that a natural healing is effected merely through time and a strict diet? Actually therein stands the essential merit of homoeopathy which evokes the vital power directly in the suffering organ to activity and assistance and seeks and employs agents which most nearly transform these organs and these conditions."

With the death of Hufeland, the Nestor of German medicine, medical literature was closed to homoeopathy. It was opened again in 1925 in Germany.

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THE NATURAL SCIENTIFIC MOVEMENT IN HOMOEOPATHY IN GERMANY.—In an early part of this study the difference between two types of homoeopathic physicians was emphasized and the supporters of the homoeopathic doctrine were placed into two groups. At this time it seems advisable to trace briefly the natural scientific movement. Spatial requirements compel a restriction of the remarks to a few personalities of different generations, whose views may be regarded as generally representative.

According to Moritz Müller,¹ the originator of the natural scientific movement, the history of homoeopathy up to 1836 can be divided into three periods. The first (1790-1821) was characterized by the clear recognition and formulation of the simile principle, the recognition of the necessity for a transformation of the *materia medica* through provings on the healthy, the doctrine of the pri-

mary and secondary action of drugs out of which arose the questions of posology and permitted an explanation of the entire process on the basis of support of the natural healing power.² The *Medicine of Experience* (1805) and the *Organon* (1810) added little that was new. The *Materia Medica Pura* had had its precursor in the *Fragmenta*.³ By 1812 Hahnemann had secured the right to teach through his thesis on "Helleborus."⁴ Now students were available to perform provings which permitted the materia medica to be elaborated. Incidentally Hartmann, one of the students, stated that Hahnemann was not a particularly good teacher.

The Leipzig period closed in 1821. This period corresponds to the first era in any innovation: foreshadowing of the principle by observation and its elaboration by a personality and the gathering of followers.

The second period (1821-1832) is concerned with an attack upon the justification of the principle. Müller's acquaintance with homoeopathy was through Gross and resulted in the treatment of a severe illness in his own family.⁵ This success was followed by attempts in practice, using single patients as trials. By 1820 he concluded: "The incurable remain incurable but curative effects frequently appearing convinced me that it contained more truth than my scepticism had anticipated, so that I was willing to approach the *Organon*."⁶ Müller did not make Hahnemann's acquaintance, a point of great significance in his development:

"I continued to practice homoeopathically, where it seemed suitable and applicable and approached more and more Hahnemann's dilution of drugs. I have not made the acquaintance of Hahnemann or his students."⁷

"From the start I took no regard of him (Hahnemann); by not being bound to him through personal acquaintance, I constantly maintained myself free from his literary despotism; I realized this position. The first task for me was the defense of homoeopathy against the general assault of its opponents."⁸ This was accomplished by becoming the silent editor of Stapf's *Archives*. In the opening article of this publication Müller wrote:

"One should avoid, what unfortunately has not been avoided, partisanship in the investigation of a debatable question which concerns one of the most important subjects for mankind."⁹ "The determination of truth is concerned with a fact and not with a personality."¹⁰ In this work are two suggestive statements.

"The homoeopathic system is based on two principles of which the first is undebatable and will retain its value if the second is not empirically asserted in the universality which Hahnemann ascribes to it. From both principles the entire system has developed pri-

marily by the way of experience, and anyone must, as Hahnemann shows, follow the same way. . . ."

"The first principle is: one must discover the action of medicinal substances before they can use them for healing of patients or in other words: one must know the relationship of the healthy to each substance, before he can discover the relationship of the patient to it."

"The second principle is: drugs heal morbid conditions when they are capable of provoking as completely as possible a similar state in the healthy or to use the terse expression of Hahnemann: they heal homoeopathically."¹¹

In regard to the first he implied that it was an error to attribute one general action to a drug, "antiarthritic," for example until such actions had been demonstrated experimentally,¹² and in pathologic-anatomical and pathologic-chemical directions. In regard to the second he considered the rejection of allopathy unjustified and urged one to proceed into homoeopathy only step by step, whereby one would appreciate the curative merit of both procedures.¹³ He held that at that time homoeopathy was a "subsidiary" method in medicine, but for the present it was entitled to a place where ordinary medicine failed and that a time might come when allo- and anti-pathic medicine might become the subsidiary methods.¹⁴

In 1821 Müller¹⁵ wrote a brief note on belladonna and its use in scarlet fever. This note has importance since the Leipzig physicians had planned to repudiate Hahnemann's therapy in an open letter to the press. Müller, who was very highly regarded by the profession, refused to sign the circular and advised that it be withheld until an exact proving of homoeopathy had been made, for he was convinced of its possible value, and that a test would show whether it was true or false.¹⁶ Nevertheless the circular appeared although many physicians refused to sign. Thus at a time most crucial to homoeopathy and Hahnemann, Müller appeared on the scene. Apparently Hahnemann did not welcome Müller's support.¹⁷ For those interested in details, König's account is the best.¹⁸

It is not without importance that Müller's denial of the universality of the simile principle in 1822 furnishes the background for Hahnemann's subsequent open break with him. Müller had said:

"Homoeopathy will ultimately be promoted, not simply through unrestricted extension of homoeopathic practice but also through determination of the undoubted and doubtful, through determination of the limits and exceptions from the rule, through its limitation to a place where it is preferable to any other method of healing."¹⁹ At the close of Müller's first publication in the Archives,

Stapf²⁰ adds that in the magazine a place should be given to an article which attempted to amalgamate the therapeutic trends. Hahnemann remained silent.

Perhaps nothing is more incomprehensible in homoeopathic history than Hahnemann's bitterness to a man who defended him at the time of the Leipzig trouble. The records suggest that Hahnemann was a poor teacher and that most students rallied around Müller. It is worthy of note that Müller was able to defend homoeopathy best because of his critical attitude.

In reply to the Jörg attack²¹ he said that he employed both allopathy and homoeopathy daily in his practice and that he was convinced that medicine had not as yet reached that height where one could say which of the two methods would heal more surely; further he is positively against the utter refusal or acceptance of any medical system.²² The replies made to other attacks may be found in the Archives.²³ Space forbids their examination here.

In 1832 Müller became president of the Leipzig Verein, in fact, the first president. In September he received a letter of warmest thanks for his services from Hahnemann. Two months later Hahnemann bitterly attacked him as a "half homoeopath."

The entire Leipzig Society with a single exception immediately went on record against Hahnemann²⁴ and in response to a letter of Kretschmer,²⁵ Hahnemann increased the feeling by the tone of his answer.²⁶ Müller refused to take a personal attitude: "the fight is concerned with the limits of homoeopathy at the bedside."²⁷ To this he added: "homoeopathy is not applicable where the power in the body cannot bring about the counter action, secondary effect, the healing action of the remedy."²⁸

Thus one unconsciously enters the third period, namely, the determination of the limits of the procedure.

The division in homoeopathic circles steadily increased with Griesselich and Schrön as leaders of the scientific group. The result was the Wolf Theses to which allusion has been made. To trace the evolution in detail would require a volume in itself, so that allusion will be made only to the broadest trend of the development, with sufficient citation so that the interested may find their way through the enormous literature available.

Incidentally this occasion may be grasped to offer a suggestion for a way of approach to homoeopathic literature. A good background can be secured rapidly in the following manner. To appreciate Hahnemann one should read Haehl,²⁹ then approach the homoeopathic problem through the studies of Bier³⁰ and Tischner,³¹ then the writings of Hugo Schulz.³² With this introduction one may turn to Hahnemann's writings, especially the essay on a new

principle,³³ the medicine of experience³⁴ and any early edition of the Organon, such as the 4th,³⁵ then return to the early work on drugs³⁶ and finally to the *materia medica pura*.³⁷ After this one can approach the lesser writings in Hufeland's Journal,³⁸ and the publications by Hufeland³⁹ to which allusion has been made.

The work of Griesselich⁴⁰ is considered in the following section and some aspects of Schrön's labors⁴¹ are mentioned later. Rau⁴² and Reil,⁴³ the latter anticipating organotropy in the sense of Hugo Schulz and Theodor Bakody, may be considered at this time. The studies of Krutz, Watzke, Zlaterovich and Rapp are worth reading.

In the middle era there are many. The Swedish situation has been summarized by Sjörgen;⁴⁴ in Italy the writings of the older Mattioli and Cigiliano, Sr.; in Bohemia Altschul⁴⁵ and the polarity law which anticipated the Arndt-Schulz rule; in France P. Jousset,⁴⁶ Imbert-Goubeyre, Leon-Simon, Cartier, Charette; in Holland, Roijen; in England, Dudgeon and Hughes; in America, T. F. Allen, the Wesselhoefts, Dake, Hale, the younger Hinsdale, and, at present, MacGavaek.

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GRIESELICH, BAKODY, AND WAPLER.—In order to delineate briefly the further development of homoeopathy in scientific directions, three representatives have been selected, each living in different but partially overlapping periods. Reference is made to others who might have been selected in subsequent sections.

The life of Griesselich has been published by König¹ and need

not be reviewed here. His early medical career was contemporaneous with the elaboration of numerous medical systems, the humoral versus the cellular versus the natural philosophic, to which might be added the German excitation theory of Roschlaub, the stimolo and contrastimolo theory of Raseri, the French physiologic medicine of Broussais. He found little satisfaction in the prevailing systems² and equal discouragement in the state of the materia medica.³ In short, he began medicine as a sceptic but believed that diet and natural healing perhaps accomplished more than other therapeutic measures.⁴ Dissatisfied with medicine he turned to botany.

His acquaintance with homoeopathy began in 1828 when he read Wedekind's work and other polemic studies. Fortunately these came at a time when: "I had rejected nearly everything, the good with the bad, and stood with empty hands, poorer than a beggar with a crust." These polemic articles occasioned his reading the *Organon* in which he found "much truth," but it contained too much "millions and billions." However to satisfy himself completely he read Hahnemann's *Materia Medica Pura*. His critical mind could not accept much of the contents and for a time the entire subject was abandoned. Later a happy clinical experience which he had anticipated would be negative, led him to subject the theory to investigation. His description of the 77-year-old patriarchal Hahnemann is still worth reading.⁵ Even his violent disagreement with Hahnemann never induced him to resort to personal attack.

During travels he met most of Hahnemann's early students, for example, Attomyr with whom he differed entirely and the moody Gross who also became an opponent. Finally at Leipzig he became acquainted with the "opposition" party to Hahnemann. He found accord with Müller who had disagreed on the smallness of dose and who had had success in acute diseases with the tinctures. In further travels he met Rummel and Wolf in Germany, Marenzeller in Austria and the early Austrian scientific group, Watzke, Zlatarovich, etc. By 1833 he had concluded that "according to its basic principle homoeopathy contains in it an essential condition for the perfection and ennoblement of medicine."⁶ A group was formed containing perhaps the largest number of significant minds ever assembled in homoeopathy (Rau, Schrön, Arnold, Roth, Kirschleger, etc.).

By 1836 he was editor of "Hygea" and employing his position to reply to the polemics of Härlin, Sachs, Stieglitz, Eisenmann, and others. Some of his publications are mentioned in the bibliography,

but his great works are found in his magazine. He died in army service.

Griesselich's writings can be comprehended only if one remembers that he never offered a medical system; that homoeopathy is not a system, but only a part of a totality called medicine.

Further he differentiates accurately some Hahnemannian conceptions as simile rule and physiologic drug provings, from the potency doctrine, dynamization theory, psora conception, and explanation of the simile. In short he closely approximates the position of Müller;⁷ both joined in an attempt to incorporate homoeopathy into general medicine, a position that Hahnemann had taken in his first writing. The attitude of Hahnemann toward the group is now generally known⁸ and the position of Bönninghausen is to be still more depreciated.⁹

The attitude of the group has been partly summarized in the Wolf theses and can be stated in the words of Schrön: "Only a few essential principles, but these are incontestably true and of incalculable value to practice."¹⁰ Though radically disagreeing with Hahnemann they held him in high esteem.¹¹

The Griesselich school, if one may employ the term, is a school of "specific drugs." Hahnemann called the homoeopathic method the "specific" method until 1808 when the word homoeopathy was introduced. The Griesselich conception of specificity resulted in many changes and the reintroduction of the word specific as applied to homoeopathy, and in time to come "specific" is a term of reproach by the philosophic group for the natural scientific organization.

They agreed with Hahnemann's conception in regard to specific drugs, that is, a drug which showed a very decided curative effect in a concrete instance of disease. They felt that Hahnemann's method of proving was the answer to Sydenham's wish: "optandum est, ut beneficio specificorum, si quae talis inveniri possint, aeger rectiori semita ad sanitatem proficeret."¹² Schrön states that Sydenham would have welcomed Hahnemann's method;¹³ and even Stapf added that the "specifics" known until now act according to the law of homoeopathy.¹⁴

However Rummel was the first to define clearly the meaning of specific in the sense of the group: "we have discovered only individual drugs which affect definite organs and functions of the body before involving others and these are usually called specifics."¹⁵ Therein two types of specifics are described. Griesselich is clear that *cinchona* in intermittent fever, sulphur in itch and mercury in syphilis are "specific" for uncomplicated cases, sufficiently so that a diagnosis can often be made with the remedy. But the essential

addition of the Griesselich school is not only generally specific drugs but drugs which are individually specific or specific for the concrete case. (Arnold uses the word idiopathic to cover this meaning.) Perhaps the entire subject can be summed up in one of Griesselich's minor writings which contained 58 statements.¹⁶ The number preceding each paragraph refers to the original number of the statement:

1. Medicine requires a critical survey of its fundamental principles. Academic science predominates far over medicine and therapy stands back the farthest.

9. Hahnemann has the undeniable honor of actually having stimulated a transformation of medicine and above all to have essentially contributed to it.

10. This transformation so far as it proceeds from Hahnemann is contained in the doctrine of homoeopathy and is based on a few fundamental principles, unassailable by theory or practice.

11. Hahnemann's medicine (Hahnemannism) and homoeopathy have become different directions in the last few years and must be sharply separated from each other.

12. Hahnemann's medicine is an aggregate of truth and untruth and can no longer be adopted in its totality by any scientific physician.

14. Homoeopathy stripped from Hahnemannism, has not progressed so far that those who embrace it, always and in every case can dispense with other therapeutic procedures, even if it surpasses by far those other methods in a great majority of cases.

15. Homoeopathy is that method which utilizes specific drugs for the removal of disease.

16. Specific drugs do not oppose specific diseases in the sense of the old school. Each case of disease is to be conceived as individual and to be treated with curative agents which stand in specific connection to the concretely existing pathologic form of the diseased organ.

17. The word "specific" likewise designates the reciprocal relation between the drug and that case of disease.

18. The principle *similia similibus curantur* expresses the reciprocal relation between disease and drug. The explanation which Hahnemann gives is entirely arbitrary and gives a false idea of the healing process.

(The group (Schrön, Rau, Widenmann, Dietz) thereby separate the signs of damage in the cause of the disease or the action of the drug, from the signs due to the reaction of the organism. The characteristic pathologic symptoms and the reactive symptoms then take the place of Hahnemann's primary and secondary actions.

The reaction symptoms in the disease picture are the expressions of natural healing and the reactive symptoms in a drug action are the expression of self restitution of normality by the organism. The drugs release the defense mechanisms of the organisms when their primary actions correspond to the pathologic symptoms of the disease, and thereby exert their healing action on the disease.)

21. There are various ways to heal.

26. All methods have as their basis the idea of a power innate in nature which is active in health as well as in disease itself.

27. In health this power is usually called the vital principle, in disease the natural healing power. The one cannot be admitted nor denied without the other. Every physician must have both in mind.

33. In the field of physiology falls the investigation of the connection of curative drugs to definite diseases of definite organs.

34. As physiology must go before pathology, and the latter be based on the first, the proving of curative materials on the healthy before the sick.

36. The entire Hahnemannian drug proving requires a new careful re-proving arranged according to very definite principles.

37. Every drug yields to us by virtue of its essential and chief symptoms, a picture of its total action in which the medicinal disease unfolds itself with most exquisite manifestations according to course and sequence, in- and extensity. The materia medica will thereby gain with its diagnosis as pathology.

(Griesselich demands here a re-proving with consideration of the organic alterations in the sense of modern pathology, so that the drug and disease will resemble each other in "type, place and character" to employ the famous remark of the Wolf Theses. This is naturally a brief for the inclusion of toxicology and animal research. It inaugurates a "pathology" of drug diseases to parallel the pathology of natural diseases.)

40. If research will pursue this direction then we shall more closely approach the nature of diseases and of drugs, since in this way diseases and drugs will undoubtedly assist in interpreting each other.

41. That the curative agent be adapted for the presenting case is the chief requirement of the specific connection. But in order to impress correctly the existing grade of vital activity in the sick organism as well as the sick organ, the second chief requirement is the choice of suitable dose of drug. Correct drug and correct dose must go hand in hand in order to influence the reaction of the organism curatively.

44. What Hahnemann states on the sole use of only the smallest doses, is also as arbitrary as it is dangerous for practice. The

method of prescribing drugs only in the 30th dilution is utmost exaggeration.

46. The theory of chronic diseases and its three basic causes (psora, syphilis, sycosis) is not to be saved and it is also not worth saving.

(In his "Handbuch" Griesselich adds: "The truth in the psora theory lies in the undeniable actuality of the so-called 'Safftkrankheiten' and the reciprocal relation between the skin and internal organs.")¹⁷

48. The entire theory of potentization of drugs is contradictory in itself and not advocated, entirely apart from the fact that Hahnemann's arbitrariness has harmed and continues to harm a good thought.

50. Pathology in its inner connections is too much neglected by homoeopathic physicians and the assertion of many that the totality of the symptoms is the sole indication is not justified in that this makes all progress in knowledge dispensable.

To proceed further with Griesselich's views would carry the discussion beyond available limits. A complete bibliography of his works may be found in König's study. To be complete it would also require the elucidation of the inter-relationships of three life-long friends: Arnold, the strict scientific investigator, Schrön, the profound theorist and experienced practitioner, and Griesselich, the promoter of these trends.

Less need be said here of Bakody although he is only second to Griesselich in importance. He reintroduced the conception of "causal specificity" into medicine, thereby leading to the conception of "organotropy" in Ehrlich's meaning and the specific organotherapy of Hugo Schulz.

Space prevents consideration of his journalistic, hospital and other activities. He was the teacher of most of the European scientific homoeopathic physicians, as Wapler, Stiegele, in Germany, Oberholzer in Switzerland, Nynens in Belgium, and Roijen in Holland.

Typical expressions from his writings are:

"According to the combined inductive empiric method of Hahnemann that curative agent (in relatively small doses) is brought into use in corresponding phases of internal disease processes, when it contacts specifically (directly locally) the same tissues in the sick organism, which it is able to experimentally induce (in relatively larger doses) in the healthy organism as a medicinal substance, that is, induce similar pathologic-physiologic and histologic alterations."¹⁸

He based the method of Hahnemann on the four following principles:

1. "The experimental proving with single medicinal substances on the healthy animal and human organism; and indeed in graded doses with consideration for all, even the most minute functional, pathologic-physiologic, pathologic-histologic, chemical and toxic alterations.

2. "The complete exact genetic (correct temporal developmental order) comparison of these alterations with similar ones which develop from a hypothetical cause of disease in natural illnesses.

3. "The employment of only single remedies for therapeutic aims and moreover by the simile law derived out of experiment on the healthy organism in the sense of causal specific tissue action conforming to the various genetic phases of the corresponding tissue disease.

4. "The use of the causal specific curative agents in form and amount corresponding to the therapeutic aim, which excludes every pathognomic accessory action on the healthy organism." (Pathognomic then meant "morbific or disease making" action, and not "characteristic" or differentially "diagnostic" as today.)

Bakody recognized dilution only as high as the sixth decimal; demanded experimental materia medica to be built on a "cellular" basis; considered that the homoeopathic physician was one who employed the homoeopathic method at the right time and place; that Hahnemann's therapy was not a universal therapy.

It is necessary to say even less of Wapler since he belongs to the present era. His mental orientation is perhaps clearly shown in his first work: A study of inducing immunity in animals against tetanus by strychnine.¹⁹

Apparently Wapler's interest in the experimental method in homoeopathy was aroused by Bakody's work on tuberculin.²⁰ In rapid review are: his remarks on how homoeopathy can be brought to general attention,²¹ on what one understands by the method now designated as homoeopathic,²² his resurrection of the Wolf Theses and the Four Fundamentals of Bakody as well as drawing attention to the homoeopathic aspects of the work of Arndt,²³ Schulz,²⁴ Hueppe.²⁵ In response to Prof. Schwartz²⁶ there was his excellent paper on the basis of modern scientific homoeopathy²⁷ in which he illustrates many examples of homoeopathy in school medicine (homoeopathia involuntaria). Likewise worthy of re-reading are his recollections of Theodor Bakody.²⁸ The already cited article based on Lux's isopathy²⁹ led to his major work on isopathy;³⁰ his polemic literature is always excellent in its constructiveness. Passing over other contributions one reads his reply to v. Hansemann's

assertion of homoeopathy as "filth pharmacy" survival³¹ in a sharp open letter.³² In his reply to Harnack³³ and Kobert³⁴ Wapler reports incidentally 60 examples of involuntary homoeopathy of these pharmacologists.³⁵ Well worthy of perusal is his reply to Strumpell's negative attitude on homoeopathy.³⁶

If these are suggestive of this worker's relation to school medicine it should not be forgotten that his criticism of the homoeopathic profession has been just as acute. His writings against irido-diagnosis³⁷ which some homoeopathic physicians have employed, his remarks on the electro-homoeopathy of Matthai which has nothing to do with homoeopathy³⁸ although Heubner would like to include it, his criticism of manufacturing homoeopathic pharmacies for "combination" tablets,³⁹ indicate the directions of his position. Nor have his studies been solely literary research although in this capacity they have been invaluable. For example his suggestion of drug proving in colleges finds fruit in Heinz' work on *drosera*.⁴⁰ Again the studies of Hufeland,⁴¹ his history of the simile principle,⁴² the simile principle as an heuristic principle⁴³ directly anticipate⁴⁴ Bier's work, and seem to bear fruit in Bier's early studies.⁴⁵ His "Homoeopathy and School Medicine" in 1925 expresses his attitude of the ultimate incorporation of homoeopathy into unified medicine.⁴⁶ Incidentally this work calls attention to the use of homoeopathy in dermatology by Spiethoff,⁴⁷ in dentistry⁴⁸ particularly by Rebel.⁴⁹ This work with that of Diepgen⁵⁰ and Friedlander⁵¹ may ultimately result in a scientific commission for the study of homoeopathy. The attitude toward the "pure" homoeopath is admirably expressed in his writing of 1930.⁵² His last great work on the incorporation of homoeopathy into a unified medicine⁵³ has been made available by the writer.⁵⁴

In a very sketchy fashion which does not do justice to either the topic or individuals concerned, a few characters have been selected to illustrate the scientific movement in homoeopathy. These endeavors have quite escaped the notice of medicine by virtue of the mutually disastrous policy of exclusion. However perhaps enough has been said to indicate that a scientific movement has been evident from the beginning of homoeopathy, and perhaps sufficient references have been given to build a path through the literature. In this connection the study of Bartels on the evolution of the natural scientific movement in homoeopathy is worthy of study.⁵⁵

With this one may turn back to the development of homoeopathy after Hahnemann in order to appreciate better the evolution of the various aspects. Most attention will be directed toward the natural scientific group.

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THEORIES OF HOMOEOPATHIC HEALING AND SPECIFICITY.—Realization of the advisability of offering some explanation for homoeopathic healing created considerable literature on the subject, without essentially advancing the solution. Since most attempts were fruitless, a detailed discussion of the individual papers seems unnecessary, although this opportunity may be taken to indicate the more important literature, the various attitudes taken, the general viewpoint gained.

Müller¹ was the first to define the issues clearly. Kretschmer,² Rau,³ Eschenmayer,⁴ Jahn,⁵ Werber,⁶ approached the subject from the standpoint of pathology, Purkinje⁷ from physiology. Among the Hahnemannian type of physicians Attonyr⁸ invoked the dubious aid of natural philosophy, Hering⁹ followed Oken and Hofmann

idealistic pathology. Some attempts were made to utilize social theories,¹⁰ but more sober observers like Rau and Schrön¹¹ had recourse to a natural healing power.

G. Schmid,¹² Watzke,¹³ Martin,¹⁴ Baekhausen,¹⁵ Fielitz,¹⁶ Koch,¹⁷ Mosthaff,¹⁸ Dietz,¹⁹ Kurtz,²⁰ Widenmann²¹ developed the theories, occasionally adding new viewpoints. Schmid, reasoning by analogy in the external world, evolved a theory of polarity, which found support in Altschul's doctrine of polarity²² and independent experimental support in the Arndt-Schulz rule. Mosthaff offered a viewpoint which deserves serious thought: while a remedy may produce symptoms in the healthy resembling those presented by the patient, when drugs are given homoeopathically, they act in the direction of re-establishing the norm, that is, as a contrarium. Müller²³ held the same opinion, arguing that while opposites tended to cancel each other in the physical world, they did not in the living; hence so far as the effect on the body is concerned, it is one of opposites, rather than similars. Thus among the older writers they were the first to differentiate the simile as a finding principle and as an effect principle. Koch attempted to show that the simile holds in physiology as well as pathology. He presented an interesting, even if not entirely new view: the factor tending to precipitate disease unites with the disposition to disease. In other words disease is a combination of an etiologic agent and "anlage" in sense of susceptibility. This combination releases two series of phenomena: one progressive in nature, the disease proper, and the other an attempt to resist it on the part of nature. The drug now produces an artificial disease which removes the susceptibility. In one sense he returns to Hahnemann's idea of cure, namely, a substitution of the real disease by an artificial one; in another sense he "desensitizes" the patient. Widenmann's position is between Koch and Hahnemann. Gerstel²⁴ considered homoeopathy effective through a derivatory process, in that the remedy produced disease of the healthy parts whereby the site originally involved became well. Liedbeck's²⁵ account is interesting because he perceived that "mechanical" stimuli as well as drug stimuli could be viewed from the simile position. Schneider²⁶ explained the simile as a derivation action; Trinks²⁷ followed Hahnemann's view. Other accounts worthy of perusal are those of Winter,²⁸ Lietzau,²⁹ Mayrhofer,³⁰ Arnold,³¹ Becker,³² Bicking,³³ and among the non-homoeopathic group, the previously mentioned Jahn, Neumann,³⁴ Kronser.³⁵ Griesselich³⁶ held that the drug, acting as an analogous stimulus in the involved tissues, evoked reactions tending to restore (normal) equilibrium. The possibilities of this type of thinking were illustrated by Miguel's attempt to vaccinate against scarlet fever,³⁷

Albers attempt in measles³⁸ and Tourtual's prophylaxis of measles with sulphur.³⁹ Trousseau and Pidoux⁴⁰ regarded the homoeopathic method as "substitutive" therapy by proceeding from the Broussais' view that almost all diseases are inflammatory. Dudgeon⁴¹ as a representative of the English school suggested the phenomena of disease should be regarded as manifestations of depression rather than stimulation: for example, inflammation represents a paralysis or paresis of the capillaries (among other lesions). A remedy which would produce paralysis of the capillaries in large doses, would cause stimulation (constriction) in small doses, that is, in its first phase—to employ an anachronism. In this way the remedy acts partly as irritant therapy. Hirschel⁴² concurred in the theory or stimulating the reaction of the organism.

If one attempts to summarize the trend the following suggestions emerge. The simile is regarded by many as a finding principle in a broader sense than Hufeland employed the word. When effect is considered, the opposite to what would have been produced in health may be obtained in disease. The reversed action is explained partly by the relatively small doses in disease, the doses in therapy actually being quite small since hypersusceptibility to "stimulation" was encountered in disease. Although a variety of phraseology is employed, most writers had recourse to a natural healing power from whence the reaction proceeds, although some have the remedy render the tissue less "susceptible."

In regard to specificity the following summarizes the situation. Ancient medicine called a disease specific when it possessed a very definite immutable character although it might appear in various guises. For example, syphilis was a specific disease although the particular form and symptoms might vary from case to case. From this general viewpoint they reasoned to "specific" remedies. Differences in opinion prevailed as to how these so-called specifics acted. Sydenham held that a remedy was a specific when it cured without causing an evacuation, as cinchona in malaria. Mercury was not specific in syphilis since it caused salivation. Hahnemann's viewpoint has been presented above. Stieglitz⁴² held a dual conception of specifics: they heal a disease in all its stages without our knowing why; they likewise act on an organ without our knowing how. Kopp⁴³ defines specific: "a drug which excites alterations preferably in one organ in healthy and morbid states, acts specifically on it." In these conceptions one will perceive two ancient types of specificity: specifics morborum and organorum. Since homoeopathy did not recognize species, families and types of disease, Sachs⁴⁴ denied the applicability of these conceptions in homoeopathy, but his dismissal of the simile is unjustified.⁴⁵ Hufe-

land⁴⁶ believed the task of homoeopathy consisted in the discovery of specifics for individual forms of disease, thereby either misunderstanding Hahnemann or comprehending the doctrine very well. Stapf⁴⁷ employed the word in the Hahnemannian sense, a remedy in a given instance of disease, and believed that ancient specifics acted by virtue of the simile in "pure" forms of disease. Arnold at first condemned the use of specific in connection with homoeopathy⁴⁸ but subsequently changed his position.⁴⁹ He believed that the physician should be concerned particularly with the phenomena of disease (in the single case) but that the "nucleus" of disease also ought to be investigated, so that by comparison of many individual cases, the general or essential could be ascertained. In other words there must be an assembly of the scattered features of the morbid picture into a unity, whereby the essential of drug action as well as of disease might be discovered. In this manner the individual situation is not lost in the generalization. Arnold had previously been professor of pathology at the University of Zurich and did much to impress the early homoeopathic profession with the importance of including an entire knowledge of etiology and pathology in the consideration of the simile. In summary of Arnold's views: homoeopaths differ from the specificists. The first proceeds from the individual instance. But they must also study "the nucleus of the phenomena, the kernel of the morbid picture, the site of the disease." Thereby they achieve a unity of disease which provides a "specific-local" point of departure for their therapeutics. A similar viewpoint had been advanced by Stoerck nearly a century before.⁵⁰ Kurtz⁵¹ emphasized the importance of the organ particularly affected by a specific but in addition urged consideration of the primarily and most severely affected organ, tissue, etc., study of what organic functions suffered particularly, and what peculiarities the pathologic state presented. By viewing all possible phenomena he would obtain the "character" of the drug. Roth⁵² adopted the same viewpoint. Schrön's viewpoint has already been mentioned.⁵³ He finds the specificity in the concrete, presenting pathologic state of the organ, as it is modified through the individuality of the patient. He called remedies specific or homoeopathic, employing these words synonymously. Martin⁵⁴ emphasized the functional state of the involved organ: squills have a specific connection to the kidney, lungs, gastrointestinal canal and skin, characterized by increased secretion. Goullon⁵⁵ recognized two types of specifics: true real specifics for some diseases having a very definite form; these could only be found by the homoeopathic procedure. Individual specifics were adapted for the individual case in diseases which varied decidedly.

Wolf⁵⁶ doubted the advisability of the specificity conception in homoeopathy since diverse meanings of the word were current, but thought that the doctrine of specifics had been advanced by homoeopathy in that a relationship between remedy and disease had been discovered by the method of finding remedies whereby this was not left to chance. Considering that specifics had often been evaluated with contradictory results, he offered the suggestion that "gastric spasm" was not a disease, but a group of diseases and that "specifics" had failed when the remedy was not adapted to the particular kind of "gastric spasm" present. The correct remedy could be found by the simile principle. The ideas of Rapou⁵⁷ are similar although he approached the subject from a historical standpoint. With the studies of Dufresne,⁵⁸ Watzke,⁵⁹ Black⁶⁰ in homoeopathy a specific or homoeopathic remedy became one adapted to the individual concrete case.

If one reviews the above suggestions it will be seen that there is a gradual concurrence toward the idea that there can be no true specific which is not first proven from a physiologic standpoint. This proving will reveal what tissues, organs, systems are involved, and moreover the manner in which they are involved, objectively and subjectively. On this basis each specific will also be a simile in that its use will be found to follow the simile principle.

The persistent occupation of the homoeopathic physician with the problem of specificity finds a partial answer in his appreciation of the ultimate inferiority of the opposite method, symptomatic medicine based on the principle of palliation. Naturally others appreciated this situation as well and the response is found partly in the magnificent development of surgery. Prior to bacteriology, prophylaxis by evasion did not rest upon a secure basis nor could a specific prophylaxis be evolved.

With the discovery of bacteria, the entire attitude toward the specificity problem changed although the relationship to the simile was not immediately apparent even though v. Behring stated that Pasteur's thinking was homoeopathic in nature. With the introduction of tuberculin the situation was unmistakable because Koch had utilized procedures common to the homoeopathic method. He had experimented with a single substance upon the healthy organism. After determining his results, he had employed the same substance upon the diseased organism. He had applied the remedy in a diluted form in the diseased organism. Through combined experiments his efforts were directed at the discovery of a causal specific remedy. The use of the term causal specific remedy here requires some explanation, for as Lux had reopened the way for specific therapy in the sense of Pasteur and v. Behring, another homoeo-

pathic physician had urged a program involving a causal specific therapy. A citation from Bakody's work will make this clearer:⁶¹

"In 1873 . . . I attended in company with my friend Dr. Clotar Müller, now deceased, the 44th general convention of the Homoeopathic Central Society of Buda-Pesth, at which assembly the foreign advocates of my theories were well represented. As president of the assembly I announced openly and unreservedly, in the form of an opening speech, the position which I took as a member of the faculty (he was professor of pathology and therapeutics of the University of Buda-Pesth), and what I deemed necessary of acceptance for the scientific development of my especial branch, and solemnly declared that I considered the doctrine of specifics in the Hahnemannian sense as the central point of my labors, and one which, on the whole, tended in our direction, but that I subordinated the specific law of similarity to the former, inasmuch as the law of similars is embraced as one of lesser extension within a more universal law of specifics. That the law of specifics was no longer unknown to the medical world, inasmuch as every physician was acquainted with the existence of remedies which, when taken into the system, show a constant and peculiar affinity to certain tissues and thereby cause a peculiar alteration in the anatomical structure and function of the part. But the fact that these changes frequently occurred on the principle of the law of similars, as yet awaited general recognition. In the second place that I designate this law of similarity as a strictly causal one, and no longer wished to see it dealt with in a superficial manner; that in making drug provings we should not be satisfied with the manifestation of mere subjective or general functional symptoms, but in accordance with the scientific knowledge of our day also include the finer pathological-physiological anatomical and chemical manifestations. The specific relations of single drugs to the various tissues must be closely studied, and their genetic changes noted, so that the nature of artificial drug disease may be better and more clearly understood. In other words drug provings should rest upon a cellular-pathologic basis, and, supported by pathological physiology, develop into a cellular therapeutics. In the third place, that it must be acknowledged that the fundamental thought of Hahnemann's Organon clearly expresses, not homoeopaths in a restricted sense, but physicians who know how to apply the proper remedy in a proper way. In the fourth place that the dilution of medicine should not be carried to a point beyond scientific recognition, and that the proper application of our direct causal acting remedies consists in using them in such strength and quantity that they will act only on the diseased tissues and leave the healthy intact.

Finally that I do not consider the biologico-medical therapeutics of Hahnemann a universal one, inasmuch as it covers only that department of practical activity where medicinal therapeutic causal cures can be effected."

This long citation also serves to indicate the evolution of the homoeopathic trend in the last quarter of the nineteenth century both in regard to the explanation of the simile as well as to the later conception of "specificity." When tuberculin was introduced for the treatment of tuberculosis the simile basis was emphasized by many.⁶² Of interest here, and perhaps worthy of further consideration, is the introduction of bacillinum, a preparation of tuberculous lung, suggested by Burnett in the last century. He believed he had attained a better "ison" by employing lung which contained the secondary invaders, lung proteins, tuberculin, and the dead tubercle bacillus itself. It would lead too far to discuss here the reasons underlying the failure of tuberculin in the hands of many workers although it is permissible to state that large doses, non-recognition of the importance of the interval between the doses, and poor selection of cases played parts.

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FURTHER DEVELOPMENTS ON THE SINGLE REMEDY.—Hering¹ was the first to contribute extensively to this subject. His essential idea revolves about the point that it is useful to give two remedies, one with a brief action and another with a prolonged effect; both remedies should correspond with at least part of the symptoms. The combination was supposed to give rise to a third action which is not identical with the action of either alone, but intermediate between the two. Hering also advised a variation of this plan in the treat-

ment of chronic diseases. In this instance the remedy should be given with a partial antidote whereby only certain effects will be manifested by the curative remedy. Obviously this is an unimportant variation of the ancient method of giving correctives.

Gross² likewise favored the plan of alternation of remedies on the basis that a single remedy at times fails to "cover" the case and that one remedy may be necessary to supplement the action of another. He also published some case reports in which the patients were treated according to this method;³ Rummel⁴ and Hartmann⁵ were of the same opinion.

Aegidi⁶ extended the practice still further by giving several remedies in rapid succession, especially when pain required rapid relief, a practice imitated by Hirsch.⁷ Kampfer⁸ considered that the practice of alternation of remedies was at times an indispensable makeshift; he changed Hering's suggestion in one important respect. Hering's practice included a purely hypothetical relationship between remedies, whereas Kampfer's plan was guided entirely by the clinical picture.

Griesselich⁹ permitted the procedure when it was impossible to find the correct remedy, prescribing the two remedies seeming to be the most suitable; Trinks¹⁰ concurred in this view. Early American writers, Marcy,¹¹ for example, had similar opinions, but in England it was denounced¹² as well as praised.¹³ Dudgeon¹⁴ felt that the procedure was unjustified in chronic diseases where one remedy should exhaust its action before a second was administered; in acute diseases whose usual course could be anticipated for the most part, the procedure might be tried.

In general it became generally acknowledged that it was permissible to use two remedies in alternation where one was found insufficient. For many the "single" remedy meant giving one drug at a time but not necessarily for several doses. These opinions arose largely out of experience and seem to represent concessions to practical necessities. While in many respects it represented a step backward and might easily lead to routine alternation, practically many physicians proceeded in accordance with their experience and often gave drugs in alternation. For the most part it was considered poor practice and often evidenced incomplete knowledge of materia medica; on the other hand certain remedies seem to act much better when given according to this plan, although theoretic objections are numerous.

The question was important since it led to the introduction of chemical compounds; for instance, in a given case of secondary anemia either ferrum or acetic acid might be indicated. In such cases ferrum acetate would be prescribed.¹⁵ From a scientific

standpoint of consistency it would have been far better to prove the compound rather than attempt to predict its action. Actually one often finds the compound possesses different effects than might be anticipated. However it is a much better plan than that of Aegidi.¹⁶ It also tended in a measure to avoid the necessity for two remedies when one did not "cover" the case.

At any rate the subject introduced further controversy in the homoeopathic ranks. Schrön¹⁷ believed correctly that the idea of alternation was contrary to the principle of homoeopathy; furthermore it prevented the compilation of any data on the actual value of a given substance. He made the correct suggestion: there is no objection to giving mixtures provided such mixtures have been proven. As a matter of fact Molin¹⁸ made such provings, for example with aconite and belladonna, and found symptoms of both drugs, although they are supposed to antidote each other. Grieselich¹⁹ made similar provings with entirely negative results and called the procedure a retrograde step. In the background of this question was another: can one use a local remedy as well as an internal remedy, a procedure which met with some favor.²⁰ Another question was also raised: should one give two different strengths of the same drug at the same time? This method has very little in its favor.

The real importance of these questions lies not so much in giving two remedies, a point which could be settled by provings, but in the problem of using auxiliaries to homoeopathic therapy. Perhaps a glance at the much maligned blood-letting is more instructive than a study of other adjuvants to therapy, because one would expect the least concession in this field of any. Among those who favored small bleedings were Kretschmer²¹ and Hering.²² Rummel favored them early in his practice but later denied the necessity.²³ Rau,²⁴ Henderson,²⁵ and Charge²⁶ are all in agreement on the occasional value of bleeding. On the other hand Arnold,²⁷ Elwert,²⁸ Schubert²⁹ and Ruckert³⁰ wrote against the practice. This particular problem was ended by Dietl³¹ who reported that bleeding was useless in pneumonia and indicated that actual harm might result from it in this disease. One might say that the homoeopathic profession was willing to adopt those procedures which were generally considered valuable, yet remained critical of the actual merit of many.

The literature reveals similar concessions in respect to the occasional use of purgatives,³² the use of stimulants in fever, the use of counter irritation, local application of heat³³ or cold, etc.

Therefore it would seem that the homoeopathic physician has not been dogmatic about the single remedy. To him it represented the

procedure of choice, although other agents could be added whenever they seemed necessary or advisable.

The use of local measures in conjunction with systemic therapy is approved by Hahnemann in many places³¹ and denied in a few. Gross,³⁵ Schrön,³⁶ Backhausen,³⁷ Griesselich,³⁸ Veith,³⁹ Koch,⁴⁰ Lippe,⁴¹ and Henriques⁴² all favored local therapy in conjunction with internal medication. In some instances this procedure resulted in the use of the same remedy locally as internally, a method with much larger possibilities than are commonly appreciated. However, as a rule, one remedy or agent was applied locally and another internally. Dudgeon⁴³ who may be regarded as the spokesman for the English profession of that time believed that local therapy was essential to cure some cases. In short, the single remedy was regarded as an ideal procedure which could not always be approximated in actual practice.

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DEVELOPMENT OF DRUG PROVING.—The suggestion of Hahnemann in this field did not remain totally neglected as evidenced by the proving society of Jörg.¹ The endeavors of Wedekind to interest the profession were fruitless and the attempt of Martin was also unsuccessful. A society of provers was started in Vienna but discontinued their efforts when one of the members became homoeopathically inclined. The provings of Rademacher can be traced to the stimulation of Hahnemann. Although Pereira² and Forbes³ perceived the necessity for provings, little was actually done. In general the method was not adopted outside of the homoeopathic profession.

Hahnemann's early drug provings contained many interesting points. Each drug was to be proven alone, in a form and amount

under conditions whereby the accuracy of the result was insured as far as possible. He administered a single dose and repeated only when the action had disappeared or none occurred. He desired by many and multiple investigations to eliminate suggestive influences, to determine whether symptoms were common or rare, definite or indefinite. He desired to know, not merely what the prover felt (subjective symptoms), but what the physician observed (objective symptoms). Statements have been cited to indicate that early, relatively large doses were employed and naturally upon the healthy individual. As the potency doctrine attained increasing importance in his mind, the doses employed became smaller until at last he advised provings with the 30th dilution. It also seems clear that the 30th dilution at that time became the normal dose for patients and there is the strong implication that his contributions in late life came from patients, so that there was a transference from relatively large doses to infinitesimal and from the healthy to the patient.

Hering⁴ also advised provings with the 30th, as in the case of Theridion, and also to people with a "slumbering psora." This method seemed to appeal to some, for example the Thuringian group,⁵ and Frohlich⁶ was not satisfied with the 30th dilution but employed the 202nd. Later Hering employed dilutions up to the 2500th. The attitude of the natural scientific group was expressed in the previously mentioned Wolf theses, and Strecker likewise objected to "high potency" provings.⁷ Watzke⁸ urged that the results were of little value even when carried out scrupulously, an opinion in which Trinks⁹ concurred. On the other hand Petersen¹⁰ would include (like Hahnemann) the symptoms which disappeared after the administration of a drug to a patient. Grieselich urged that provings only with high dilutions would lead to many errors and that the reports would be quite exclusively subjective, whereas the objective phenomena were at least as necessary in the totality of drug action. Moreover the first task of the materia medica was a determination of the action upon the healthy by pure pharmacodynamic experiment, a task which had hardly been begun, not alone completed. Finally the inclusion of symptoms which appeared in the patient or which disappeared was never justified in a "pure" materia medica.

The rules for proving were somewhat modified by Piper.¹¹ Incidentally he suggested that provings should be made in fasting individuals, an idea which has again been advanced by Bier. Piper desired to include the symptoms of idiosyncrasy, therein concurring with Hahnemann's viewpoint.

Schrön¹² emphasized the relative nature of health and thought

that provings should also be performed on the sick. These impressions should be used to confirm impressions previously gained on the healthy. He also clearly perceived the preponderance of males in the provings and urged the use of more females. Equally clearly he emphasized the use of young individuals on the basis that remedies which affect the thymus could hardly be expected to display many symptoms in adults. Another important suggestion, unfortunately largely disregarded, was that the immediate future should be concerned not with encumbering the materia medica by the addition of countless substances, but with the more thorough study of those already known.

He likewise opposed proving with the 30th dilution and demonstrated his point clearly by showing the more satisfactory knowledge of the drugs proven by Hahnemann in his early days than in the later. Very important but again not regarded was his endeavors to have two groups of symptoms recorded; those common to all provers and those almost individual.

Griesselich¹³ continued his ideas on constitution, urging that there must be susceptibility to drug action just as to disease. He reported his own experiments, showing that he was personally susceptible to the action of relatively few substances. The importance of his observation is difficult to over-estimate. In any proving with a large number of individuals, at least 25% will usually not respond.

To list the actual new provings would require too much space but they may be found in the writings of Stapf, Gross, Hering, Wahle, Hartlaub, Trinks, Franz, Helbig and many others.

With Watzke¹⁴ began the actual labor of re-proving Hahnemann's assertions on drug effects; this work was extremely important since Hahnemann's provings lacked all information on the sequence of drug effects. In regard to the critique practiced on existing provings perhaps the work of Roth¹⁵ will save a long discussion. Here the remarks will be confined to the studies of Nenning:

"The symptoms of Cajetan Nenning ought upon no account to remain in the materia medica. The prover himself admitted that the provings were conducted without due caution, but this has been forgotten.

". . . This is the language of a fine honest fellow but one who is totally deficient in the necessary qualifications of an accurate observer. To make provings of medicine is one of the most difficult tasks, so difficult that I have never been able to bring myself to publish my own provings, 26 in number, and all of them, even the very newest, that were made with Dr. Tripper, shall be consigned to oblivion. How little Nenning possesses the necessary qualifica-

tions, one can easily convince himself if they read with attention his practical essays in the Allg. Hom. Ztg. Dr. Watzke has demonstrated this clearly in the same Journal. If it were but a few scattered symptoms that Nenning has furnished, we might pass over this, but the evil is greater than many persons think. The following is a table of his contributions to the *Materia Medica* from 1828-1836 in Hartlaub and Trinks' *Annalen* and Stapf's additions to the *materia medica*.

Aethusa Cynapium	143	Magnesia Sulphuricum	355
Agaricus	26	Millefolium	77
Alumina	662	Natrum Carbonicum	594
Ammonium Carbonicum	465	Natrum Sulphuricum	340
Ammonium Muriaticum	448	Niccolum	446
Bovista	226	Nitrium	359
Baryta Carbonicum	309	Oleum Animale	525
Cantharis	489	Phellandrium	369
Causticum	173	Phosphorus	531
Castoreum	276	Plumbum Aceticum	287
Chelidonium	138	Sabadilla	18
Duleamara	51	Sarsaparilla	347
Graphites	178	Senega	19
Helleborus	77	Strontium	206
Indigo	266	Sulphuric Acid	249
Kali Carbonicum	365	Tinctura Acris	285
Kali Hydriodicum	303	Tonga	185
Laurocerasus	739	Tabaccum	104
Magnesia Muriaticum	646	Zincum	456

"A grand total of 11,447 symptoms, not one of which Nenning has observed on his own person. This he has not concealed but so states in the Allg. Hom. Ztg.

"Thus we have good reasons for doubt in respect to Nenning, in addition to those expressed by Hahnemann himself, though many of his symptoms may hereafter be confirmed. It is our opinion that they ought to be rejected at least provisionally. These we see exceed 11,000 symptoms and good reasons exist for treating many thousands more by other observers in the like manner."

This long quotation has been included for several reasons. Hahnemann called Nenning a symptom buyer and distrusted the symptoms although he included these symptoms in "Chronic Diseases." The article also refers to the fact that later provings were performed under such rigid conditions that it was difficult to secure provers. It also exemplifies the destructive critique practiced by physicians of the natural scientific group on the homoeopathic *materia medica*. This quotation should also suggest to those who rely upon a repertory the character of the materials with which they work, since these symptoms are included in most repertories.

The secret of reporting too few symptoms rather than too many, the rigid elimination of incidental and accidental symptoms have been overlooked too frequently.

It is impossible as well as unnecessary to go into an extensive critique of the homoeopathic materia medica. Allusion has been made to the work of Roth¹⁶ and reference may be made to the study of Wesselhoeft (1877), or Dake.¹⁷ While Allen's Encyclopedia intended to cover all that had been reported an analysis of the first three volumes shows:

Drugs in first three volumes	248
Without any provers at all	22
With 1 prover	68
With 2 provers	30
With less than 5 provers	29
With less than 10 provers	30

Thus 69 or about 35% might be considered as having sufficiently the minimum of quantitative proof. An analysis of some high potency provings can be found in the above mentioned writings of Dake and Wesselhoeft. To the same group of entirely inadequately proven substances belongs *Lac caninum* and *Kentian* materia medica in general.

By 1865 there was a thorough appreciation that the materia medica of Hahnemann was "antiquated, insufficient for the science of that time, partly impure and partly incorrect."¹⁸ Roth had stated that Hahnemann's *Materia Medica Pura* was "a mound of symptoms, an accumulation and collection of errors of various kinds which owe their origin to false quotation, subjective symptoms which are not the effect of the proven medicine, symptoms observed while the patient was using the medicine for curative purposes, symptoms from cures." By Roth's efforts some 16,140 symptoms were eliminated from the contributions of six workers as impure.

All scientific homoeopathic physicians seem in agreement on the absolute necessity for provings; they are regarded as indispensable and cannot be replaced by animal experimentation. But the hyper-subjective materia medica of Hahnemann, which was a product of his time, was subjected to considerable retesting and modification and the important supplement of organotropic effects added from animal experimentation.

Two practices which shaped homoeopathic practice should be mentioned here: as time elapsed certain symptoms seemed so useful clinically that they became regarded as "keynote symptoms" and that in place of the innumerable symptoms found in the textbooks, relatively few actually guided the choice of the remedy. In short,

the symptoms which were prominent in the pathogenesis as well as those constantly reacting to the drug when used in disease were deemed important. But at the same time another practice which Hahnemann both deplored and used also came into vogue; the dangerous procedure of using clinical symptoms as a source of provings: this differs from the preceding in that when drugs relieved symptoms, it was presumed that they are also capable of producing those symptoms in the healthy. It seems hardly necessary to point out that this reasoning is based on very fragile evidence.

Here one may perceive another trend of difference in the two groups of homoeopathic physicians. Whereas the natural scientific group became more wary of all unusual subjective symptoms and tended to emphasize the common or major phenomena, the purists attempted to "preserve" the status of the materia medica and not rarely to prescribe on the basis of the rare symptom, basing the process on the speculation that if the symptoms corresponded in respect to the rare, they would also correspond in respect for the common.

In summary it may be said that the materia medica underwent marked change in the period following Hahnemann. Many drugs were reprovén; others received critical study; new drugs were added. At the same time a wide variety of substances, which still clutter the textbooks, were introduced on evidence which at best is little more than meager.

In regard to the application of this knowledge, as time went on one group paid more attention to the "important," common, usual symptoms with increasing attention to objective phenomena. The other group tended to preserve each fragment and maintain emphasis on the subjective symptoms.

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THE DEVELOPMENT OF IDEAS OF THE HOMOEOPATHIC AGGRAVATION.—Schrön called the idea of homoeopathic aggravation "an unfortunate dogma" and denied Hahnemann's views in toto.¹ Moreover he stated that it was described most frequently by those possessing insufficient knowledge of the natural course of disease. Rummel² held that while the homoeopathic aggravation was rare it was occasionally seen. Kurtz³ stated that aggravations occur when the drug is too strong or too weak; in the latter instance they are associated with lack of control of the natural disease. They do not occur with a truly homoeopathic remedy. Gross⁴ described two types of aggravations, the first early and evanescent, the second occurring later. The first were ascribed to too small doses and the latter to too large. He also thought that with larger doses an irritant action led to the expulsion of the medicament and that this resulted in delayed specific action.

Schmid⁵ believed that aggravations occurred only from too small doses and were evidence of their inefficient attempt to overcome disease. In his opinion most aggravations are associated with the natural course of the disease and he believed that they do not appear with his moderate or large doses. Kampf⁶ divided aggravations into those which were followed by improvement and those followed by no change. Hirschel described several types of aggravations: aggravations due to hypersensitivity of the organism, those due to the drugs being incorrectly chosen and producing new symptoms, aggravation followed by cure and aggravation without resulting improvement.⁷ Trinks⁸ accepted the idea of natural aggravations due to the course of the disease and also a homoeopathic drug aggravation, but denied that the latter was essential to cure.

Schneider⁹ described several types of aggravation but called Hahnemann's homoeopathic aggravation "a phantom." Romano¹⁰ accepted Hahnemann's aggravation theory, and moreover stated that he saw them frequently, while Rau¹¹ subscribed, at least, to the first part of this statement. Griesselich¹² was impressed by the importance of the aggravation, but added that he had often seen it

in patients not receiving medication, a view with which Braud concurred.¹³

Griesselich stated that there was too great a tendency to ascribe everything which happened after the administration of a remedy to the remedy and furthermore that imagination played a great role in the aggravation theory of homoeopathy: the homoeopathic aggravation is the psychic effect of homoeopathic theory. While, undoubtedly, it does occur, it is often absent and certainly not essential to cure. Arnold¹⁴ likewise thought the aggravation occurred but was rare. Goullon¹⁵ also expressed an opinion. Veith¹⁶ failed to observe aggravations after relatively large doses.

In future years the homoeopathic aggravation played a minor role; in general it was appreciated that it might occur but was not essential. The literature indicates that it was most often reported by the "high-potency" group.

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DEVELOPMENT OF IDEAS ON PRIMARY AND SECONDARY DRUG ACTIONS.—It has been noted that Hahnemann's early ideas were quite clear in spite of the fact that the evidence on which they were based was very confusing. It should also be emphasized that Hahnemann's ideas of primary and secondary action differ in some re-

spects from those which will be reported in the section on the modern viewpoint. However the literature was long in a confused state and little that was essential added in the period under discussion.

Hering¹ regarded Hahnemann's secondary actions as *restitutio ad integrum*; but it was not the restoration of the normal by nature, it was the cessation of action of the drug. Piper² regarded all the symptoms produced by the drug as medicinal symptoms and discarded the idea of primary and secondary actions. Helbig³ considered them parts of alternating actions. Watzke⁴ regarded the symptoms as of two types in which the primary symptoms or medicinal symptoms, or the secondary symptoms (reactive) might predominate. Attonyr⁵ misunderstood the subject so completely that his views need not be repeated. Kurtz,⁶ Trinks⁷ and C. Müller agreed that the division into primary and secondary symptoms was not tenable. Schrön⁸ made the remarkable suggestion that the primary symptoms are those common to all provers while the secondary occurred only in a few. His views on drug action have been cited before; the statement being introduced merely to indicate that the words primary and secondary were confusing and various subjects were discussed under this topic. Arnold⁹ thought Hahnemann's views one-sided and Hirschel¹⁰ stressed the complexity of so-called secondary effects.

Gerstel¹¹ called the symptoms evoked by the drug, the passive or primary symptoms, and the reaction symptoms of the organism, the active or secondary. Schneider¹² wrote a *materia medica* dividing the symptoms accordingly. The views of Griesselich have been mentioned.¹³

In summary it need be said merely that little was contributed to the development by the followers of Hahnemann. Confusion was the chief result of the introduction of a variety of interpretations to the words primary and secondary. In general the views of Hahnemann are clearer than those of his followers.

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DEVELOPMENT OF IDEAS ON CHRONIC DISEASES.—Hahnemann imparted his ideas to Stapf¹ and Gross² who hailed them as a great discovery. A similar view was taken by Petersen except that he regarded psora and leprosy as identical.³ Rau⁴ with his more rational thinking admitted the possibility that some chronic diseases were due to itch, but regarded the doctrine in general as an attempt to supply a defect in Hahnemann's system, namely, of looking into the organism for an explanation of the morbid phenomena. Wolf stated that the entire matter was unfortunate, but happily it had no effect on practice.⁵

Schrön⁶ added the important observation that the very men who now endorsed the psora theory were the ones who had previously reported cures without psoric remedies. He added that it was just as inconsistent to speak of a universal cause of disease as it was to mention a universal panacea.

Hering carried the psora idea somewhat further than Hahnemann,⁷ and introduced psorine as a prophylactic for the condition. Puffer's writings⁸ may be regarded as quite typical of those who defended the psora doctrine and those interested may refer to them.

Griesselich regarded the psora theory as supplying a defect in the hyperdynamic doctrines of Hahnemann. Arnold⁹ regarded the theory as the opening wedge for all types of speculative forms of treatment. Henderson¹⁰ regarded the entire matter as a mistake on the part of Hahnemann and traced the pre-Hahnemannian views on the subject. Lebouche¹¹ concurred with Henderson. Thus it may be said that the psora theory was immediately and uniformly rejected by the natural scientific group of physicians.

Perhaps the most vitriolic of the writers in the homoeopathic school who wrote on the psora theory, was Gentzke.¹² He said:

"To tell the truth and answer the question, why only a proportionately small number of professional men follow the doctrines of homoeopathy and why many others secretly make use of its curative principles and are afraid to acknowledge it publicly . . . we must admit that the cause is to be found in the sad elements which for a long time, like parasitic growths, have deprived the plant of its sap and tried to engraft their own fruit upon it; although in the course of time, much has been done to extirpate these parasites, the

object has been but partly attained. Similar to the hydra, new heads arise as soon as the old ones have been trampled down. It cannot be denied that the greatest enemy to homoeopathy is to be found among its own followers and when considering all the nonsense which they have, in opposition to reason and experience, hatched and identified with homoeopathy, those who wish to proceed earnestly on to the path of a really scientific investigation regime, require a great deal of courage and a most sincere conviction of the excellence of its doctrines to acknowledge publicly that they are followers of this new doctrine. . . .

“Even Hahnemann left, at a later period when the weight of years had paralyzed his mental power, the original path of investigators and being misled by defective observations, he was reduced to patch his doctrine by many tenets, which, although without any real basis have been praised as something extraordinary and trumpeted forth as new perfections by those credulous followers who have been accustomed to see only through the eye glasses of their master.

“The most fabulous and miraculous ones have been already performed by homoeopathy and all journals have published them. Hahnemann himself had repeatedly mentioned that the homoeopathic method of curing possessed a high degree of perfection, that it was as sure to cure diseases as to solve a mathematical problem, when suddenly like a *deus ex machina*, Hahnemann’s work on Chronic Diseases was published, with the exposition of his theory on their pathogenesis and with his antipsoric medicines.

“At once the views of his echoing gang were changed, the eye glasses hitherto worn were thrown into the lumber room and the new ones were used according to the pattern of the master.

“It was a singular fact that the same medicines which shortly before were selected most carefully according to the principle of *similia* and *similibus*, and had effected the most miraculous cures, had suddenly lost their efficacy, and the mystic trio (*psora*, *syphilis*, *sycoosis*) were scented everywhere; the terrible *psora*, especially infected the brains of a number of chiefs and taking hold of their ‘*thalmi nervorum opticum*,’ caused them always to see the prodigious.

“These and similar scenes have been repeatedly enacted either alone or mixed with each other at various periods and I believe that it is unnecessary to mention the roles unnecessarily played in homoeopathy by the homoeopathic aggravation, the famous decillionth, the prescription of smelling a single globule, the solution of a single globule in water and other tom-fooleries.”

This sarcastic quotation contains considerable truth, and it again

urges one to look behind the symbols occasionally set up in order to determine the factual basis lying beneath. Strange as it may seem, even in 1914 Wapler concluded the greatest danger to homoeopathy as well as its greatest source of difficulty was to be found in its literature and in the fact that some of its adherents attach every will-of-the-wisp to the clear-cut and definite problems.

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DEVELOPMENT OF THE DILUTION THEORY.—It should be recalled here that the 30th dilution or 30th potency has two different meanings in the writings of Hahnemann. At one time 1 part of the drug is added to 99 parts of the vehicle to make the first centesimal dilution and this process is repeated 30 times. Again the process is performed only once and this shaken until it acquires the "strength" of the 30th dilution.

Early Hahnemann implied that material subdivision occurred up to the sixth dilution, but the idea of spiritualization took the fancy of some of his followers. Korsakoff then proceeded to make "potencies" up to the 1500th centesimal.¹ As stated previously Hahnemann regarded this as impractical and urged that the limit must occur somewhere. He expressed his disapproval of going beyond the 30th.

Nevertheless this restraint had little effect, and there soon appeared Gross' "blood powers"² and the equally miraculous tales by Plaubel.³ The idea of succussion without dilution was taken up by Jenichen⁴ and substances were "potentized" highly. Gross,

Stapf, Hering, Bonninghausen used these potencies and extremely absurd stories were related about their power.⁵ Dudgeon⁶ remarks that fortunately Jenichen shot himself when he reached the 16,000th dilution or there is no telling what heights he might have reached. Naturally the high potency viewpoint was adopted only by the "pure" homoeopathic physicians.

Scientifically inclined homoeopathic physicians completely repudiated these claims. Segin⁷ showed by microscopic examination that the so-called infinitesimals were actually very material. Mayrhofer⁸ investigated the metals and found discernible traces in the 10th dilution and possibly in the 13th; although gold could not be found in higher than the 5th, precipitated gold could be found in greater dilution. Other studies may be found in the works of Arnold⁹ with cow-pox vaccine, in studies with shaken and unshaken *drosera* with no difference in the result.¹⁰ Werber,¹¹ Wolf,¹² Fielitz,¹³ Schmid,¹⁴ Lietzau,¹⁵ Strecker,¹⁶ Schneider,¹⁷ Aegidi,¹⁸ Hartmann,¹⁹ and Veith,²⁰ all denied the dynamization theory. The viewpoint of Rau²¹ is excellent and was accepted by Griesselich. The interested may also consult Schrön,²² Kretschner,²³ Trinks,²⁴ Rummel,²⁵ and Kampfer.²⁶

Griesselich²⁷ emphasized that substances may be placed in two groups: those acting without previous pharmaceutical preparation, those requiring division or dilution (for solubility).

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REMARKS ON SO-CALLED HOMOEOPATHIC POTENCIES.—Since no opportunity is afforded to discuss this problem elsewhere, attention may be directed to it here. In retrospect it will be recalled that homoeopathy had been practiced without reduction of dose, then with relatively small doses, and finally by some with infinitesimals. The points on which there was general agreement do not require further discussion: the advisability of reduction in the amount in order to avoid too severe aggravations; the desirability of increasing the drug surface by trituration and facilitating its solubility by dilution.

In regard to trituration, it may be conceded that this procedure will result in increased activity of the solid preparations because the particles are finer and there will be a better opportunity for absorption. In modern homoeopathic pharmaceutical technic, 1 part of the drug is triturated with 9 parts of sugar of milk to make the D 1, the first decimal trituration. In the second trituration 1 part of D 1 is mixed with 9 parts of sugar of milk to make D 2, etc. The question immediately arises to what extent increased division will compensate for the reduction of total mass; that is, whether or not the increased surface of D 2 compensates for the fact that only 1/10th as much drug is present. Moreover, there is not any proof that sugar of milk is sufficiently "hard and sharp" to cause further subdivision after the process has been repeated a

few times. It is very difficult to sustain the argument that increased trituration causes increased surface after the process has been repeated a few times, for example after D 6, especially when it is unknown how far the increased fineness compensates for decrease in the amount of absorbable drug material.

Analyses of the lower triturations, for example, up to D 4 show that the content varies considerably. For explanation of this variation one obvious factor is the container. If the container is new, there may be adsorption on to the wall so that the preparation contains less than the calculated amount. If containers have been used before, the drug may be given off from the walls and more than the predicted amount will be present.

Equally obvious is the fact that cleansing of mortars is impossible in a "homoeopathic" sense. If chemical means are employed, new chemicals are absorbed into the walls; mechanical cleansing is even less satisfactory.

Further one must consider the problem of purity of the sugar of milk. Crude analysis by ignition shows a residue of 0.050% in so-called chemically pure lactose. Analysis of several lots of sugar of milk revealed a content of 0.0003% iron. If one limits himself to triturations of iron for example it is impossible to make a tablet with less than 0.0003% iron since this amount is constantly added by the sugar of milk. For this reason the lower triturations contain a variety of "potencies"; after one reaches D 6 further reduction in the amount of iron is impossible. To make a higher potency one might as well begin with sugar of milk and triturate it 6 times the usual time.

It is much the same with other substances. Average analyses of so-called chemically pure sugar of milk will reveal approximately the following results.

K.....	0.0174%	P.....	0.011%
Na.....	0.0143%	Cl.....	0.0064%
Ca.....	0.0095%	S.....	0.0041%
Mg.....	0.0032%	Si.....	0.003%

If the above results approximate those of other investigators, then one should not forget that this analysis is very fragmentary since the primitive state of chemistry does not permit tests for many substances when present in amounts less than 1/100,000 grams per liter. Indeed there is strong probability that sugar of milk contains all mineral substances in dilution of above D 11. But the above is sufficient to show that at least 8 substances are present in the D 5 or lower, and implies that what happens in further reduction in dose beyond D 5 is at least highly problemati-

cal and quite unpredictable. Again the obvious conclusion is that equal results might be attained by sugar of milk alone.

Incidentally it may be observed that results obtained with triturations above D 6 cannot be analyzed therapeutically since one does not know what substance is responsible for the result.

In connection with the remarks above it is interesting to note that the supporters of Schüssler's biochemic or tissue remedy procedure now admit that all 12 of the tissue salts are present in sugar of milk itself.¹ Above the third decimal trituration the impurities in the sugar of milk predominate over the amount of the substance intended for the patient and furthermore the impurities are triturated and subjected to the same conditions as the medicinal substance.

Entirely the same arguments prevail with respect to alcohol as a diluting agent. Pure alcohol, chemically speaking, is notoriously impure, homocopathically speaking. Adsorption by the walls of containers is equally evident here. Likewise silicate contamination from the walls of glass containers can be easily shown. Moreover glass alkali produced by containers affects alkali sensitive drugs, for example, the alkaloids. Though the action may be temporarily increased, the effect is later destroyed.

The same general argument obtains in respect to "dissociation" through dilution. To use HCl as an example, it may be said that $n/10$ HCl is 91.9% dissociated and $n/100$ is 93.3% dissociated. Thus dilution may increase the dissociation in the case of electrolytes. But it is immediately evident that in the second dilution only $1/10$ the number of ions is present, compared to the first dilution, and it may be reasonably doubted whether an increase of 1.4% dissociation compensates for the discarding of 90% of the ions.

The attempt made to preserve the doctrine of high "potencies" through the doctrine of dissociation, of course, has nothing to do with the question, since many of the drugs do not dissociate in the usual sense of the word. However, to analyze the situation it may be conceded for the purpose of discussion that dissociation does occur.

It is possible to determine the number of molecules present under certain conditions by the Loschmidt number (Avagadro's hypothesis refers to gases but can also be used). Two examples may be employed for the purpose of illustration. The first column represents the dilution, the second the number of molecules or electrons present in the case of copper sulphate and adrenalin, respectively.

Naturally the figure will vary according to the substance used.

	CuSO ₄	Adrenalin
D 20	4000 molecules	80,000 molecules
D 21	400 "	8000 "
D 22	40 "	800 "
D 23	4 " (477 electrons)	80 "
D 24	30.8 electrons	8 " (784 electrons)
D 25	3.08 "	78.4 electrons
D 26	0.3 "	7.8 "
D 27		0.7 "

but presuming substances pure, the vehicle clean, that the container did not absorb, that the substances dissociated perfectly, then in D 26 there would be 3 chances in 10 for a single electron to be present in the case of copper sulphate, and 1 chance in 2 for an electron in the case of adrenalin in D 27. It is immediately apparent how remote the possibility is for a single electron to be present in the D 200 or D 1000, advocated at times by the high potency group of physicians.

In the face of such evidence a retreat has been made to electronic dissociation. A brief example from the case of HCl should suffice to show the untenability of such an explanation. One may assume for the purpose of discussion that the acid has one electron outside of its nucleus which will be called the chlorine atom. One may further assume the nucleus to have 17 electrons on its border, 3 hydrogen atoms and 8 helium atoms or alpha particles. Finally one may assume for the purpose of discussion that the solution containing this single molecule of acid is shattered; then the solution contains 30 "particles." Thus if the D 20 contained 1 molecule, the D 21, 3 "particles," D 22, might or might not contain a "fragment," etc.

It is equally obvious that if the molecule has been shattered it no longer possesses the properties of HCl, but the properties of hydrogen and helium. Carried to the ultimate this argument ends in the use of hydrogen only for all diseases.

Practically none of the presumptions permitted actually exist in pharmaceutical technic. Mortars as well as containers are re-employed. Neither the sugar of milk nor alcohol is homoeopathically "pure." In the preparation of many high potencies, distilled water as well as alcohol is employed which adds other impurities and in the so-called fluxion potencies or very high potencies, the water is not even distilled.

To make an actual high potency would require absolutely pure substances which are unknown; a perfect container which neither adsorbed nor gave off materials; the operation would have to be carried out in a perfect vacuum to avoid contamination. It would also require other conditions impossible to obtain.

In response to the query that results have been obtained with so-called high potencies, the following may be said: there is no evidence that D 200 has ever been made, although the operation may have been carried out. If and where results have been obtained there can be no decision on what produced it; analyses of so-called D 200 of several alleged substances have shown the presence of numerous other substances in the D 4-5. Occasionally the result might be explained by the following experiment: a homoeopathic vial is filled with a saturated solution of methylene blue. After the vial has stood for some time, 9/10ths of the liquid is decanted and the vial refilled. This procedure can be carried out 30 or more times. Usually the vial still remains blue because of the large amount of dye absorbed. Frequently after some hours a considerable amount of dye can be found in what might be called the D 30, but actually the figures are in the vicinity of D 4-6.

These reasons which represent but a fragment of the situation show that no extensive critique of the high potency problem need be introduced. Unless one chooses to disregard the divisibility of matter, the entire knowledge of physical chemistry, the purity of vehicles, the problem of a perfect container and other factors, there is no scientific evidence favoring the so-called high potency, which can stand critical analysis. Many of the assumptions are entirely unwarranted, for there is no proof that shattering of the atom is possible by homoeopathic pharmaceutic technic. The same argument could be used in respect to the problem of radio-active disintegration where radium is employed as an example. But with the exception of potassium, and possibly a few other elements, there is no proof that such disintegration occurs in elements with an atomic weight of less than 200. But even if it extended to all it would have no bearing upon the homoeopathic situation.

There has been some scientific work with high potencies, or, as the workers call them, high dilutions, such as the studies of Junker,² Krakow,³ Kolisko,⁴ and König.⁵ But since these works could not stand the critique of Kotsechau,⁶ no extensive discussion is necessary; the same holds for the work of Persson which the writer has made available. Moreover other examinations of this type of work are available, as Fenner's critique of Kolisko's work⁷ and the study of Seybold.⁸ Similar experiments have failed to eliminate oligodynamic action as described by Nageli,⁹ Saxl,¹⁰ Freundlich¹¹ and others. Since the writer has¹² had occasion to make available the work of Kötsechau¹³ as well as that of Ostwald,¹⁴ no further discussion seems necessary here.

It is appreciated that high potentists bring into force arguments based on some unknown type of energy. Outside of the lack of

existence of any proof of this energy, the fact remains that as far as is known, energy is not infinitely divisible.

The reader should appreciate that degree of dilution is a subject not actually connected with homoeopathy at all. But since it has been mistakenly injected into the problem, it was necessary to examine it briefly.

There is probably no more important aspect in homoeopathy than the question of the minimum effective dose, and no greater damage and source of confusion exists than the identification of homoeopathy with the high potency problem. Homoeopathy had long been successfully practiced before the introduction of the high potency. Anyone who uses such high "dilutions" must appreciate that he does not know what he is using.

All too frequently homoeopathic writers see a connection between extreme minuteness of a dose of a substance and the high potency theory. If Heubner has shown that the guinea pig heart is susceptible to the effect of camphor in a dilution which approximates the 15th decimal, this states nothing but that some substances are active in extremely small amounts. A calculation would show that there is a definite number of camphor molecules in this dilution; in short that camphor is still active when hundreds, thousands or millions of its molecules are present. The same holds for the acute olfactory sense of dogs. The only record on this point known to the writer is the recognition of mercaptan in the 12th dilution.¹⁵ Undoubtedly with other substances and with other animals the limit might be set higher, but "physiologic" or "biologic" does not mean beyond the limits of physics and chemistry.

Most reactions known to chemistry as delicate are in the region of the 8th decimal. The action of colloidal platinum on hydrogen peroxide is detectable in the 5th,¹⁶ the depression of this reaction by hydrogen sulphide in the 8th; the action of iron on spontaneous oxidation of cystein also occurs in the 8th;¹⁷ destruction of hydrogen peroxide by colloidal osmium in the 8th;¹⁸ reactions of oversaturation and under cooling in the 8th-9th;¹⁹ microchemical tests for gold in the 9th,²⁰ for antimony and cobalt in the 9th-10th;²¹ sodium spectroanalytically in the 10th,²¹ copper in the 10th,²² methylene blue in the 10th, NaOH in the 10th,²³ HCl in the 11th,²⁴ radium C in the 17th,²⁵ fluorescein in the 20th.²⁶

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DEVELOPMENT OF IDEAS ON THE SELECTION OF THE REMEDY.—

Rau¹ made the suggestion that one should treat the totality of the disease since this included the proximate causes as well as all phenomena determinable by the senses; he also attempted to replace the "totality of the symptoms" by this expression. Hahnemann accepted Rau's re-definition. The same point is stressed by Hartmann,² whose entire work is based upon the idea that no homoeopathic physician would ever employ a remedy whose pathogenetic effects did not clearly indicate the correct relationship to the cause of the disease and its effects.

He adds that many important indications originally were derived from this source, as arnica for the effects of bruises, china for the

symptoms following loss of blood, *nux vomica* for the gastro-intestinal symptoms following over-indulgence in alcohol, etc.

Müller³ who had gained Hahnemann's enmity for refusing to accept the *dieta* of the latter wrote very intelligently against the pure comparison of symptoms and showed the difference between therapy directed at the totality of symptoms and one which was directed at the most prominent symptom or symptoms, in short, differences in so-called symptomatic therapy. The works of Schrön,⁴ Kurtz,⁵ Wolf,⁶ Roth,⁷ Watzke⁸ and others are written in the same vein. Hirschel⁹ summarized the indications for a remedy on diagnostic and etiologic anatomico-physiologic, extrinsic and intrinsic factors, etc. Hering,¹⁰ in spite of the miscomprehension of his writings by many of his followers, emphasized the importance of pathology.

Bönnigshausen¹¹ and his works practically always represent a retrograde movement. In this case it is the arbitrary deduction as to what is characteristic and what not, and the same might be said about many other practices which are intrinsic to the dangers of repertory prescribing. It is remarkable that this man, who had no medical training, should still be considered by some as qualified to give opinions on important and complex medical topics.

Grisselich¹² emphasized three important phases of the selection of the remedy: the individuality of the patient; the symptoms from the moment of the onset of the illness to the present; the ascertainable cause which had provoked the symptoms. The views of Bakody have been presented in an earlier section. Other writers of interest are Schmid,¹³ Mosthaff,¹⁴ Rummel¹⁵ and Heibig.¹⁶

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DEVELOPMENT OF HOMOEOPATHIC POSOLOGY.—Although this question has been considered elsewhere, it has received so much emphasis that the major opinions expressed by homoeopathic physicians at the time should be mentioned. Otherwise one might misunderstand the problem and think that the only issue involved was dilution near the 30th.

Hartlaub¹ immediately questioned Hahnemann's views, and while agreeing with him on the importance of the small dose, nevertheless he mentions the use of conium in the tincture and the first dilution. Wolf,² representing the scientific group, also denied Hahnemann's arbitrary fixation of the dose at the 30th and considered that patients ought to be given the necessary amount of the drug, regardless of whether this was the tincture or some dilution. Rau³ urged that the sensitivity of the patient was the deciding factor in posology. Contrary to modern opinion he believed the more acute the case, the smaller the dose, the more chronic, the larger. Werber⁴ admitted the value of small doses, emphasizing however that this did not mean small doses or the smallest doses exclusively. Aegidi⁵ reported cases in which high dilutions failed, the patients being subsequently cured by lower dilutions. While he occasionally used dilutions which are not recognized by science at present, he denied the dynamization theory of Hahnemann. At any rate he repudiated the idea of fixation of the dose. Rummel introduced a point which was later the point of considerable controversy, namely, that the dilution was immaterial, the selection of the correct remedy being all important.⁶ There is, within definite limits, something in the point. The same thought is reiterated by Stapff⁷ who later became imbued with the high potency ideas of Jenichen, and the same is true of Gross.⁸ Veith⁹ felt the necessity of employing triturations and dilutions and administered dilutions as high as the 18th. Kammerer¹⁰ attempted to unite the high and low potency groups and favored the use of all doses. Schmid¹¹ began with high dilutions, but later gave larger amounts. He accepted the dynami-

zation idea but believed that it ceased with the 1st trituration. Watzke¹² wrote lucidly as always; he administered high potencies at one time, at another employed large doses and finally reached the domain of the 3-6th dilution. Trinks also favored the idea of low dilutions and the tincture. Schrön¹³ tried all dilutions including the Jenichen and found that the 3-6th are the most satisfactory, but that many drugs are valuable in the tincture or 1st dilution. Elwert employed the 1-8th dilution and believed that all cured and that lower dilutions such as the 1st might produce aggravation.¹⁴ No useful purpose is served by further citation of opinions as the same general ideas may be found in the works of Vehsemeyer,¹⁵ Noack,¹⁶ Goullon,¹⁷ Lietzau,¹⁸ Schneider,¹⁹ Wahle,²⁰ Kampfer,²¹ and many others.

The dose question has divided the homoeopathic profession more than any other single problem. However a vast majority of the school belong to what may be called the low potency group; that is, they use preparations between the tincture or mother substance and the sixth decimal trituration or dilution. With extremely powerful drugs or unusual sensitivity of the patient, they use a dilution one or two steps higher, but this does not mean stepping off into space. Occasionally one employs the 12th decimal dilution. A vast majority of the homoeopathic physicians with whom the writer is acquainted use the tincture to the third decimal dilution in acute diseases and the fourth to the sixth decimal dilution, occasionally a step higher, in chronic diseases.

Among the high potency group drugs are prescribed in all dilutions. Usually for them the "low" potency is around the 30th and the high potencies run up to the 100,000th or more. As a rule they are concerned with more or less selected practices in that they deal largely with chronic problems. It would create a false impression to imply that these high dilutions are always employed, but the general trend is, that an excursion by them into the realms of the third dilution is about as rare as the excursion of the scientific group into the realm of high dilutions.

In order to demonstrate the effect of a high potency clinically it would be well for such workers to report the treatment of some diseases in which the psychological influence of the physician can be excluded as far as possible. Such a disease would be syphilis. Then it would be necessary to prepare a high "potency", for example the 30th, using the precautions already mentioned to the extent that they can be applied.

Many physicians with whom the writer is on the most friendly terms use high potencies. He has never seen a result in the treatment of syphilis with the so-called high dilutions, nor in other cases,

which would withstand a strict critique, namely, that the preparation is a high potency on the one hand, and that the result can be attributed solely to the drug.

Since there is no opportunity to discuss this subject elsewhere it should be stressed here that "potencies", "dynamization", and related theories have nothing to do with the homoeopathic problem. They have been considered here merely because they have loomed as important subjects in non-critical literature.

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DEVELOPMENT OF IDEAS ON REPETITION OF DRUGS.—Aegidi was among the early writers to criticize adversely the long intervals

between repetition of doses in the treatment of chronic diseases, for example, several weeks.¹ He agreed that medication should not be repeated as long as improvement was noticeable, but held that the remedy should be repeated if no change was noted after a few days or if the improvement ceased. Wolf² described cases which were benefited by rapid repetition of remedies and other instances where a longer interval seemed advantageous; he also called attention to remedies which seemed useful when repeated often.

Hering³ counselled repetition, particularly when improvement ceased. Gross, Kretschmar, and Rau favored the repetition of the remedy at relatively short intervals.⁴ Rau⁵ advised repetition when improvement ceased or if the remedy had not acted within the anticipated period. Kampf⁶ emphasized that drugs had a much shorter duration of action than Hahnemann had supposed and that remedies should be repeated often and frequently in increasing amounts. Atomyr⁷ taught the importance of the cumulative effect but otherwise his theories look better on paper than in practice. Koch⁸ favored repetition and developed rules which still guide the profession, namely, large doses and short intervals for acute diseases. Griesselich⁹ with his fine critical sense emphasized the necessity for speaking of the duration of an action of a dose, rather than a drug, and also stressed the importance of the conditions under which a given dose operated. Therefore, he might repeat a drug in ten minutes or not for several days, according to the circumstances and he emphasized the importance of the rule: no repetition as long as improvement was noted. He fully appreciated the short interval in acute diseases and the long interval in chronic, but urged that cases be individualized in this respect. Trinks¹⁰ had no important views on the subject except that he spoke at a time when it sounded like treason to imply that repetition might be necessary. The views of Arnold¹¹ approximate those of Griesselich. Bönninghausen¹² quite naturally attempted to outdo Hahnemann on the length of the interval.

Thus it may be said that there was no essential disagreement on this point. The short interval and relatively large dose for acute diseases and the long interval and small dose for the chronic, summarizes the rule of interval. Naturally individualization must take precedence over the rule.

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DEVELOPMENT OF ISOPATHY.—Limitations of space permit only a brief discussion of this subject. Hering¹ spent considerable energy developing the isopathic idea, and introduced some remedies of merit, others quite ridiculous. However, he may be accredited with the introduction of nosodes into homoeopathic practice. Regrettable over-enthusiasm cast a spell of doubt over his valuable ideas and this has prevented him from becoming hailed as the re-discoverer of specific therapy in the usual sense of the term. Hering began his publications on isopathy in 1830, Lux in 1833. This point is not without historical interest, but it is particularly worthy of note that two of Hahnemann's students, so to speak, may be properly denominated as innovators of this splendid practice.

Gross² also anticipated Lux but, since many regarded him as a "hunter of novelties," his impressions did not receive the attention they merited. Stapf³ recognized the principle involved as far as the infectious diseases were concerned, but later denied that it could be extended to organ constituents. Rau⁴ also restricted the principle to infectious diseases, but later became disgusted with the freedom with which all types of substances were introduced under the name of isopathy.⁵ Dufresne⁶ regarded the introduction of the isopathic idea as a great advance, an opinion shared by Müller.⁷ Kammerer,⁸ Kurtz,⁹ Genske,¹⁰ while Veith thought the application limited¹¹ and Buchner¹² condemned it, except for infectious diseases. Hermann¹³ extended the principle to organ products and reported some miraculous results, which perhaps contain a modicum of truth. His work was refuted by Genske.

For these reasons it would seem that the homoeopathic profession was practically united on the merits of isopathy, but to different degrees. Hahnemann regarded vaccination against small pox as one of the greatest evidences favoring the claims and truth of homoeopathy. Physicians who refuse to vaccinate according to the commonly accepted methods cannot find support for their attitude in Hahnemann or homoeopathy.

As the individual sections have been summarized at the close of each account no recapitulation seems necessary. However, it is proper to call attention to the apparently arbitrary arrest of the account of the development of homoeopathy at this point. This decision seemed justified for many reasons; however it is sufficient to mention merely two important considerations.

The work of Virchow and the development of bacteriology belongs to the present era of medicine. Any attempt to discuss the evolution of simile thinking during that transition era with the intention of separating the recent past and the present would probably be futile since the gradations between 1875 and 1935 merge with almost imperceptible gradients. For this reason it seemed advisable to interrupt the narration of the evolution abruptly at the point where the modern era begins. Moreover this period, at least until the turn of the century, found the homoeopathic profession busy with the establishment of institutions, local, state and sectional societies, boards of examination, enactment of protective legislation. The chief result of this diversion of energy, from the standpoint of the study, was a stasis in scientific advance. To discuss the legal controversies would require not only a large volume but might tend to rekindle almost extinguished flames.

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PART II

THE MODERN CONCEPTION OF THE SIMILE

INTRODUCTION.—While the sections which follow immediately may seem, at first, to have little relevance to the subject under discussion, quite the opposite is true. Whether or not the viewpoint advanced finds approval is quite unimportant; but if the modern conception of the simile is to be comprehended, appreciation of the attitude expressed is absolutely essential. To minimize the possibility of confusion, a brief introduction precedes the next section, by means of which the general purport of the text may be emphasized.

Years of contact with medical scientists convinced the writer long ago that the elimination of traditional difficulties, mentioned or implied in the preceding sections, can accomplish much in the way of removing barriers often created by the passive acceptance of hearsay reports about the simile. For this reason the origin and evolution of important aspects of the simile were reviewed. On the other hand, the writer has gained the equally firm conviction that the clarification of historical issues, interesting and valuable as this may be, is, by itself, insufficient to excite active interest or to ensure real participation in the elucidation of the problem. The chief source of this tolerant but passive attitude seems to arise from the position adopted by most medical investigators toward science. Moreover, there is strong presumptive evidence that the recent and gradually increasing interest in the simile finds its major source of stimulation in the equally evident re-orientation of this scientific attitude.

The viewpoint prevailing in medicine, almost exclusively in the recent past and to a large extent at present, is usually designated as the "mechanistic." Most mechanists do not regard the "causal law" as a theory but as a natural law of supreme importance. On the other hand, it may be confidentially asserted, for reasons advanced later, that from the very nature of the simile, little interest can be expected among those oriented exclusively by "mechanism." The reason is discovered in the fact that the simile is not conducive to the formulation of comprehensible problems for solution by "mechanistic" thinking. It is equally true that the simile is not a "natural law" and, while the methods for its

investigation are not totally dissimilar to those employed in "mechanistic-causal analysis" and "law" investigation, the formulation of the problem and the experimental set-up, do differ decidedly. It is, therefore, not surprising that passivity and disinterest continue to prevail in many quarters. More important however, is the fact that if "mechanism" is exclusively correct, there is a high degree of probability that the explanations advanced for the simile are wrong, and the significance of the simile may be far less than many supporters believe.

The attitudes and methods suggested in the text are not novel, but they are not commonly employed, and are still more infrequently advocated. The popularity of other attitudes and methods rests, to no small extent, upon their fruitfulness. It has therefore seemed advisable to create some justification for the suggestion of supplementing them by less popular viewpoints. Again it is highly probable that a majority of readers, consciously or unconsciously, subscribe to the "mechanistic" viewpoint. For these and other reasons it has seemed most profitable to proceed from the generally known and widely accepted to the generally neglected and consequently largely unknown, in short, to approach the modern simile by examining some of the obstacles to its acceptance, and these chiefly concern "mechanism."

Although the most confirmed mechanist will not deny the existence of other methods of consideration, his practices and utterances leave no doubt, in the vast majority of cases, that he regards the "mechanistic" approach alone as valid and exclusively correct. The following sections are intended to show that there are other fruitful methods of consideration. Moreover, "mechanism" in place of being hypothesis-free and exact actually contains serious and unsuspected dangers when its extremely hypothetical nature and inexactitude are forgotten. Finally there are two alternatives to "mechanism," which are compatible with simile thinking.

MECHANISM.—As the word "mechanism" is employed loosely in medicine it seems advisable to discuss the various forms separately. In general there are two varieties, dogmatic and methodologic. Dogmatic mechanism asserts the organism *is* a machine or mechanism. As such it makes a positive assertion about the ultimate nature of the organism. It tends to be opposed by an equally metaphysical vitalism and, since both parties make a prophecy which only the future can settle, there is an immediate stalemate. All the various forms of dogmatism seem to possess a common feature: they assume that everything is already known in principle and the future of science will consist merely in filling in details. In medicine such an attitude is unduly presumptuous.

Methodological mechanism makes no assertion about the ultimate nature of the body but states that it can be investigated scientifically only by treating it *as if* it were a machine or mechanism. To logically accept this attitude, it is essential first to examine thoroughly the nature of mechanistic explanation, second to show that no other method of thinking is possible or can possibly be called scientific. Adoption of the latter course usually results in logomachy regarding "scientific." Usually a point is reached where scientific and philosophic thinking are differentiated, whereby scientific thinking is identified *by definition* with the mechanistic view. In extreme forms science is identified with mathematical physics, everything falling outside this field being regarded as extra-scientific. Obviously the amount of biological material amenable to treatment by mathematical physics is extremely small, although it represents a legitimate field for inquiry. For the sake of consistency such mechanists ought to delete extra-scientific conceptions from their vocabularies, but they seem to find it impossible to proceed without talking about cells, evolution, organs, organisms, etc. For these reasons it seems best to discuss the various types of mechanistic explanations.

a) MECHANISM IN THE SENSE OF CLASSICAL MECHANICS.—Mechanism as the equivalent to explanation by the principles of classical mechanics in the sense of Newton and Hertz, is no longer common in medicine. Vestiges are still encountered, for example, in the following remark by a physiologist:

"Physiology as the doctrine of life must therefore confine itself to the material vital phenomena of organisms. It is self evident, however, only such laws as govern the material world will be found governing vital phenomena—the laws, i.e. of mechanics. Explanatory principles of vital phenomena must therefore be identical with those of inorganic nature—that is, with the principles of mechanics."¹

If physiology "must confine itself" to certain material phenomena, apparently there are some non-material phenomena also connected with life. If so, according to the definition, physiology is not the doctrine of life but simply a part of it. Again, for the matter to be "self-evident," the entire world would have to be a perfectly uniform homogeneous gas, in which case there would be some basis for the assumption that all parts were governed by the same laws. But obviously this situation does not obtain. Again, it is not true that the laws governing the material world are exclusively those of mechanics, at least, as the physicist understands them.

Since an appeal is made to the mechanical explanations of physics, it might be well to note the physicists and chemists are

by no means as assured about mechanism as one might presume. Whitehead² states: "the appeal to mechanism on the behalf of biology was, in its origin, an appeal to the well attested self-consistent physical concepts as expressing the basis of natural phenomena. But at present there is no such system of concepts." Weyl³ remarks: "It must, once and for all, be said quite clearly, that physics is no longer able to support, in its present state, the belief in a closed causality of material nature resting on strictly exact laws." Broad⁴ finds no necessity for making an assumption of pure mechanism: "I think we are justified in saying that the possibility of dealing scientifically with a given region of phenomena, does not imply that it must be known to obey even microscopically the more rigid forms of mechanism. And if anyone says that its explicability must depend upon its actually doing this, whether the fact be known or not, he is asserting pure dogma, for which, from the nature of the case, there can be no evidence." It would seem that not only the hypothetical nature of the borrowed idea has been forgotten, but also the hypothesis is considered dubious in its own field. Moreover, physiologists would seem to be somewhat naive toward physics, treating it more dogmatically than the physicists themselves, for Bridgeman⁵ regards the desire for mechanical explanation "perfectly unjustifiable" in physics.

To make it good measure another aspect may be mentioned. In physics all mechanical explanations imply that the phenomena under discussion obey Lagrange's equations or some substitute for them. As far as the writer can find, no physiologist has attempted to determine whether or not the phenomena of physiology are actually amenable to such treatment. Apparently it is presumed that they are.

In summary it appears that instead of this form of mechanism being exact and hypothesis-free, it is actually based upon a hypothesis borrowed from physics; moreover the validity of this hypothesis is seriously doubted in physics; finally its presumptions have apparently not even been tested in medicine. It seems to base itself upon a "self-evident" proposition, which is not only not self-evident but actually repudiated by the senses. Another supporter of this form of mechanism advances the doctrine as the "dream and faith . . . of the scientific man."⁶ This is a more modest attitude, but science would seem to be in a bad way if the sole and exclusively correct method of thinking rests upon such a basis. At least it would seem to be scientific folly to seriously discredit attempts at exploration of other ways of scientific thinking.

b) MECHANISM AS THE EQUIVALENT OF PHYSICO-CHEMICAL EXPLANATION.—This meaning of the term is the most common in medicine at the present time. It is assumed that an explanation of life is possible by resolution of the organism into partial events which are independent from each other and capable of isolation. The laws of life are physico-chemical laws. No special theory of life is necessary, since life can be explained completely by knowing the single parts and events physico-chemically. Usually it is assumed that the physico-chemical structure must also be known and thereby the machine explanation is interwoven: the organic events are still resolvable into physico-chemical processes, but these run their course as an aggregate of machines which make up the organism.

Many medical scientists presume there is only one science. Moreover, they assert that the strict natural sciences, physics and chemistry, form the sole scientific basis of medicine. Medicine is obviously primarily concerned with mankind. Again while the medical investigator may choose whatever means he desires in order to solve his problem, in this case most regard physico-chemical means and conceptions, exclusively correct. Then man with all of his physical and psychical problems can be conceived scientifically only physico-chemically. If this is not the case, then it is possible that other means are given for conceiving man, in which instance the physico-chemical viewpoint becomes merely one among others. The assertion that there are "only" material things in the world perceptible to man is such an obvious desertion from science and entrance into the domain of belief⁷ that it hardly requires discussion. Even such a presumption seems somewhat premature at a time when some important branches of medicine and physiology are compelled to employ "biological" conceptions almost exclusively. If one believes that the suggestions made above are overdrawn, he ought to recall that Virchow⁸ reminded the mechanists of his day that their procedure of laying a fairly narrow scheme of physico-chemical formulas on natural phenomena led to a conclusion "which is not less dogmatic than the dogmatism they attack so zealously." Only recently Buytendijk⁹ found it necessary to recall to physiologists that the great masters of physiology did not "limit themselves to explaining all material living events as physico-chemical actions." In medicine Bier¹⁰ emphasizes that eternal truths were found by other than the "naturalistic" methods and adds "all that is not adapted to its system is rejected." If there was not a widespread adherence to an "exclusive" physico-chemical mechanism in medicine, there would hardly be an occasion for an increasing number of writers

as Verworn,¹¹ Krehl,¹² Bier,¹³ v. Bergmann,¹⁴ Goldscheider,¹⁵ Sauerbruch,¹⁶ O. Müller,¹⁷ E. Meyer¹⁸ to object to it. In substance they all concur with Krehl's summary: "biology cannot achieve an understanding of the living processes with the conception of mechanistic causalism alone."

It should be stressed here that the physico-chemical method and conception have proven extraordinarily fruitful, and undoubtedly more important discoveries will be made by its application. There is every reason for assuming that the known biologic products, represented for example by the endocrine substances, form an extremely small fraction of the probable number existing in the body, so that enormous progress in this direction may be reasonably anticipated. But the question is: whether or not the physico-chemical method of consideration is "exclusively" correct. The citations introduced above indicate that many and great discoveries have been made likewise by non-physico-chemical methods. One thinks of Mendel and Darwin.

In recent years biology has taken its methodology under advisement. While it remains the "science of organisms, of living things," it regards itself as a "natural science," that is, a science of things which are recognized by perception as objects of the outer world, in space. In this definition the "psyche" is not denied, but by definition it is relegated to the domain of psychology, whereby biology becomes a "natural" science. The problem is not whether or not a similar division ought to be made in medicine, nor whether a ("psycho-somatic") unit can be profitably subdivided into domains whose workers proceed with startlingly little awareness of results obtained in fields outside their specialty. Nor is the question simply one of the validity of assigning the "subjective" aspect of the only form of life capable of reporting this to another science, although this could be examined in reference to the "oneness" of science. For the purpose of discussion it will be assumed that such a division can be made and that it is methodologically advisable, and an attempt will be made to determine whether or not having eliminated the "psyche," the physico-chemical approach is exclusively correct.

The chemist investigates the organism by separating out single constituents, molecules, atoms, electrons; the physicist considers the heat of the body as the movement energies of molecules,* etc. Physico-chemical investigation attempts to resolve events and substances into elementary parts, in short, a definite substance or event is detached from the living and analyzed. Protoplasm is shown to consist of proteins, carbohydrates, fats, etc.; the actions of enzymes are studied. Moreover the investigation is summative;

it proceeds from the viewpoint that there are "building" stones, that these form cells, aggregates of cells which form the organism. This procedure apparently characterizes several aspects of biology and medicine: physiology considers the body an aggregate of cells; developmental mechanics, an aggregate of determinants; genetics, an aggregate of genes. Ultimately in each there is a physico-chemical mechanism and the total organism can be resolved into single physico-chemical processes.

In speaking of mechanism, Wilson¹⁹ states: "existing mechanistic interpretations of vital phenomena evidently are inadequate; but it is equally clear, as some one has said, that they are a necessary fiction." In another place²⁰ in speaking against Loeb's expression of a chemical machine he remarks: "even the most superficial acquaintance with cell activities shows us this conclusion (chemical machine) cannot be taken in any crude mechanical sense—the difference between the cell and even the most intricate artificial machine still remains too vast to be bridged by present knowledge. Nevertheless we accept the hypothesis that the difference is one of degree rather than kind, because it has proven fruitful in discovery and has kept us moving in the right direction." Accordingly the "exclusively" correct method seems to be a "hypothesis" and a "fiction." As stressed above many important facts have been and probably will continue to be discovered by this method, but "knowledge" does not come from a "heap of facts," nor do they prevent a science from being a "medley of ad hoc hypotheses." The method has been fruitful, but a statement implying "it has kept us moving in the right direction" means that we know where we are going and that we are following the right route. There is reason to doubt the complete accuracy of these implications.

One obvious limit of the energetic conception lies in the fact that living substances and events never occur as such but always in connection with living organisms. The physicist may speak of free fall, the chemist of sulphuric acid, but the biologist does not encounter protoplasm growing "wild" in nature. He may, of course, speak of maintenance of irritability of protoplasm. But if reflection indicates there are not living substances and events, these always being referred to organisms, then a limitation of a method is apparent since the event is placed in a realm where only an energetic conception is possible.²¹ In other words the physicist proceeds from single components, but biology must regard the organism as a totality.²² The physicist, upon dividing a block of iron into two parts, finds that each part displays the same properties and reactions. But obviously there is not a "dog" substance, nor a "lion" substance. If tissue is removed from the

multicellular organism or protoplasm from the unicellular it loses its "living" properties and "dies."

Protoplasm is not found free in nature, but always in conjunction with cells. According to cytologists the cell is infinitely complex and it contains a highly elaborate system of parts. Each part has a remarkably intricate organization if, for example, there is any truth in the chromosome theory of heredity. Moreover there are a large number of "formed" bodies, the mitochondria, Golgi bodies, etc.

A chemist may grind up a number of cells in a mortar; he may apply the term protoplasm to such ground up masses. Both the term and the method are perfectly justified. But clearly no such mass is found either "wild" in nature, or in the living organism. If a large bomb was dropped upon a populous town, the term "townplasm" could be applied to the debris which remained. But it would be quite absurd to say that towns were composed of townplasm and that a sufficient knowledge of such debris could explain the "organization" of towns. Unless the biochemist confines himself to fluids as blood and urine, which can be withdrawn from the body, he must, it seems, "not merely ignore any organization above the chemical level, but must also destroy it in order to apply his methods."²³ The information obtained is of utmost importance, but it is confined to the "chemical" level. It is unfair to expect it to transcend those limits and absurd to pretend that it has no limits.

It is becoming increasingly evident that "we murder to dissect" to employ Wordsworth's terse expression. One never chemically analyzes the actually living, but always that which has been killed.²⁴ It is completely uncertain how many single substances into which the chemist resolves protoplasm are actually present in the same way in the living organisms and how many are artificial products. The structural chemistry of proteins offers little solace here since the atom grouping may occur only in death;²⁵ moreover the phenomena of death are in no way identical with chemical fragmentation.

Apparently the "organization" of protoplasm is important. In this way "chemical" and "physical" attain new meanings, and the confirmed mechanist may find another alternative than "vitalism." A lump of iron is a chemical entity in which "iron" stands for a chemical conception. If the iron is fastened into a padlock, it is still susceptible to chemical analysis, but the padlock cannot be fully described in terms of chemical composition. It is said to have attained an "organization" above a chemical level. As stated above, the physico-chemical approach is enormously fruitful;

but its information is confined to that level. In organization the "totality" is the important element. In many respects this is quite the opposite of the "isolating" policy of the physico-chemical attitude. To employ the latter exclusively is to ask information which it cannot furnish, and one may wonder if it has kept us moving in the "right" scientific direction.

The popularity of the method is easy to understand: problems may be easily developed, fruitfulness is reflected in equal ease in obtaining results. The result is reflected in an enormous literature composed of isolated facts. Data are provided in great abundance; interpretations are of great complexity. "The continual heaping up of data is worse than useless if interpretation does not keep pace with it. In biology this is all the more deplorable because it leads us to slur over what is characteristically biological in order to reach hypothetical causes" (Woodger).

The physical laws so far discovered are relatively simple, but they have required the most brilliant mathematical talent for their elucidation. There is no reason for believing the "laws" of biology equally simple. For example many aspects of medicine and physiology deal largely with chemical changes, for example, nutrition. On the chemical level investigation has proven interesting and valuable. But it is more than doubtful whether the problem of nutrition can be solved physico-chemically; for example, if physico-chemical analysis will teach how food gets into the stomach in the first place and how it happens that meat gets into some stomachs and only grass into others. One need merely read Virchow's polemic²⁶ against Robin to discover that nutrition has been "explained" in the past. While the modern scientist rightly disregards Robin's "molecular renewal," in many instances he accepts "alterations of the colloidal milieu" and other conceptions borrowed from physical chemistry quite naively as "explanations" for living phenomena.²⁷

The policy of isolating an event or substance has also led to the development of consideration by analogy. It may be presumed that no one doubts that an "isolated" event of the organism in many respects pursues the same course as within the body: enzymes decompose material in a test tube as well as in the body. Likewise inorganic models can be made to imitate many bodily processes. Rhumbler's work contains an enumeration of such "living analogies."²⁸ The intestinal wall is represented by a dead membrane, and behaves in accordance with the laws of endosmosis. The manifestations of the circulation are explained by laws of hydrostatics and hydrodynamics. Respiration is explained by the laws of aerodynamics, absorption and diffusion.

There are several obvious obstacles to this method of consideration. In the first place, all of these devices require a "creator," an idea absolutely repugnant to the physico-chemical viewpoint. In the second place, the materials employed in their manufacture have no semblance to these of the imitated object. Thirdly, they are composed of homogeneous and stabile materials, whereas the living are made of heterogeneous and labile. Fourthly, they exhibit no evidence of the most characteristic phenomenon of the living cell, namely, metabolism.

Moreover physiology actually teaches apparently the opposite of these "analogies." The fat droplet is engulfed, passed through the intestinal wall, but the much smaller fragment of pigment is rejected. In normal life, in the absence of a "catastrophe," the worthwhile is incorporated, the useless rejected; this holds even for single celled organisms. The mammary glands select out of the blood stream, which varies in composition, those substances exactly in the proportion in which they are required for the growth of nurslings. In circulation the movement of blood is passive; the living phenomenon is the active function of the heart. A bellows once in motion will expel and take in gas according to the laws of dynamics. The gas is passive. How did the bellows develop, how does it maintain itself, what set it into motion? These are problems of life.

Thus what the physico-chemical attitude apparently succeeds in grasping are largely heteronomic events. v. Bunge²⁹ said: "all the processes which can be explained mechanically are just as little phenomena of life as the movement of the leaves and branches of a tree, shaken by a storm, or the movement of pollen which the wind scatters from male to female. Here we have to do with a movement which is indispensable to life. And still no one would maintain it was a vital phenomenon, simply on the basis that the pollen behaves absolutely passively in the movement."

This passivity also emphasizes another aspect of the heteronomic nature of the event. The work performed by such "analogies" has no relation to maintaining themselves or type, whereas this is characteristic of "living" phenomena.

One compares the eye to a camera obscura. The retinal picture occurs in the posterior chamber of the eye according to the laws of refraction as the picture of a photographic plate. This is not life, for the eye is passive, the picture occurs in the dead eye. The development of the eye is a living phenomenon. How does this complicated apparatus come to exist? How do the cells of the tissue add themselves to one another for this wonderful structure? The succession of developmental stages can be observed, but this

is not the "how" of the matter. The process of accommodation is a living process, etc. As Ungerer states:³⁰ "the events of the body of a living dog form a totality to which each event contributes in that it runs its course in a definite way. The events in the body of a dead dog may be fully compared to the weathering of a stone by the wayside."

Schultz³¹ emphasizes this point in his interesting discussion: "wherein does such a mechanism differ fundamentally from the living in the reaction to a stimulus, its movements from those of life? In that all the reactions of the organism serve directly or indirectly for the maintenance or for re-establishment of the necessary form."

The question may also be approached from another angle. Naturally any mention of "purpose" is foreign to an exclusive "physico-chemical" conception. For this reason the mechanist cannot speak of adaptation, purposefulness, individuality, totality, unity, organization, harmony, regulation, activity, autonomy, organism, and remain consistent. For even a physico-chemical machine is made to realize some conscious human purpose, and its parts work together for that purpose, even though it is not to secure its own persistence. Mechanism finds itself unable to work biologically without the assumption, at least, of an "internal teleology," and consequently is in constant contradiction with its own premises.

It is important to note the consequences of this attempt at consistency and they are implied clearly in Haldane's writings:³² "if . . . we are teaching the physiology of the kidneys we must teach the main facts bearing on a possible mechanism of the secretion of urine. We must discuss the possible influences of filtration, diffusion, etc., in the process, leaving out of account all details irrelevant to this discussion; and when at the end it turns out that the essential mechanism of secretion is quite unknown there is nothing further to do than to pass on to the next subject. Actually it is known that, mechanism or no mechanism, the kidney fulfills its functions of regulating the composition of the blood and that it does this with marvelous delicacy; but the facts relating to this, do not fit into the plan of exposition of the subject and have too much of a smack of old fashioned teleology about them. Hence they are completely ignored or scarcely touched upon . . . the fact that the body lives as a whole, each organ or part fulfilling its proper functions and adapting itself to every change, is scarcely touched upon, while a vast mass of unrelated and unassimilable mechanical detail is carefully recorded and described."

It has been urged above, and again in this citation, that the

body lives as a whole; but the physico-chemical method is a procedure of abstraction, of isolation.

Haldane also urges that part of the subject is ignored. The reason for this is not difficult to discover. Elsewhere he has said: "if we are investigating secretion, we are measuring the mass or volume of the substances secreted, or their chemical composition or perhaps their osmotic pressure, or concentrations of ions in them. If we are investigating muscular contraction we are measuring the rate and the extent of contraction or the accompanying heat production or electromotive phenomena. The phenomenon which we observe is always some physical or chemical change. The methods we use are physical and chemical methods and the resulting facts are consequently physical and chemical facts."³³

In other words only that part of the event is measured which is measurable. No one would care to assert that what is perceived is more than a small surface zone of the actual event. Of this only a small fragment is measurable. Mathematical treatment of the event would represent remarkable progress if one could conceive the organic event in its entire complexity according to definite formulae. But usually the non-measurable fraction is relegated to the "irrational." Such treatment can hardly be called "exact" regardless of how replete the work may be with formulae and figures. Undoubtedly numbers and measures are yardsticks for the measurable and mathematics may be valuable in the quantitative estimation of nature, but it does not describe nor explain the characteristic qualitative attributes. Those interested will find Dingler's account of the limitations of the mathematical method in science worthy of perusal.³⁴

Attempts to apply mathematical-physico-chemical explanations to biologic phenomena frequently result in tautology whereby the situation is complicated rather than clarified. Heidenhain³⁵ has reported an example in Pordes' elaboration of the Dessauer theory of x-ray action: "Considered from the logical side, with Pordes it involves what Study³⁶ has designated as tautology. One can write the hypothesis of Pordes in the form of an equation: clinical observation showed varying power of resistance against radiation; the conclusion was: varying sensitivity of the cells. Pordes asserts: varying sensitivity = varying ultra-microchemical stability. Ergo: varying power of resistance (Widerstandskraft) = varying power of stability. Expressed exactly the left side of the equation is German, the right side Latin, but both are the same."

Power of resistance and sensitivity are biological conceptions by which at least something is understood. What progress is made by replacing this comprehensible terminology by a physico-

chemical formula, which is almost empty of content and which unnecessarily complicates the situation?

Heidenhain has also stressed the paradoxes to which exclusive mechanistic conceptions lead:

“Dessauer said: ‘A swallow of hot water or a hot compress introduces into the body a multiple of energy in comparison to a fatal x-ray radiation.’ How Dessauer arrived at such a calculation he does not say. This form of thinking shows above all, that one must not measure by mechanical means, the influences of the environment on a living organism which stands under peculiar inner laws not known to us. How many gram-calories are contained in a few centigrams of opium or some milligrams of strychnine?”

In speaking of the selection of nutriment, the incorporation of the worthwhile and rejection of the damaging, v. Bunge³⁷ recalls the observations of Cienkowski made on *Vampyrella*, an amoeba:

“*Vampyrella Spirogyra* is a microscopically small, naked, reddish colored cell which seems entirely structureless. Cienkowski was not able to find a nucleus in it and the fine granules in the protoplasm are perhaps only nutritional rests. This microscopically small protoplasmic droplet seeks among all types of aquatic plants for a very definite type of alga, the *spirogyra*, and refuses all other nutriment. One sees it send out pseudopodia, sees these move about until they touch a *spirogyra*. Then it attaches itself on the cellulose wall of its cells, dissolves it at the point of contact and sucks in the contents and then wanders off to the next cell and repeats the same maneuver. Cienkowski never saw the *Vampyrella* attack other algae nor take any other material; *Vaucheria*, *Oedogonia*, which he placed before it intentionally, were constantly avoided. In another monad, *Colpodella pugnax*, Cienkowski observed that it fed exclusively on *Chlamydomonas*: it ‘taps the *Chlamydomonas*, milks out the chlorophyll and goes on.’ ‘The behavior of these monads’ states Cienkowski, ‘in the seeking and ingestion of nutrition is so remarkable that one must believe they see the actions of a conscious nature before them.’

“If this capacity of selection of nutrition appears in the simplest cell, the formless, structureless protoplasmic droplet—why not also in the epithelial cell of our intestine? As the *Vampyrella* selects the *Spirogyra* among all aquatic plants, so the epithelial cells of our intestine, differentiate the fat droplet from the pigment granule. We know that the epithelial cell of our intestine does not permit the inclusion of a great series of poisons although these are quite easily soluble in the gastric and intestinal juices. Indeed we know

that when we inject these poisons directly into the blood, reversely they are excreted through the intestinal wall."

Near the end of his discussion are found some remarks which may not be amiss here:

"In the activity—there is the riddle of life. But the conception of activity has not been created out of sensory perception but from self observation. We transfer that created out of our own consciousness to the object of our sense perception, to the organ, the tissue element, to any small cell. There is the first attempt at a psychologic explanation of living phenomena.

"If it also seems that with the sole help of physics and chemistry we are not able to explain vital phenomena, then we may still ask: what may we expect from the adjuvant sciences of physiology, what may we expect from the morphologic disciplines, anatomy and histology?

"I assert that they also will not bring us nearer to the solution of the riddle. Because if with the help of the scalpel and the microscope we divide the organism down to the last element, even if we attain the simplest cell—then the greatest riddle lies before us. The simplest cell, the formless, structureless, microscopically small protoplasmic droplet, still shows all the essential functions of life: nutrition, growth, regeneration, movement, sensation, indeed the same functions which at least substitute for the 'sensorium' the psychic life of bigger animals. I recall once again the observations on *Vampyrella*, but believe it advisable to detail a more striking observation which Engelmann has recorded in *Arcella*.

"*Arcella* are likewise single organisms but more complicated than *Vampyrella* in so far as they have a nucleus and secrete a shell. This shell has a convex-concave form. In the middle of the concave side of the shell there is an opening from which pseudopodia emerge and at the border of the shell a glassy protuberance appears. If one brings a drop of water which contains *Arcella* under the microscope then it often happens that the *Arcellae*, so to speak, fall upon their back, that is, with the convex surface touching below so that the pseudopodia appearing at the border of the shell do not find any point of contact. Then one sees an air vesicle develop in the protoplasm at the side in the region of the border; this side becomes specifically lighter, it raises itself; the animal then comes to stand on its opposite narrow border. Now it is able to lift itself with the pseudopodia on the under surface and to turn over so that all the pseudopodia lying on the border touch the under surface. Then the air vesicle deflates and the animal moves around. If one brings a drop containing *Arcellae* on the under surface of an air chamber, then

at first, in consequence to gravity, they collect at the lower surface of the drop. If they find here no point of contact, then they develop great air vesicles through which the entire animal becomes lighter than water in specific gravity so that they rise in the droplet of water. If they arrive at the glass surface in such a position that they cannot fasten their feet then the air vesicle will be made smaller on one side or larger on the other or at times simultaneously one becomes smaller and the other larger until the animal touches the glass surface with the border of the shell and can turn itself over. As soon as this occurs one sees the air vesicle diminish: the animal can now crawl on the glass surface. If by careful contact with a fine needle one loosens it from the surface so that they again fall to the lower surface of the drop, they develop a new air vesicle, rise again, etc. And as one labors to bring it into an unfavorable position, they will see through the development of an air vesicle at the corresponding place and of corresponding size in order to reverse the situation into a position suitable for movement. As soon as this goal is attained, the vesicle always diminishes again. 'One cannot deny' states Engelmann 'that these facts indicate psychic processes in the protoplasm.'

"Whether this conception is correct or not, I shall not attempt to decide. Indeed I unconditionally concede the possibility that the manifestation will find a pure mechanical explanation. I have only introduced these facts in order to show with what complicated vital phenomena we have to do, even here, where the microscope has already attained the limit and how little has been attained up to the present in mechanical explanation of vital phenomena. Because the events in this single celled nature are at least just as complicated as the events in each cell of our body. Each of the innumerable microscopically small cells which compose our complicated organism, is a wonderful structure, a microcosm, a world in itself. . . ."

"But we must also concede the possibility that the obstacles and difficulties which rise up mountain high at present before physiologic investigation, will finally be overcome. But at the moment it is not apparent how we shall make an essential step farther with the sole help of physics, chemistry and anatomy. In the smallest cell—there already exists all riddles of life before us and in the investigation of the smallest cell—there we have already attained the limits with the available assisting agents.

"But we can perfect our assisting agents! We can increase magnification! The cell which appears structureless today, will allow a structure to appear tomorrow. The cell which is not nucle-

ated will show a nucleus by the use of some new staining process. And likewise the nucleus is no longer structureless; it already shows a complicated structure so that the mere observation and description requires the complete working powers of many students! But a complicated structure is not an explanation; it is a new riddle: how does this complicated structure arise? And will an insight into this structure also give an understanding for the simple processes which we can observe in *Vampyrella* and *Arcella*? Will it completely solve the great riddle, the greatest riddle of all—the riddle of inheritance—inheritance through a small cell! And if this holds even for a small cell, how much more for our complicated organism!"

Limitations of space prevent further discussion of this form of mechanical explanation, but perhaps sufficient has been presented to create doubt in regard to the exclusive validity of physico-chemical mechanism as ordinarily viewed. It is fruitful, relatively easy to apply, productive of quite immediate results, and leads to the production of many papers and the discovery of innumerable isolated facts. However it is not exact nor hypothesis-free. These are not, in themselves, shortcomings, except when the existence of fictions is forgotten and purely hypothetical presumptions tend to be regarded as proven. With it one tends to measure the measurable and likewise tends to disregard the remainder. It proceeds by a policy of "isolation" of single events, thereby disregarding the totality, the order, the organization. It seeks to answer all questions on the level of physics and chemistry when actually other higher levels exist. It employs analogy conclusions based upon extremely remote analogies. It speaks inconsistently by employing a terminology not comprehensible in the frame of physics and chemistry. It renders understanding of events difficult by the introduction of tautologies and leads to paradoxes. It measures and records heteronomic events that are as little characteristic of life "as the movement of the leaf in the wind." For these reasons the outlook of biology is extremely dismal, if physico-chemical mechanism is the "exclusively" correct conception. It seems all the more forlorn when Tschermak's remark is recalled: "if physiology has the task of 'explaining' living events by tracing back the phenomena completely to inanimate materials, today, it has as good as not yet begun its task."³⁸

One should not overlook that a fruitful "mechanism" substituting for a sterile "vitalism" may crystallize into an equally rigid dogma. The temporarily "successful" explanation may conceal further problems. Too often the purely hypothetical nature of the presumption is forgotten and the explanation attains greater reality

than it was originally supposed to possess. When an eminent mathematical physicist asks, "What is the sense of talking about a mechanical explanation when you do not know what you mean by mechanics?"³⁹ biologists perhaps ought to take heed and perhaps wonder whether they actually possess infallible principles of interpretation.

c) MECHANISM IN THE SENSE OF THE MACHINE THEORY.—As it was necessary to refer to the machine theory in the preceding section, no detailed discussion is needed here. It may be added, however, that the metaphor "machine" in itself is questionable since there are no machines which maintain themselves, regenerate or adapt themselves, nor for that matter no machines which come into existence without the participation of human efforts. In the machine theory one also finds it impossible to carry out the postulate without employing foreign conceptions, for example, "aim" and "purpose." If one states that machines are constructed for a purpose, this necessitates a "builder." Moreover energetics deals with the performance of machines, not their development. v. Uxekull⁴⁰ points out that all theories deriving structure of organisms from physics, chemistry, and general mechanics may be dismissed from the start. Even if one had all the aids provided by physics and chemistry for constructing a machine, it is impossible to build them, living or dead, without the "immanent" factor, namely, the building "plan."

Machines can be devised to react to influences in a stereotyped manner, so-called "machine conditions." Here they react to definite stimuli; but they cannot react purposefully to requirements not foreseen in advance.

Naturally the mechanists have not been so obtuse as to not recognize the problem of the "builder" of the machine, which is answered by the selection theory. Bertalanffy has depicted the situation:

"One thinks of a hog which roots with its snout in a heap of letters. Through rooting of the animal all possible combinations of letters occur. For an infinitely long time the results of this activity was merely meaningless compositions; the philosophic hog however has time and roots through all eternity. And then see: finally a moment occurs where, accidentally thrown together, Goethe's Faust appears, who also owes his existence, not to sentient thinking, but the great powers: *sacre majeste le hazard.*"⁴¹

In other words the builder question is answered by accidental development, selection, summation of single variations. Jordan⁴² has written well on this subject and those interested are advised to read his account. However it may be noted that Darwin concerned

himself with small alterations of properties, as the length of an organ, etc. Such results were applied deductively to the development of organ systems.

To apply Darwin's thinking, the organism must be subdivided into many parts, until each part is so small that its appearance could be comprehended as an accident, but still this part has value in and of itself for selection. As an example one may take certain parts of the accommodating eye. This possesses a lens, enclosed in a capsule, which is made tense by a wreath of fibers, into which muscles insert, the muscles forming a definite angle, a nerve from a definite center connecting the accommodating impulse to the muscle, a nerve leading from the retina to this center so that visual accommodation may occur reflexly through tension of the accommodating muscle. Each of these parts is typical; in isolation they are meaningless. The muscle without the nerve would be "pathologic," and its possession certainly would not confer superiority over other forms. "Darwinian organ systems are based upon a sum of diseases, not a sum of useful alterations." Bleuler⁴³ has calculated the approximate probability of the accidental development of the correct position of the cornea, lens, retina; it amounts to $1:10^{42}$ th. How much this would have to be increased for the development of a "purposeful" organism is suggested by recollection of the fact that there are at least ten known, absolutely necessary events which transpire in a liver cell, in a volume about equal to $1/100,000$ th of a head of a pin. "Is it believable that such a chemical laboratory, in comparison to which our chemical laboratories seem to be mere bungler's work, could be thrown together by accidental play of molecules and atoms?"⁴⁴

Bleuler also emphasizes that if new types are formed by accident and survival, there must be an enormous number of variants, almost all of which are unfavorable, for the possibility of a plus variant is not greater than for a minus. Sapper⁴⁴ was unable to find evidence supporting the elimination of types in fossils or recent flora and fauna.

In this connection one should not overlook the essentially historic character of life. In the inorganic systems the earlier history is quite without significance. If a pen drops from the desk it is immaterial in regard to the fall, how the pen happened to be on the desk. As Driesch remarks, the non-living system is always in the Now. While the past is not invariably foreign to an event, as in hysteresis,⁴⁵ in the living even the conception of "anlage" is based upon the historic character of life.⁴⁶ Even in Rashevsky's inorganic model for conditioned reflexes, the colloidal systems uti-

lized are not known to physical chemistry, the author merely demonstrating the possibility of such systems.

Finally the inorganic event is essentially a decomposition of elements, whereby one finds decreasing complexity; but from "amoeba to man" there is the trend of increasing complication.

In conclusion it may be said that the machine theory is an extremely valuable heuristic fiction. It is neither logically nor factually tenable in its current form and ought not to be regarded as the solely valid approach to the conception of life. It is extremely important to note that the machine theory is not the sole possibility for a physico-chemical theory of life.

d) MECHANISM AS CAUSAL EXPLANATION.—This use of the word has little to recommend itself since vitalism also strives for a causal explanation. For this reason the writer prefers the term *mechanistic-causal analysis*, although for brevity and in keeping with tradition, the first part of the term is dropped in this discussion. Usually mechanism as physico-chemical mechanism and as mechanistic-causal analysis are confused in that it is believed that all sciences must explain causally (mechanically), so the mechanistic (physico-chemical) explanation is the sole method available. The error is found in the presumption of merely one type of causality, whereas there may be a "biologic" causality, not to mention a "psychic" causality. No attempt will be made here to examine the causality question itself but allusion will be made merely to some of the problems arising when it is applied without limitation to the living organism. One thinks here of many forms of so-called "causal therapy."

It would seem that the idea has been applied most successfully in various industries, where the element of predictability of the outcome is extremely important. For example, if a doorbell fails to ring, one immediately thinks of some interruption of the circuit; incomplete circuit, no ringing. This leads immediately to a search for the point of interruption and permits the prediction that soon everything will be in order. One is able to make such predictions in the technical sciences because the number of participating factors are few and a fairly definite knowledge of the total event has been gained. When one leaves the relatively simple fields of industry and enters the more complicated fields, such as meteorology, this situation no longer holds. As Schmauss⁴⁷ urges, the smallest causes often exert greatest effects in meteorology: in other words, the real situation is unknown.

In technic one labors to exclude small undesired influences; one deals with relatively lucid natural laws, few in number and under fixed conditions. In nature, on the other hand, all influences are

effective, an infinite number of events proceed simultaneously, in sequence, in contrast, in independence; the conditions are infinite in number and for the most part unknown. In short the more perfect the technic, the more remote the event from nature. "Man permits only single causes to act, nature works only with the complex."²⁷

The demonstration of a cause in the sense of a single factor does not explain any natural event. If an electrical stimulus acts on various sensory nerves, the light, the sound and the taste sensation, the muscle contraction, the glandular secretion produced are not "explained" by the demonstration of an electrical stimulus. Perhaps this may become clearer by a few citations.

Mach states:⁴⁸ "We call cause an incident which is inseparately bound to another (the effect). Frankly it can be shown that this relation is usually very superficially and incompletely conceived. Usually we select only two particularly striking constituents of an event as cause and effect. But then the exact analysis of such an event almost always shows that the so-called cause is only a complement of the entire complex of circumstances which determine the so-called action. On this account one esteems or overlooks this or that constituent of the complex, so that the questionable complement may be judged very differently. . . . In the highly developed natural sciences the use of the conception of cause and effect is ever more limited and more rare. This is due to the fact that this conception delineates the content only incompletely and insufficiently. . . ."

"In speaking of cause and effect we arbitrarily give relief to those elements to whose connection we have to attend in the reproduction of a fact in the respect in which it is important to us. There is no cause and effect in nature: nature has but an individual existence; nature simply *is*. Recurrences of like cases in which A is always connected with B, that is, like results under like circumstances, that is again, the essence of connection of cause and effect, exist, but in the abstraction we perform for the purpose of mentally reproducing the facts. Let a fact become familiar and we no longer require this putting into relief of its connecting marks, our attention is no longer attracted to the new and surprising, and we cease to speak of cause and effect. Heat is said to be the cause of the tension of steam: but when the phenomenon becomes familiar we think of steam at once with the tension proper to its temperature. Acid is said to be the cause of the reddening of tincture of litmus; but later we think of the reddening as a property of the acid."⁴⁹

Pfeffer stated:⁵⁰ "Even if the closer demonstration of an occa-

sioning cause (of a stimulus) signifies an essential progress, still in any case it is wrong, if, as so often happens, the knowledge of a single factor is seen as one all sided sufficient causal explanation of a complex vital phenomenon."

The same idea is stressed by Roux⁵¹ when he states: "the complete cause of a flying cannon ball is not merely the spark, the powder and the ball but also the barrel of the cannon; all these together form the factors of the flight of the cannon ball." In another place⁵² he adds: "as complete or entire cause of an event I designate the totality of the directly and indirectly participating causes in it, the so-called factors and their order. . . . One factor alone cannot act (Newton). To each event there are at least two factors, also a combination of factors is necessary. In consideration of the entire cause of human tuberculosis the cause is not simply the tubercle bacillus but also the man concerned with all of the general and special properties necessary to this abnormal event (the so-called disposition)."

This mention of the causes of infectious diseases recalls the remarks of v. Hansemann:⁵³ "One has not yet succeeded in producing a furunculosis with bacteria taken from a furuncle. On the other hand atrophic children and diabetics have a tendency to furunculosis. It is known that one can introduce pus producing bacteria into the abdominal cavities of animals without thereby bringing about a peritonitis, indeed without even producing disease if the resorptive function of the abdomen is normal. If before the injection of the bacteria one produces an aseptic inflammation, for example, through the injection of some tincture of iodine or of some absolute alcohol, then a peritonitis invariably occurs even if only traces of bacteria are introduced. Indeed one has succeeded through the production of such an aseptic peritonitis, in creating a purulent peritonitis when the bacteria had localized themselves in an entirely different place. The normal bladder mucous membrane is fairly insensitive to the usual inflammation producing bacteria. Very regularly however a catarrh can occur when the emptying of the urinary bladder is not normal, for example, in paralysis in consequence to spinal cord diseases. If there is a stenosis present, whether it is due to prostatic hypertrophy or through the stricture of the urethra or through retrovesical diverticula, then even the least trace of bacteria when introduced into the bladder is sufficient to produce a severe purulent and necrotizing inflammation. On the other side one can inject large amounts of pus-producing bacteria into the urinary bladder of animals without thereby producing an essential inflammation, as long as no disturbance of emptying is present. The same holds for the gall bladder, which

is particularly liable to show disturbance in emptying. When inflammation of any type occurs in the intestine then a very special type of intestinal flora develops. In mercury intoxication appears the well known mercury dysentery. Thereby a definite type of intestinal flora develops. If one did not know of the mercury poisoning, then the alteration of bacteria would be perceived as the cause of the dysentery. Some fungi grow only under certain conditions as in diabetics. Through experiments in Rubner's laboratory it was shown that even a very marked fatigue was sufficient to permit bacterium coli to enter the blood stream."

In these examples the cause is only a series of conditions, the totality of antecedents without which the action could not occur. All single influences on the organism, either exogenous or endogenous, are never "causes" but merely one of many cooperating conditions, belonging to the totality of the complex event.

If now one turns to the current conceptions in regard to "causal," there is little agreement; some follow the functional conception of Mach, others the releasing factor in the sense of v. Kries, Fischer, Lubarsch, another the condition viewpoint of Verworn, v. Hansemann, etc. One of these, Verworn for example,⁵¹ may be cited briefly:

"We encounter some embarrassment when we take the conception (the causal conception) under the lens in order to analyze it. The answer is not easy to find although one is accustomed to move around with the causal conception and as a rule one tends to designate the 'causal natural analysis' as the acme of exactitude in natural investigation. From whence arises the conception? Like all conceptions the causal was also created by man in order to characterize a type of experience, but its origin is lost in the darkness of prehistoric time. Where we can grasp it first, it signifies an agent not perceptible to the senses to which, in analogy to the human will, one ascribes a definite significance for the event. It is true that scientific thinking has gradually sought to clarify this originally completely mystical conception and we still retain causal conception. But even this contains a fragment of the original mystery. One tends to say: every state or process has 'a cause.' Thereby the factor determining an event or process, the cause, appears in the singular. Even here there exists an error. There is no state or process in the world which is dependent upon merely a single factor. There are always a number of factors which determine it. Let us take an example. If I bring hydrochloric acid and sodium carbonate together, then the gaseous carbon dioxide arises. What is the cause of the development of carbon dioxide, the acid or the carbonate? In actuality both are necessary conditions. But

there are several more conditions likewise necessary for the development of carbon dioxide, for example, water, a certain temperature, a definite pressure. If one of these conditions is not fulfilled, then carbon dioxide does not develop. These conditions are also equivalent collectively, because they are collectively necessary for the process. But no condition can be more than necessary. It is therefore positively unjustified to take one condition out of a complex of conditions, perhaps the hydrochloric acid, and give to it a dominating role as 'cause.' This holds for every state and every process in the same way. What I can demonstrate are only the conditions on which it depends. There remains no place for a cause. For this reason one should renounce speaking of a cause in the singular and employ for the conception of cause the total determining factors of an event. Thereby the conception of cause relapses into nothing because it has become identical with the conception of conditions." Even if one need not go as far as Verworn in placing the conditions equivalent, this discussion is not pointless.

The comparison of research with industry deserves emphasis in another direction, for study of investigations will usually reveal the application of the methods of technic to biologic research; this is particularly evident in the procedure, so useful in physics and chemistry, of stressing an individual condition. Since an infinite number of cooperating conditions exist in nature, an attempt is made to silence them, for example, by studying the organism in a medium of known composition or isolation of a tissue. The other method usually employed consists in emphasizing the variable of interest to the worker so that other variables cannot be manifested. This is accomplished by permitting the influence studied to act so intensely that other influences are quite without significance. Practically speaking the tissue investigated varies constantly and this again results in further emphasis of the strength of the stimulus. By combining the two methods, one secures fairly constant results; in this sense one approaches cause in the sense of industry. But are the events observed normal phenomena of nature? Does one then study nature or does one secure what Müller has called interesting but not valid results?⁵⁵

Brief allusion should be made to another important aspect. Nature knows neither beginning nor end but the humanly constructed causal course knows both. In a study of gastric hyperacidity and its correction by alkali, usually the investigation is continued through the period of neutralization. For a long time this arbitrary ending of study failed to indicate the secondary hypersecretion, an increase in acidity often beyond the original point. It has become increasingly obvious that attempts to fix the conditions in

the organism, the indispensable item in technical research, fail in medicine since the body makes every effort to react against change. In short nature knows neither fixed conditions, nor, for that matter, strongly emphasized conditions. To be sure emphasized conditions may occur in various catastrophes, but their very emphasis indicates the excess beyond the limits compatible with life.

The selection of conditions for establishment of laws is likewise apparent in the inorganic world, for example, in the law of gravitation; if one concluded that each substance moves toward the earth, simple observation would teach that gases lighter than air actually rise in real nature. The same holds in the human organism; while water tends to collect at the lowest point, actually the influence of gravity on circulation is entirely offset in health. As Schwarz states⁵⁶ "my arm never follows gravity unless it is paralyzed or I 'permit' it to follow; I use it for my purpose." If one abolishes the marked emphasis of a condition, the fixation of conditions, then a viewpoint is approached wherein causes are found in nature in general only when the observation is made under abnormal, artificial conditions.

In this manner one approaches a second characteristic of rules; they are observations in nature. Fixation of conditions and emphasis of a condition which suppress the autonomy of the cell and permit only heteronomous phenomena to appear, no longer indicate the characteristic of living cells, but hold equally well for dead cells. As v. Uexkull states: "it is actually the clearest definition of death when we can say of an organism, it no longer proceeds purposefully but only causally."⁵⁷ Kulenkampff⁵⁸ adds: "mechanistic causality belongs to the dead cell, to the living is the biologic, the living causality." v. Bunge has emphasized: "as the epithelial cell of the stomach secretes an acid, yet remains alkaline, so the pancreatic cells secrete ferments yet remain ferment free. . . . We see the same in every plant cell. The cell juice which fills the clefts in the protoplasm is acid, the cell itself alkaline as all contractile protoplasm. The cell juice is often decidedly colored, the cell which produced the pigment colorless. But as soon as life ceases, as soon as the vital phenomena recognizable to our eyes, the amoeboid movement, cease, and the puzzling property of separating materials disappears; the law of diffusion appears undisturbed in power; the protoplasm imbibes the coloring matter." The same general idea was emphasized by Hufeland.⁵⁹

It seems advisable to indicate how peculiarly the causal attitude is used in medicine and likewise to show that this has not been without unfavorable influence. In regard to the first: v. Kries⁶⁰ states, and he is supported by Fischer and Lubarsch, cause is that

which for any reason possesses the greatest interest or significance for us. Winterstein⁶¹ implies that it is whatever satisfies our need for causality. It is therefore not surprising that Bier⁶² became sarcastic and said: "causal in medicine is that which the investigator concerned would like to have the cause." One perceives where this leads. If ten individuals witness an automobile accident and are asked the cause, the physician, the engineer, the psychologist, the lawyer, the philosopher in the group would probably give quite different "causes." This hardly yields the exactitude and precision which is implied by causal-mechanistic explanation.

As the last element considered here, attention is directed to the fact that the causal viewpoint has not been without disadvantages to medicine. The examples immediately following have been selected from medical literature of the recent past since error is more apparent there, than it might be in some fallacies pursued at present. One thinks of the "causal" treatment of high blood pressure by vaso-dilators, fever by antipyretics, alkalosis by the introduction of acid, gastric hyperacidity by the introduction of alkali, etc. Without further multiplication of examples, it can be seen that what was once regarded as "causal therapy" is now viewed as the treatment of a prominent symptom.

That this does not belong only to the past may be indicated by a more recent example. Groner⁶³ finds the characteristic of asthenics to be an outspoken lability of certain cations in the blood and a diminution of blood phosphorus. Therefore he proposes to treat them by increasing the calcium and phosphorus content of the blood. Thereby he has selected but one event of asthenia; moreover, he overlooks the suggestion that the change in phosphorus may be just as valuable to the patient as an increase in temperature in fever; less teleologically that like antipyretic therapy, this is treatment of a symptom rather than of the disease. Such thinking overlooks the viewpoint: "causal thinking has now become a dogma and particularly for the reason that it is so convenient. There is no doubt about the convenience when one can say that a disease is brought about through a cause and if this cause is removed the disease can be removed, a simple process, theoretically considered, sounding extraordinarily plausible and decidedly convenient. Unfortunately it does not agree with actuality in many cases."⁵³

It would lead too far to consider the infectious diseases, but this has been a particularly fertile field for the application of the causal idea. Suffice it to state that prominent bacteriologists as Much⁶⁴ incline toward the opinion that the patient is more important than the microorganism. v. Bergmann⁶⁵ has emphasized that changes in virulence in bacteria are insufficient to account for the

appearance and cessation of epidemics. Hueppe⁶⁶ has always stressed that the prevailing theory of infectious diseases leaves no place for the "nature" of "specific disease" (Sydenham) nor the sick cell (Virchow) nor the local and temporal disposition (Pettenkofer) the "specific" disease-producing bacteria of Pasteur. He urges that it is much more all factors together. In this connection Böttner⁶⁷ and Diepgen⁶⁸ may be read with interest. Rost⁶⁹ holds the same general argument is valid in the consideration of merely external factors in eczema. v. Bergmann now holds the local treatment in gastric ulcer is on a par with a very primitive dermatology, etc.

One can read much about the factor which explains non-specific actions in therapy, one author stressing thrombocyte destruction, another the lipoids, another the reticulo-endothelial system, another the leucocytes, another fever; probably it is all.⁷⁰ The "misplaced" energy is recalled in the forty different explanations for the heart sounds in a fifty-year period, a matter which is assignable in all probability to exclusive devotion to one explanatory principle by each worker.⁷¹ Whether or not this is conducive to "chaos"⁷⁰ in medicine must be left to the reader. For those who see in detail work and the discovery of single facts sufficient justification for exclusive causal analysis, some interesting discussions are indicated in the bibliography.⁷²

e) MECHANISM AS EXPLANATION OF TIME-SPACE PHENOMENA FROM TIME-SPACE CAUSES.—This is the true antithesis of vitalism which employs transcendental non-spatial factors. This use of the word has little to recommend it since by definition every natural science must proceed "mechanistically." The usual reasoning adopted is that there are no transcendental vitalistic factors given in natural science, so there is only physico-chemical lawfulness. The obvious fallacy here originates in the implication that there are no levels of organization above the "physico-chemical."

In conclusion it may be well to summarize some of the more important reasons for regarding "exclusive" devotion to the mechanistic explanations as undesirable. A detailed account will be found in Woodger's excellent work.²³

1. Mechanical explanations are abstract; consequently they cannot be exhaustive. Abstraction is a process of emphasizing certain lines of thought and neglecting others. The conclusion reached will be valid only under the conditions of the mode of abstraction. Other modes of abstraction ought to be explored, first to check conclusions reached by the first method, second to determine just how "irrelevant" the "neglected" actually is.

2. Biologists and physicians interpret physics more realistically

and dogmatically than do physicists themselves. It would seem the safer and wiser course for biologists to appeal to biological subject matter than to accept notions borrowed from other sciences, particularly when the borrowed conception, in place of being impregnable and "unmoving rock," appears to be more nearly akin to shifting sands.

3. Mechanistic analysis destroys the characteristically vital level of organization.

4. Mechanistic explanation employs a hypothetical method, using a method elaborated in one sphere and extending it hypothetically to another. If one uses physical and chemical hypotheses exclusively, physical and chemical results must be the only results. "Vital" levels of organization cannot be attained in this way.

5. Biology regards organisms as the outcome of an evolutionary process. If there is no organization above the chemical level what has happened in evolution?

6. Organisms display at least to some extent an "internal teleology." This subject finds further discussion later under the teleologic method of consideration. A detailed account of these reasons as well as others will be found in Woodger.

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LAW OR RULE.—The opinion generally prevails that the essential difference between law and rule is quantitative, that is, a law invariably holds whereas a rule permits exceptions. This suggestion of a mere quantitative difference between law and rule is emphasized by Nernst¹:

“Biological laws, as perhaps that of development or the theory of heredity, are qualitative in character and only conditionally applicable in quantitative treatment. In spite of their great significance we can scarcely designate them as natural laws but better as rules to which one closes the eyes in the face of exceptions.”

Many also believe that natural laws are derived from experience, yet observations have shown that a natural law cannot be proven exactly in unaltered nature. For example, it is admittedly true that bodies fall according to Galileo's law, yet this law is not yielded by retesting in nature. A succinct statement by Roux² may clarify this point:

“The laws of physics designate for the most part events which do not occur in free nature in exactly the manner designated in the law. . . . A thing in nature never falls exactly and absolutely according to the law of falling bodies, a projectile never describes a parabola because the resistance of the wind makes it impossible and in the region of the earth, light does not progress in a perfectly straight line, for this is possible only in a perfectly uniformly thick medium, and there is none present over a great extent of the earth. The mathematical laws of hydraulics all contain the presumption of a ‘frictionless fluid’ which practically does not exist.”

Thus a natural law is not a description of a natural event. In a natural law, all complicating factors which might tend to disturb the “lawful” nature of the phenomena are eliminated. On the other hand an event in free nature is characterized by the inevitable presence of such complicating and disturbing factors, each of which is subject to special individual laws.

Natural laws are not observations in nature but arise from genial thinking superimposed on observation. Otherwise it would be difficult to account for the fact that thousands of individuals saw apples fall without obtaining the ideas of Newton.

Bertalanffy seems to have stated the “law” problem most clearly.³

“Biology today finds itself in its pre-Copernican period. We possess an enormous number of single facts, but we still have no insight into the laws which govern the same. This lack of laws moreover has its foundation in the fact that, up to the present, we have innumerable biologic theories but do not possess an unobjectionable, finished theoretic biology. Theoretic science and law

science are one and the same; the non-development of theoretic science does not permit biology to make the step from a mere empiric and descriptive science to an exact law science.

“One will probably concur reluctantly with this statement and moreover may suggest that there are certain laws in biology. For example one will refer to the Mendelian ‘law’ of heredity. But we have already seen above how this, the most progressive and exact field of biology at the present time, is in no way free from fundamental reservations. One may regard these objections as they please: in any case attention must be drawn to the fact that a vast intervening step lies between principles like the Mendelian and the laws of physics and chemistry. If this holds even for the most progressive field, for the field most extensively amenable to mathematical treatment, how much more it holds for all others! Even the most fleeting glance teaches that in physics we speak of ‘laws’ in every case, but in biology only rarely and in isolated cases. In physics the name of the physicist appears with the law discovered by him and named after him; but in ontogenesis there is just as little a Roux law or Driesch law as there is a Kleb law in botanical morphology, a Loeb law in physiology. In spite of the significance of the results of such outstanding workers it is impossible up to the present to connect even a minor lawfulness with their names as the enduring product in science.

“But these considerations naturally remain on the surface. With deeper consideration it is evident that those few principles which are often designated in biology by the title of law, do not deserve this name, but must be contented with being merely empiric rules. What is the difference between law and rule? The rule is derived inductively from experience, on that account possessing no inner necessity, and holds always merely for special cases, at any time can be disproven through opposing facts. The law on the contrary indicates a logical connection of a mental construction; on this account it is deducible from supra-ordinated laws and on its part permits the derivation of subordinate laws: as such it possesses logical necessity in the agreement with its supra-ordinated premises; it is not merely a probability principle, but in the concession of its premises has compulsory, apodictic logical value. This means the law generally does not belong to the domain of empiricism but is a logical connection between ideal mental creations. For this reason law science is identical with theoretic science. If we apply these considerations to the so-called biological laws, then we see that these are merely to be designated as rules: they are generalizations drawn from empiricism, they are neither derivable from higher principles nor can lower laws be

derived from them; they are 'accidentally' contingent in the meaning of philosophy. We possess no explanation as to why these rules and no other obtain; they possess neither logical necessity nor determination. If perhaps we think through the law of Mendel according to these points, then it is seen distinctly how even the most progressive biological field today has scarcely the character of a law science.

"In order to perceive this relation more clearly, we must present to ourselves the question of how one comes characteristically to natural laws. It is the question of the relation of induction and law science.

"The general conception prevails that natural laws 'are found by empiric, above all, experimental ways.' In this sense one dates the beginning of modern natural science with the 'inductive method' of Galileo. But the conception that a natural law can be derived from experience is fundamentally wrong.

"Dingler has instructed us by a splendid analysis. One speaks of the fact that Galileo obtained his law of fall from experience and perceives in this inductive scientific method, the essential advance of modern natural investigation over Middle Age metaphysical thinking. But it is entirely impossible to set up the law of fall by the experimental way. Through the resistance of air, etc., the fall of a body is so altered that it can scarcely be recognized. The experimental demonstration of the law would move in a circle: in order to derive the law of fall from an experiment, one must first know the amount of air resistance; the air resistance, friction, however is definable only through the preconception of undisturbed movement. Galileo in a more logical way selected the simple accelerated movement, although this is never perfectly developed in experience. It is also absurd to say that the experiment of Galileo proved the law of fall; on the contrary his opponents employed an experiment in fall from the leaning tower at Pisa as disproof.

"Expressed generally: the derivation of natural laws from pure experience is impossible because this would lead in a circle: in order to derive the law from experiment, we must first recognize the disturbances of it in actuality; but these disturbances on their part are recognizable only through the presumption of the law. Actually the fathers of our physics proceeded in an entirely different way. They did not derive their laws from experiment but worked as Euler has expressed: 'I already had my results, only I did not know how to obtain them'; that is, one first presents the law as an ideal case and compares this with reality in which it is always realized in a highly disturbed form and for this reason it

can be perceived by the 'inductive' way. Galileo's pupil Torricelli has expressed the situation in the form of a paradox: 'And if the ball of lead, of iron, of stone do not accommodate themselves to that determined law, so much the worse for them,'—a statement which almost literally recalls the notorious remark of Hegel: 'if actuality will not accommodate itself to his system, so much the worse for actuality.'"

The procedure followed in deriving a natural law has also been described by Kraft: "a synthetic summarizing thought process which is not a resume, but which contains something new. The actuality of the law is still unproven and unidentified, merely conjectured. Then mental experiments are arranged which may yield the possibility of testing the conjecture and then proving by deductive processes. Experiments are in reality provings of ideas."

Thus one takes a freely selected ideal assumption and with strict logic makes deductions from it through the introduction of special conditions which are comparable with experience and verifiable by it; and this constitutes their only strict value.

On the contrary that which is read directly out of nature is not a law, but when it is frequently or regularly observed it is a rule. This has been clearly stated by Roux:² "A rule is an expression of a frequent relation of an empiric event; it designates the event at least in more than 50% of the cases.

"A natural law designates an 'action' of given components and since all actions are fixed, that is, proceed equally under equal conditions at all times, so a natural law must hold without exception, it does not permit a single exception or it is false."

It is also important to note that a rule being observed in nature explains nothing. It is obtained by description and comparison. On the other hand law derivation proceeds on the necessity of the events occurring under definite, ideal but not actual conditions. From this is yielded that we cannot expect to "explain" the processes in the organism extensively in a physico-chemical sense. To quote Kötschau:⁵

"For example what influence has the law of gravitation in the living organism? One might say that the organism does everything it can to oppose the effect of gravitation. Although it contains more than 90% water, still water does not collect in the extremities as long as the organism is healthy and capable of reaction. The blood flows in the same direction in the arteries or the veins regardless of whether the arm is up or down. And so the organism characteristically opposes all natural laws. It protects against the dissipation of heat. It defends against every

physico-chemical effect. If one introduces alkali into the stomach, then the organism produces an excess of acid contrary to every chemical law. In its isotonia, isoionia, isothermia, etc., the organism shows its ability to maintain a definite equilibrium in spite of all physico-chemical effects."

The subject deserves further elaboration in several directions. For example, a natural law must necessarily be clothed in a mathematical formula (Nernst). But detailed discussion of this and related features is prohibited here by lack of space and ought not to be necessary because of the availability of exhaustive treatment elsewhere. However, one important aspect of the situation cannot be dismissed without mention.

The first step necessary in the development of any science is the complete and exhaustive description and order of its object. In biology this is found in the systematic aspects such as the cataloguing of plants and animals; in medicine it is evidenced by the high development of anatomy. In other words science begins with asking "What." The complete description and arrangement of data permits the formulation of observational generalizations called rules. As long as investigation is confined to this plane, no attitude, mechanistic or otherwise, need be adopted.

The second step of science is made when a complete description of what or what happens is available. On the other hand, in some branches of medicine, with relatively little information on the "What," the jump has been made to the second level, namely, "explanation." It seems particularly true that pharmacology has accepted the demand for explanation relatively early in its career. This course would contain less potential danger if it were more generally appreciated that other explanations than causal-mechanistic are possible and here again if almost exclusive devotion to physico-chemical mechanism did not prevail. For example, in place of almost exclusive devotion to "How," one may ask teleologic questions as "For what purpose": the query of the function of organs and their appropriateness for the existence of the organism, the problems of adaptation under a variety of conditions, etc. Naturally other possibilities of explanation exist in addition to the description of the causal and teleologic connections in the organic world. It would seem obvious that in the absence of complete descriptions of what occurs, explanations of how it happens are premature; the history of medicine is replete with examples of seemingly satisfactory "explanations" which placed problems on the shelf as solved until discovery of new facts and rediscovery of old ones revealed the explanation was not tenable. One may think of the many things explained at present by elec-

tricity, by histamine, etc. Naturally this is true of most branches of biology, for example, the assumption of the radiation of potassium as the "cause" of its action, the mitogenetic rays of Gurwitsch as the "cause" of cell division, etc.

It would seem, to the writer at least, that the safer course for science would be to remain on the descriptive level in the present rudimentary state of some medical sciences; or if scientific demand for explanation is irresistible, at least to check the conclusions by as many other approaches as possible. If the teleologic approach is regarded as sterile, one might at least check the isolated event by investigation of the organism as a unit. Valid rules will be the outcome of the collection of complete descriptions in which all possible methods of approach and comparison are employed.

The third step in the development of science will be to determine the laws governing living events; this has been mentioned above.

The simile is not a natural law; it fails to qualify in the manner of derivation, exclusive validity, lack of mathematical formulation, and absence of explaining value. Moreover being an observational generalization, remote from the strongly emphasized "conditions" and "law" investigation prevailing in some divisions of medicine, as pharmacology, it has failed to intrigue the interest of many.

No detailed discussion is necessary to show that generalizations of the rule type have been valuable guides, both in theory and practice, when they are not regarded as "eternal truths." In addition to furnishing a valuable stimulus to investigations, they also represent practical necessities in medicine. It is elementary to state that at present no one could possibly know all of medicine in its many ramifications, even if this were desirable. Practical necessity forces everyone to place the most essential aspects of each science into general rules which permit the worker to look over the entire field. It is unfortunate that this device is forgotten at times by detail workers. The "heuristic" value of such rules is well illustrated by the problem of antisepsis and asepsis.

One would think that throughout the centuries empiricism, esthetic feeling, etc., would have led to cleanliness in the treatment of wounds and thereby furnished the key to asepsis. But even rather clear ideas of "primary union" and "cleanliness" failed to gain general popularity in medicine. One may recall Hunter and Semmelweiss in this connection. However, the belated recognition of their ideas can be attributed to no small degree to their inability to set up a convincing rule, which was brought about by Lister. No extended apology is needed to justify the "practical" nature of such rules in a field like therapeutics. It may

be that the material which follows will tend to suggest the simile as a biological rule of more or less importance. However this may be, there can be little doubt about it as a "heuristic principle."

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THE SIMILE AS A FINDING PRINCIPLE.—While the simile has been formulated in a variety of expressions, the most common expression is *similia similibus curentur*, let likes be treated by likes. This is generally interpreted to mean that a "remedy" capable of evoking certain responses in the healthy under certain conditions will be useful in the treatment of a disease characterized by similar phenomena. Nothing is stated or implied as to just how cure or amelioration is supposed to take place. In other words the simile is essentially a guide for finding "drugs" possibly of use in the treatment of disease. The contrarium however is not the opposite of the simile. The contrarium rule is always considered an effect principle. It will be perceived that the simile makes no postulation beyond implying, for example, that "drugs" capable of producing fever in the healthy, under certain conditions, may be useful in the treatment of "febrile" diseases. It makes no assertion as to whether or not the fever will be temporarily increased. On the other hand, since it emphasizes the conditions, health on the one hand, disease on the other, it is entirely consistent to state that a drug found by the simile may act as a contrarium.

In order to indicate that this is not merely an academic distinction a few examples may be cited. Iodine has long been employed in the treatment of acute rhinitis on the basis that it produces symptoms similar to the common cold in the healthy. Recently Bier reintroduced iodine for the treatment of certain forms of acute rhinitis, a suggestion subsequently emphasized by Horwitz.¹ Bier's suggestion came solely from awareness that iodine produces symptoms similar to those of colds. On the other hand, Müller urges that there is nothing new in the idea since he had long employed iodine as a prophylactic against those infections of the

central nervous system whose portal of entry was supposed to be the nasopharynx. In other words he proceeded from the viewpoint: iodine is an antiseptic, therefore it will sterilize the nasopharynx. By extending this idea he employed iodine on the basis that it might effect sterilization of the upper respiratory passages or at least lessen infection in this area by direct action upon the bacteria responsible for these infections. Improbable as it may seem that iodine or for that matter any other substance tolerated by the mucous membrane could disinfect the mouth and nasopharynx, the point remains that two separate workers arrive at the same drug but reached their conclusions by entirely different methods, one by a finding principle (similar symptoms) the other by an effect principle (antiseptis).

Another example: veratrum was formerly employed in the treatment of certain forms of cholera. It was regarded as more or less "specific" when a certain definite group of symptoms was present, and here again the cases responding to this therapy were said to exhibit symptoms similar to those produced by veratrum in the healthy. At that time veratrum was also widely and gladly employed by others unaware or disinterested in the above mentioned observation. It was employed by them on the basis that veratrum killed the micro-organisms responsible for cholera. Hugo Schulz thought it advisable to submit this suggestion to experimentation with the result that he was able to grow the micro-organisms in question in the presence of fairly strong concentrations of veratrum, at least many times stronger concentrations of the drug than could be attained in the human intestine. He therefore concluded that since the pathologic lesions produced by cholera and veratrum were very similar, the remedy was curative by virtue of the production of similar symptoms (finding principle), not by virtue of an antiseptic effect. Still the demonstration of its lack of direct antiseptic action gave occasion for increasing unawareness of the drug, illustrating again the influence of theory on practice, whereas theory should come from practice.

Exactly the same situation holds for the formerly employed bichloride of mercury in the treatment of some forms of bacillary dysentery. Many employed it in those cases where the intestinal symptoms were similar to those of dysentery, and it is generally appreciated that the two diseases may be quite identical histologically. But it has also been employed by others on the basis that it is an antiseptic for the purpose of killing the causative bacteria. Interesting enough the same dose is recommended by both, for 1/500th of a grain is considered efficient (Hare's Practical Therapeutics). It seems highly improbable that this amount, or much

more could make much of a direct impression upon the bacterial flora of the intestine, recalling that this structure is some 20 feet in length, composed of protein walls which unite with bichloride, and whose contents would seem to render an antiseptic action problematic to say the least. But the point remains, that here again the simile and contrarium arrive at the same end.

The same situation obtains in regard to the question of antitoxin therapy, although other problems are involved. If diphtheria antitoxin is given to a patient suffering from diphtheria, the actual administration is based upon the contrarium principle; one has proceeded on the basis that the toxin in the blood is "neutralized" by the antitoxin. But in the preparation of antitoxin or in the production of immunity one proceeds on a purely simile basis. In this case the result of simile procedure is applied to the patient; in the other to the horse.

Although the action of digitalis receives more detailed scrutiny elsewhere one point may be mentioned here. In normal animals or man the minute output of the heart is definitely decreased by digitalis and its isolated active principles as far as they have been investigated in regard to this point. On the contrary no effect is more spectacular than the increased output of the heart as the result of the administration of digitalis in certain forms of heart disease. Here again one perceives that a finding principle may be entirely different from an effect principle.

Again those aware of the simile have long employed iodine in certain forms of thyroid disease, here again particularly in so-called Graves disease or exophthalmic goiter. They arrived at this method by virtue of the fact that iodine can produce a syndrome quite identical with that of Graves' disease. On the other hand it is general knowledge that iodine, as perhaps no other remedy, is extremely useful in the preoperative treatment (at least) of this syndrome. Whereas as in the healthy, iodine increases the basal metabolic rate, in Graves disease with its heightened rate, iodine medication is followed by a lowering of basal metabolism in this disease.

Perhaps enough has been said to indicate that the simile as a finding principle ought to be kept separate from an "effect" principle. Likewise it should be noted that the simile and the contrarium are not necessarily opposite to each other. Essentially they are modes of thinking and actually the same conclusion may be reached by these different routes.

At times "simile" or "contrarium" depends upon the orientation of the observer. In giving food to the hungry, one proceeds on the basis of the contrarium. In maintaining health by giving

food, one proceeds from the simile. Thus the simile and contrarium are not eternal truths, but are methods of thinking which have resulted in useful biologic rules.

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THE ISON.—The isopathic rule was formulated by Hippocrates who stated: the same factor which produces a disease will cure it. Various attempts to apply this rule have been reviewed in the section on the origin and evolution of antitoxin therapy.

Although the rule is simple and clear, it should not be imagined that it is easy to apply. Although only months separate the discovery of sera for the prevention of diphtheria and tetanus, years elapsed, with thousands of workers laboring industriously before the serum for scarlet fever was added to the list. This perhaps will serve to emphasize the great difficulty which may be encountered in the practical application of a simple rule.

It is hardly necessary to do more than remind the reader that medicine is in possession of a number of antisera, some of highest value, others of doubtful utility, some extremely curative, others markedly prophylactic and feebly curative, some antitoxic, others antibacterial.

The outstanding curative properties of diphtheria antitoxin would hardly be questioned by any intelligent person who has ever attempted to treat diphtheria with it. While the serum becomes increasingly less valuable as time elapses between the infection and its employment, and while its value is questionable after the toxin is firmly "anchored" to the tissues, this time element underlies all biologic actions. This shortcoming is a reflection on diagnosis and tardy application of an extremely useful agent rather than a defect assignable to the product itself.

Diphtheria antitoxin is supposed by some to act indirectly to the extent that it neutralizes diphtheria toxin. The toxin is said to repel leucocytic infiltration, for example, into the tonsillar tissues, whereas if the toxin is rendered inactive, infiltration of leucocytes may occur with death and removal of the provocative organism. Naturally antitoxin is also available for rendering harmless unbound toxin in the circulation, etc.

In the above instance the isopathy is applied in the horse used to produce antitoxin, namely, by the injection of the toxin. More in accordance with the simile is the use of modified toxin, anatoxin, for the production of diphtheria prophylaxis or immunity.

The procedure of diphtheria prophylaxis or immunity is widely and successfully employed wherever diphtheria prevails and people are intelligent.

Not all sera are equally curative. There are many who question the curative value of antitetanic serum. But the results obtained in the late world war will convince anyone of its excellent prophylactic qualities if further evidence were needed.

Of distinct merit is the antitoxin for botulinus poisoning which represents a variation from the previously described sera in that the toxin and not bacteria is usually ingested. Its apparent early problematic value found a partial answer in the discovery of different biologic types of causative organisms, a defect which will be largely overcome by the use of polyvalent sera. Likewise to be mentioned in passing is the successful development of a serum of considerable curative value for so-called malignant oedema, at least for the appalling cases of infection by bacillus *Welehii*, vibriion septique of Pasteur and *Bacillus Oedematis malignii*. The literature suggests the value of serum in dysentery due to the Shiga-Krause type of infection. More recent and very valuable has been the successful use of a serum in scarlet fever. There also seems to be promising evidence for the production of a cholera serum.

Because of the extreme complexity of biologic types of streptococcus the value of specific sera here is less certain, but the experiences of the last few years suggest that erysipelas may offer a welcome exception to this. The remarks applied to streptococci also seem to hold for staphylococcus infections.

Some progress has been made with the pneumococcus antisera particularly in type I infections, and while there is much to be desired it may be hoped with the discovery of type specific carbohydrates, that much progress will be made in this direction. Also very worthy of mention is the polyvalent serum for the treatment of meningococcus meningitis which has reduced the mortality in this terrible disease.

Of far less value are the sera for gonococcal infections, particularly for the arthritis, and the serum for whooping cough. An intermediate position is occupied by the serum for anthrax. Passing down the scale of efficacy one comes to the relatively useless sera for coli infections, influenza, and typhoid. The writer has had no occasion to try the sera available for plague (protective), tularemia, typhus, epidemic encephalitis, post-vaccinal encephalitis, etc.

However, sufficient has been said to imply the merit of the isopathic rule in the treatment of infectious diseases (and especially their prophylaxis). Even if no other sera were found in

the future the rule would be amply justified. However, it is only by the recognition of the rule that other sera may be anticipated although naturally the rule will be found increasingly difficult to apply. No one seriously doubts that equally valuable preparations will be found for numerous infections now missing from the above list.

Time, patience, industry and medical science will probably make this already respectable list include most of the infectious diseases. and, as v. Behring stated, the basis is the simile (or if one wishes the isopathic rule).

If one desired to elaborate fully this subject it would be necessary to turn to the enormous literature on agglutinins, lysins, opsonins, bacteriotropins, for all these fall under the same rule which has been applied above to antitoxins and antiendotoxins although they are not necessarily factors in "immunity." They are, so far as is known, the results of the reaction of living tissue to a stimuli.

Since no one seriously doubts that the dead bacteria of vaccine therapy are considerably modified, perhaps this may be more readily appreciated as the simile than so-called isopathic rule; the same applies for the use of attenuated organisms or even active organisms at times used in treatment. Here comes into expression. to mention but a few items, the vaccine therapy of streptococcus and staphylococcus infections as in abscesses, furuncles, some cases of acne, secondary infections in tuberculosis, in rectal fistula, in actinomycosis, in several forms of arthritis.

Into this group falls the universally practical smallpox vaccination, the typhoid prophylactic vaccination, the excellent prophylactic vaccination against hydrophobia and others.

Several procedures which at present are practiced so "routinely" that their curative value is less obvious, as tuberculin in tuberculosis, find no discussion here.

In all these cases, while there are differences in the results and manner of procedure, the underlying rule is the same: the factor which produces the disease will also cure it, or as Lux stated: diseases carry in their cause, their cure. And it is equally evident that none of these could have been found by the contrarium rule, as v. Behring so clearly emphasizes. Frequently now that these procedures have become universally practiced, the basic idea, the simile, is left out of the picture, although this rule probably furnishes the guide to equally valuable but as yet unknown therapeutic triumphs.

One may also turn to the generally recognized "desensitization" therapy which has been employed with excellent results in the

treatment of hay fever, allergic forms of bronchial asthma, the numerous forms of allergic skin diseases which may take on the symptomatic picture of eczema, pruritus, urticaria, etc. Here again one ought not be deceived by the brevity of the list at present. The rule is difficult to apply. Only recently the importance of the role of allergy in the manifestations of tuberculosis, in the symptomatic and pathologic picture of chronic deforming arthritis (at least atrophic type), acute rheumatic fever, the "secondary sicknesses" of scarlet fever and many others has been appreciated.

It may be of interest to note here that Storm van Leeuwen, an international authority on the subject of allergy, has clearly stated the principle involved: "All methods of specific treatment of the allergic diseases are based upon the same principles, namely that the injection of very small amounts of allergens can prevent the breaking out of an attack which has been caused by this allergen."¹ Here one sees the principle of small dose added to the conception of the "idem."

The principle of desensitization has long been consciously practiced by those appreciating the simile particularly for sensitization to foods² and the use of *Rhus toxicodendron* (poison ivy) for the prophylaxis of poison ivy. It would be wrong to believe that only literature published in rare journals has been overlooked in this respect. Actually the work of A. Bier anticipated most of the work on allergy although he too is usually forgotten. As early as 1901 he wrote (and in a prominent medical journal): "I had been interested for a long time in transfusion and about 10 years ago made the following experiment which I thought might promise success. Following the principle that the organism becomes accustomed to many things, I thought that through a graded procedure, animals of one type might become accustomed to the blood of another. I injected defibrinated sheep blood into the ear vein of rabbits at intervals of 3-9 days. At the beginning it looked as if the animals rapidly became accustomed to the foreign blood. But all at once they died showing the most severe transfusion symptoms."³ Here again one perceives what transpires when biologic rules are not developed.

Whenever claim has been made that the practices mentioned above are founded on the simile, the claim has been denied on two grounds: the first states that the procedures of "immunity" are concerned only with proteins, whereas the simile implies the use of many non-protein "drugs"; the second, that the procedures are specific; that is, diphtheria antitoxin is produced only as the result of the administration of diphtheria toxin.

These objections are raised without realization that the simile

principle is a broader finding principle. What has protein to do with the fact that Bier¹ has treated x-ray burns with x-ray?—an excellent possibility for simile therapy. Here as elsewhere the rule is difficult to apply and will meet with extensive success only when the dose, the interval of treatment, and other factors are determined.

What has specificity to do with the treatment of x-ray burns by radium⁵ and thorium,⁶ carbon arc light,⁷ ultra red⁸ and blue light?⁹

Another aspect of the question is clearly indicated by Bier's work with the ether therapy of post-operative (ether) bronchitis. In the first publication¹⁰ only a relatively small number of cases were reported, but in the second study the cases number 187¹¹ and evidence has been advanced to show that the method is becoming very popular in Germany.¹²

Some investigators have attempted to explain this work on ether on some other basis. Apparently no one who has tried it in the class of cases for which it was devised has failed to secure results. Some assert: "it is counter-irritant therapy." (The ether is injected hypodermically.) Once more one forgets that it was discovered by consciously employing the simile principle as a finding principle. Explanations will continue to vary. But few objections to the method have been heard since Schneck reported a series of 300 cases of crushing of the upper part of the body in which not a single case was lost as the result of pulmonary complications.¹³ One sees here an extension of Bier's suggestion to proceed from the ison to the simile, for he had suggested ether in other forms of acute bronchitis than simply the post-operative type due to ether.

The question naturally raises the problem of employing this rule in the treatment of poisoning, especially since the contrarium rule has not been promising in many intoxications particularly after the poison has entered the system. Only a few investigations have been made in this most promising field.

Most interesting and deserving of further study is the communication by Richter.¹⁴ He reported a group of cases in which there was a possibility of idiosyncrasy to metals or an actual poisoning with them. His first case concerns a patient with neo-salvarsan poisoning. The patient was treated with small doses of neo-salvarsan intramuscularly with rapid recovery. The second case is similar. The third patient suffered from a neo-salvarsan icterus and a similar favorable result is recorded. The fourth case presented hemorrhages from the mucous membranes following neo-salvarsan and was successfully treated by the same agent in small doses. Another patient with a rash and icterus also

showed favorable results. Similar favorable results are reported with bismuth and mercury in poisoning from these agents. Baader has reported extremely interesting studies with lead.¹⁵ Thus it will be seen that the rule extends far beyond the mere implication of "proteins."

That hypersensitivity to bichloride of mercury and phenol has been successfully treated by "desensitization" is now generally appreciated, and the importance of this subject to many occupational diseases would be rapidly appreciated if physicians passed beyond the symbolism of proteins.

To be sure, the chemically definable materials may combine with proteins to become "antigenic," but this idea perhaps is not the essential for the practical treatment of common idiosyncrasies to potassium iodide, iodine, iodoform, formalin, salvarsan, pyramidon, veronal, acetyl salicylate, antipyrine, phenacetin, veramon, nirvanol, mercury or mercury compounds, quinine, morphine, codeine, nickel salts and countless other substances.

In this fashion one proceeds a long way from the early conception of the limitation of the reaction to pollens, feathers, etc., and at the same time secures a much broader viewpoint in respect to the practical application of the isopathic rule. After this introduction, one may turn to a closer examination of some aspects of specificity closely allied to the simile rule.

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A NOTE ON SPECIFICITY.—In ancient medicine based upon humoral pathology, the therapeutic conceptions were founded largely upon "general" measures, although divisions of pharmacologic drugs resembling modern classifications were not infrequent. With the application of quinine to malaria and mercury to syphilis a new conception of specificity came into existence. A substance which affected a given disease so markedly that a diagnosis could be made from the therapeutic result was "specific." Progress was gradually occurring in respect to specifics of this kind when the blinding brilliance of specific immunity and specific anaphylaxis cast everything else into a shadow. This had considerable influence upon the simile.

Before the discovery of "specific" immunizing agents it had been known that erysipelas not rarely cured tuberculosis of the skin, syphilitic lesions of the skin, more rarely leukemia and at times even neoplasms. These results were so generally known that in 1883 Fehleisen injected pure cultures of the streptococcus of erysipelas into the skin of lupus patients and in 1886 Emmerlich reported that the intravenous injection of the same organism effected cures in otherwise fatal experimental anthrax infections. Likewise Pawlowsky and Bouchard reported healing of general and local anthrax by the injection of Friedlander's bacillus pyocyaneus and other bacteria.

Up to that time the immunizing procedure was not regarded as the simile presumably because it was deemed necessary to use the same agent for cure, that is, isopathy. On the basis of observations of the type recorded above, gradually medicine adopted the additional conception of heterobacteriotherapy but the idea of the

simile was unappreciated, since it was stated that "immunity" was produced only by bacteria. Even if this had been true, the principle involved was the simile.

The time was not far distant when Buchner noted that sterilized cultures of Friedlander's bacillus prevented an otherwise fatal anthrax infection. He explained this on the basis of stimulation of leucocytosis and fever. Likewise Koch in his epochal work described the reaction of the tuberculous with tuberculin and Buchner and Römer showed that this could also be obtained with the alkali derivatives of proteins from other bacteria. This was confirmed by Matthes and Krehl. Before long the defensive properties of various bacteria, of animal and human sera, of nuclein were appreciated, bouillon had been discovered and it became generally known that by it one was able to save animals from otherwise fatal infections with cholera, typhoid, streptococci (Klein, Sobernheim, Klemperer, Metschnikoff, Chantemesse and Widal, etc.). Only as recently as 1914 did these observations find more proper application in the so-called non-specific effects of typhoid vaccine as in the work of Ichikawa, Krause and Mazza, Ludke, Dekastello, Zupnik, Müller, Leiner, Galambos, Feistmantel, Luksch. Ludke, Leiner and Galambos. Zupnik emphasized the importance of deuterio-albumoses in therapy, Nolf stressed peptone injections, Luksch sodium nucleinate, and Saxl milk injections. Similar observations had been noted in the field of serum therapy. In 1907 Deutschmann introduced a "paraspecific" horse serum prepared by injecting horses with yeasts and employed it in various infectious diseases. Following the introduction of convalescent serum in infectious diseases came normal human sera. Incidentally sera had been introduced by workers for the treatment of some of the phenomena associated with the toxicosis of pregnancy (especially the skin lesions) whereby the door was opened for the non-specific treatment of skin diseases. Favorable results were reported by Linzner, Zeiler, Hueck and others. Thus the time was ripe for "non-specific" serum therapy of infectious diseases and Bingel's report appeared. In this communication 466 cases of diphtheria were treated with normal horse serum and without essential difference in the result as compared to the use of diphtheria antitoxin.

When the simile nature of many of these practices was again emphasized, it was again denied, this time on the basis that only proteins are capable of releasing the reactions essential to cure. However, the terms heterobacteriotherapy and heteroserumtherapy were relegated to the background. With recollection of the work of Matthes and Krehl on protein split products and the suggestion of Weichardt, based on the so-called high-molecular protein split

products, the word proteinotherapy could not last long. It was soon replaced by protein body therapy. Once more it was finally remembered that many preparations had proven quite satisfactory, yet they could not be placed in this class. For example, turpentine, formic acid, sulphur, silicea, sugar solutions, indeed, even distilled water produced similar clinical results. After attempts with "colloidotherapy" one turned again to proteins but the phrases "protein equivalent therapy," "protoplasmic activation" were remote from the original conception of the sole utility of proteins or bacteria.

These remarks are not intended to minimize the importance of "specific therapy." The sole purpose is to emphasize the much neglected non-specific therapy although both of the two great procedures are founded chiefly on the simile finding principle.

With this has gradually come an appreciation that the recovery from infectious diseases is not exclusively dependent upon the formation of specific antibodies, but that it also depends upon non-specific actions. It makes little difference whether one assigns this to increased destruction of body proteins as do Piek and Hashimoto, to disturbances of the body colloids which led to the introduction of the term colloidotherapy, to the appearance of cell-destructive hormones of Gottlieb and Freund, to the trans-mineralization of Kroetz, changes in water regulation and that of electrolytes as suggested by Straub, Meyer-Bisch, or to reactions of the reticulo-endothelial system as emphasized by Siegmund, Oeller and others, the reaction of the hemopoietic system as urged by Schittenhelm and Weichardt, to alterations to the vegetative nervous system, the principle underlying the procedure is the simile. More comprehensive though liable to some misunderstanding are the terms healing inflammation and healing fever as introduced by Bier.

The value of "specific" therapy in infectious diseases has been incalculable, and there is suggestive evidence that the rule has much wider application than technic permits at present. Like all extremely fruitful ideas, the emphasis on the symbol "specific" and the tendency to regard proteins as exclusively important in the treatment of infectious diseases has prevented, to no small degree, the extension of the idea of non-specific therapy. Had the simple principle been applicable only to infectious diseases, it would have been a useful rule, even now not exhausted. But with the possibility of extension to non-specific realms, for example, to the therapy of x-ray injuries, the rule is potentially and actually more useful. If one will pause to recall the progress made in

therapeutics during 1900 years under the almost exclusive guidance of the contrarium principle, in comparison to that made in the last forty years with limited utilization of the simile, the situation becomes clearer. However, there remains the danger that one may not look beyond the symbols of "specific" and "protein" and may imagine that the rule has no further application.

Important changes are already taking place in regard to the so-called antigen-antibody phenomena. Zinsser¹ defined antigens as substances which give rise to a specific alteration in the reaction capacity of cells of the treated animals and that every true antigen is a protein. Wells² likewise remarks that such specificity depends chiefly upon the chemical structure of the proteins. Undoubtedly these statements are true, but they are susceptible to misinterpretation.

Substances able to alter proteins chemically may act "antigenically," for example, formaldehyde, iodine, etc.^{1, 2, 3} In other words, the normal proteins of an organism are not antigenic to it but when treated by some chemical capable of evoking alterations in them they may become antigenic. Thus non-protein substances may act in conjunction with proteins. Certain forms of atoxyl can combine with body proteins making them antigenic,⁴ and complement fixation reactions have been reported by this procedure. In short the introduction of a new group or radical may entirely alter the specific immunologic behavior of the entire molecule.⁵

Likewise serologic reactions have been demonstrated with chemical compounds of simple constitution⁶ and also the introduction of azodyes has protected guinea pigs sensitive to azoproteins.⁷ Landsteiner⁸ who has worked on this and allied problems particularly now concludes that "specific serologic precipitin reactions can take place with other substances than proteins." This has been demonstrated by bacterial antigens⁹ and is suggested by the polysaccharides of Heildeberger and Avery.¹⁰ Moreover, conceptions are changing in respect to the substances involved and whereas formerly a high molecular weight was deemed necessary, this is no longer held. The work of Walbum in respect to specific immunization by non-specific substances is considered later.

In this section a few remarks have been directed at one type of specificity. Medical literature reveals that progress has resulted in continual alteration of the conception as evidenced by the evolution of the thought of "immunity" against specific bacteria. The suggestion is advanced that the fruitfulness of the "ison" should not close the door to the investigation of the "simile."

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A NOTE ON SOME CHEMOTHERAPEUTIC SPECIFICS.—The subject of "causal specific" therapy is so important that it seems advisable to deviate from a sequential presentation of the modern simile in order to indicate at once the relation of the simile to the most valued and justly popular methods of applying "causal specific" therapy available to the internist. This required allusion to the problem of specificity, serums, vaccines, vaccination, desensitization, etc. Reference was also made to the existence of a second kind of specificity in which the administration of a remedy was followed by satisfactory results in such a high percentage of cases that a diagnosis could usually be made in case it was previously doubtful. It would not be fruitful to discuss "how" these remedies accomplish their results since agreement does not exist in many important respects. However, since the simile is supposed to be a finding principle, it is not without interest to determine how many of these substances came to be introduced, particularly since some historical evidence is available on this point. An important corollary is the question whether or not they could have been found by the simile. Space permits reference to only a relatively small number of the substances belonging to the chemotherapeutic specifics and here again to merely brief discussion.

QUININE.—As detailed accounts of the history of quinine are available, no extensive narration concerning this substance is necessary.¹ There has always been a small school supporting the notion that the curative properties of cinchona were discovered by the

Jesuits.² This assumption does not rest upon positive evidence; apparently the fact that the Jesuits might have been impressed by the extremely bitter taste and therefore tried the bark, furnishes the chief basis for this conviction.³ The early names as Pulvus jesuitarum, Pulvus patrum, Polvo de los Jesuitas, Jesuits' powder, refer, of course, not to the discovery but to the important role played by the Jesuits in popularizing the use of peruvian bark in Europe as well as to the fact that the Jesuit apothecary Piero Paolo Pucciarini was active in the preparation of large amounts of the bark in the early years. On the other hand, there is a larger group, many of its representatives more nearly contemporary with the introduction of cinchona and likewise supported by the majority of modern opinion,⁴ who attribute the discovery of cinchona bark in "malaria" to South American natives. La Condamine relates the quite improbable story that natives introduced it after observing a sick puma gnawing cinchona bark. Goeffry's saga describes the origin to a native who accidentally drank water from a stream into which a cinchona tree had fallen. In brief the various stories imply: its origin and introduction is enshrouded in obscurity, it was accidentally discovered either by natives or Jesuits, and agreement exists only on the accidental feature of the situation.

If now one turns to the middle of the last century the leading pharmacologist of his time reports:⁵ "but the diseases in which this remedy manifests the greatest therapeutic powers are those which assume an intermittent or periodical type. Now, in such, the methodus medendi is quite inexplicable and therefore the remedy has been called a specific. . . ." In this case specificity appears to be applicable to drugs whose mode of operation was unknown and it is difficult to see how the remedy could ever have been discovered except by accident.

Naturally the situation was somewhat changed by the discovery of the provocative plasmodium. Three remarks from current text books of pharmacology will serve to indicate that much information is still desirable in this field; Solis-Cohen states "Malarial organisms in drawn blood are killed by 1:5000 or less."⁶ It would therefore seem that the author would probably subscribe to a view of direct parasitocidal action. Cushny states:⁷ "Moreover recent studies (Macnaughten) have shown that lower concentrations affect some other functions of leucocytes, whose phagocytic powers are lessened by concentrations of 1:24,000; the bacteriocidal action of the plasma is also reduced by this concentration. There is no reason to suppose that this action on the white cells occurs when quinine is administered in therapeutic doses, which

would not give rise to this concentration." While the future may reveal a direct parasitocidal action apparently evidence of this has not as yet been obtained and the available facts suggest that the concentration required to kill the plasmodium (1:5000) is not attained in the blood stream (less than 1:24,000). It may be, of course, that some transformations of the alkaloid or some condition of the body may "sensitize" the plasmodium so that it succumbs to direct action. Sollmann states:⁸ "Attempts to explain the specific action of quinine have so far been unsatisfactory; a remark which holds true also for the chemotherapy of all other protozoa. The evidence indicates that the effect is not due to a direct toxic action of quinine on the parasites *in vitro*; this is not materially greater than with non-specific drugs, and the concentrations of quinine which are required to kill the parasites *in vitro* are much higher than those which exist in the blood in quinine treatment. Nor has it been possible to demonstrate the production of specific or non-specific immune bodies; nor is the action due either to an antipyretic or to a colloido-clastic reaction, for other agents which produce these effects are not specific against malaria. It is conceivable but not proved that quinine stimulates some other natural defense mechanisms; for instance the phagocytosis by the large mononuclear lymphocytes or somewhat vaguely it renders the parasites less resistant to these mechanisms." In short, endeavors at "explanation" have not met with much success.

Whether or not quinine could have been discovered by simile thinking is a matter of speculation, but the fact remains that this particular drug did form the point of departure for the reintroduction of the simile.

ARSENIC.—The various arsenicals, particularly different compounds of the arsphenamine type, are so extremely valuable in the treatment of syphilis and especially in the early forms with marked involvement of the skin, that they have been appropriately called specifics.

Arsenic was well known in antiquity. According to Throne⁹ it is mentioned in the Indian materia medica. *Rasaratnasamuechaya*, from a period near 1500 B.C., and was advised in leprosy. Hippocrates repeatedly mentions "sandaracha," probably a sulphide of arsenic in the treatment of ulcers.¹⁰ Dioscorides¹¹ devotes a section to arsenic emphasizing its usefulness in the treatment of diseases of the skin. The same may be said of Galen. *Aetius* living in the sixth century knew that arsenic given internally produced a skin eruption.¹⁰ The Arabian school was well acquainted with the arsenical treatment of skin diseases. The Paracelsian school employed arsenic in syphilis if one may interpret "Franz-

osen" as a name for this disease. The work of Fowler,¹² perpetuated in "Fowler's solution" dealt primarily with malaria. However his successors, as Girdlestone and others, extended the use of this solution to the treatment of leprosy, psoriasis, lichen, prurigo, syphilis, all diseases in which the skin tends to be involved.¹³ Indiscriminate employment and overdosage, poisoning, etc., subjected arsenic to considerable discredit and voices were raised against its internal use and restriction of external application (Junker, Boerhaave, Triller, Lieutaud, Heister, De Haën, Quarin, Stoll, Peter, Hufeland, etc.). Naturally skin manifestations of arsenic were frequently observed as urticaria by Fowler, "taches arsenicales" by Devergie, keratosis and arsenical cancer by Hutchinson.

The new chapter in the treatment of syphilis began with Bunsen's discovery of cacodylic acid, Bechamp's use of atoxyl, and Ehrlich's discovery of salvarsan.

How arsenic was found to be useful in the treatment of disease is unknown, but apparently its particular effectiveness in diseases involving the skin is recorded in the oldest extant medical writings. Soon after the introduction of syphilis into Europe, if one accepts the post-Columbian tradition of origin, arsenicals were advised in the treatment of this disease. It seems reasonable to assume that since arsenic had proven useful in the treatment of skin diseases in general, it was tried empirically in this "new" skin disease. However it is worthy of note that it was promoted in this connection by the Paracelsian school, for example, by Becher.

In regard to the simile method of thinking, everyone is and has long been aware that few drugs equal arsenic in frequency with which they produce dermatitis medicamentosa. Hardly any drug rivals arsenic in its tendency to produce the most variegated and extensive skin eruptions which may be erythematous, vesicular, bullous, papular, pustular, exfoliative, etc. Andrews¹⁴ states: "all types of lesions are encountered and in any one case they may be multiform." Likewise salvarsan is no exception to this rule. Kolmer states:¹⁵ "the rashes that may follow the intravenous injection of arsphenamine and its substitutes are extremely varied and so many types may be encountered that it would appear almost useless to list them all on a morphological basis."

In view of the relative ease with which arsenic produces eruptions and the variegated pictures resulting, and on the other hand recalling the marked tendency for syphilis to involve the skin in a high percentage of cases, it does not seem unreasonable to suggest that simile thinking could have suggested the possible utility of arsenic in syphilis.

It will be appreciated that it has seemed more consistent to present this subject on a very primitive level by employing a pure symptomatic comparison as the guide in the application of the finding principle. It would have been equally possible to present the subject from the standpoint of the similarity of round cell and plasma cell perivascular infiltration with syphilis as well as with all the agents successfully employed in its treatment. However it seemed inconsistent to discuss these aspects in connection with possible "finding" of remedies since "perivascular" infiltration was obviously a late discovery in the tissue diagnosis of syphilis.

In regard to the modus operandi of salvarsan there is little unanimity. The situation is well described by Walbum:¹⁴

"The experiments mentioned here have demonstrated that mice and rabbits infected with virulent tetanus spores and mice infected with virulent tubercle bacilli, could be sterilized by exceedingly small doses of various metallic salts, so that here we are dealing with a 'therapie sterilisans' which has been accomplished with small doses. It is scarcely to be doubted that this action occurs only in an indirect way and that every direct action of the injected metal salts on the injected bacteria must be considered as unlikely. . . . The correctness of the theory on which Ehrlich constructed his experiments, namely the capacity of the remedy to act directly disinfecting and specifically in the organism was doubted soon after the appearance of salvarsan. In this connection I recall merely Uhlenhuth and Lesser, who considered the action as indirect, that is, brought about by the stimulation of cell activity. Although the Frankfurt Institute tried to prove the direct effect, they were unable to do so in a convincing manner and the possibility of an indirect effect on the antibody producing organs was immediately recognized by Ehrlich. However he was continuously of the opinion that the main effect was due to the direct disinfecting action of the remedy. This dispute was of considerable interest in pure scientific respects but of no practical importance, because the action of salvarsan was recognized very quickly. On the other hand the conception of Ehrlich, according to which it was a matter of applying a chemotherapeutic remedy in as large a dose as possible, and not simply to sterilize the organism at once but also to avoid making the provocative organisms 'arsenic fast,' had fateful results as its consequence. The successful experiments of Ehrlich with protozoa naturally raised expectations of finding substances with similar effects against the bacterial diseases. Numerous attempts have been made, particularly in Germany, to find substances of this nature, but the result was, as we have seen, not very satisfactory. In spite of 15 years of work in this direction it was not

possible in a single case, starting from these theoretical presumptions, to find a substance whose action towards bacterial infections could be compared with salvarsan action against trypanosomes and spirochetes. The main factor in this lack of result after many years of work is found in the fact that in these investigations—according to Ehrlich's theory—success depends primarily on applying a given substance in the largest permissible dose, as near as possible to the 'dosis tolerata' and thereby it was hoped to obtain an optimal effect. In this country after the appearance of sanocrysin we had occasion to notice a tendency in this direction. I believe I have proven by my experiments on the therapeutic characteristics of the metal salts that this is based, to a large extent, upon a completely erroneous foundation in respect to the physiology of the event and it may be considered as a definite fact that the injection of large doses of such compounds into an infected organism—apart from a possible direct metal poisoning—to a great extent suppresses the natural defensive mechanism of the organism against the attack of the parasite and by this fact alone improves the living condition of the latter so that the individual will perish quicker than without treatment. That the principle of large doses has suffered its defeat, finds here its explanation and its experimental proof. Even in Germany, the motherland of chemotherapy, the more or less uncritical injection of all kinds of substances with unknown or uncertain action (often large doses of various metal salt compounds), which has become very popular in recent years, has been strongly criticized in authoritative circles (Bier, Krehl, etc.). It is particularly harmful in infectious diseases and it cannot be doubted that the deeper cause of this misunderstanding is due to unlimited confidence in Ehrlich's theories concerning an effective chemotherapy. It is readily comprehended why it has taken so many years for this reaction to occur. It is due chiefly to the protecting influence of the exceedingly great authority of Ehrlich and furthermore to the lack of experimental evidence which could satisfactorily explain the phenomenon of *sterilisatio magna* in another manner."

While this citation introduces other points, as yet not discussed, it serves to emphasize that under the prestige of Ehrlich's authority thousands of workers have been laboring in the field of "chemotherapy" utilizing the chemical structure of the compound as a finding principle and without much success. In view of rather dismal outlook for research which considers that the agent acts directly and the infected host in no other capacity than a test tube in which the action will take place, it would seem that attention might be turned to other finding principles like the simile.

How salvarsan cures syphilis is unknown. The inability of this and related compounds to kill the spirochete in relatively strong concentrations was responsible for the introduction of theories in which the host was supposed to transform the compound into some more active substance and again some special relationships to sulphhydryl radicals have been postulated. As implied above most attention has been directed to the chemical compound and the provocative organism, comparatively little but increasing interest displayed toward the host.

A start in this direction has been made by Roskin¹⁵ and collaborators,¹⁶ Marzinowsky,¹⁷ Orlow and Lewinson¹⁸ in their as yet unconfirmed work that mice infected with durine and recurrent fever spirochetes, rabbits infected with syphilis, have a markedly increased response to salvarsan if the animal is exposed to ultra-violet radiations shortly after the injection of derivatives of arsenobenzol. It has been suggested by Feldt,¹⁹ Kritschewski,²⁰ Jungeblut,²¹ Kelly,²² Kolmer and co-workers²³ that animals whose spleen has been removed show a diminished response to salvarsans. There is also an increasing literature on possible antibody formation in syphilis and the relationship to salvarsan. Restriction of attention to the spleen and the reticulo-endothelial system of the spleen, liver and bone marrow and neglect of the skin as an organ of immunization may possibly account for many failures in this field. This is suggested by simile thinking in that both syphilis and arsenic show an elective tendency to involve the skin.

MERCURY.—The story of mercury and its use in syphilis is quite the same. According to Darby²⁴ mercury was employed as an inunction in the treatment of "syphilis" in 2500 B.C., by the Chinese. Alexander of Tralles employed it in condylomata²⁵ and the early Romans in a variety of ulcerative skin diseases. Hardly a writer of the Arabian school fails to mention mercury in the treatment of scabies, pediculosis, leprosy and other diseases involving the skin. Therefore it is not surprising that mercury should have been tried empirically when syphilis ("Mal de Naples") became widespread at the end of the 15th century. It had proven useful in other skin diseases, it might in this one. Fracastoro eulogized its mythical origin describing it as a gift from the Gods.

On the other hand syphilis and mercury poisoning often resemble each other so closely that the two syndromes may be confused with each other. Schulz²⁶ has devoted a most interesting chapter to this similarity.

The reader may well anticipate that almost innumerable theories have been offered to explain the action of mercury in syphilis during 400 years' experience with the disease and remedy. While

mercury is invaluable in the treatment of this disease, actually a specific remedy, the fact that almost countless preparations of mercury have been introduced on the one hand, and partial displacement of mercurials by the arsenical compounds on the other suggests, what is generally known and often forgotten, that no specific will cure every instance of disease for which the remedy is supposed to be specific. As arsenic or even splenectomy is often found necessary in the treatment of malaria, so in syphilis, numerous specifics besides mercury are at times necessary, for example, the preparations of bismuth.

Many writers adhere to the theory of direct antiseptic action, a viewpoint steadily becoming more improbable. If Bronfenbrenner and Noguchi demonstrated that the spirochete is killed by 1:1000 bichloride of mercury in a test tube, this fact is of little importance in clinical syphilis.²⁷ Metaphen will kill staphylococci in a 1:10⁻⁸ dilution in a *water* solution, but this strong mercurial compound is quite useless in the treatment of syphilis. To state the matter another way, Lomholt and Kissmeyer have shown that at the height of a mercury cure in syphilis, the blood contains 1-3 mg. Hg per liter, while 20 mg. Hg per liter is not sufficient to retard the growth of the spirochete.²⁸ On the other side, since the time of Girtanner there has been a steady increase in numbers of those accepting the theory of an indirect action of mercury. Many regard mercury as an agent stimulating the body;²⁹ some attribute the cure to excitation of oxidative and metabolic processes;³⁰ some a potentiation of the defense reactions.³¹

It will be perceived that while the writer has not attempted to discuss even a small fragment of the literature dealing with the problem of how these drugs act, that some emphasis has been placed upon the fact that a "direct" disinfecting action will not explain the action of any of these "specifics." The purpose underlying this emphasis has been to support indirectly the statement made earlier that reflection will show that in none of these diseases can the term "causal therapy" be applied in a strict sense. In all instances the simile could have "found" the remedy, in case one prefers this explanation to that of "accident." In one instance there is a rule given for the finding of remedies (and naturally it will be difficult to apply); in the other case advance in therapeutics will have to await fortunate accidents.

Schlossberger has written in this connection: "chemotherapy cannot, as is frequently done, be considered 'inner disinfection' of the diseased body, for it requires the active co-operation of the organism in order to accomplish healing effects, the natural defense efforts which it attempts to support. This leads to the fact that

particularly our most effective chemotherapeutic substances, for example, salvarsan, germanin ('Bayer 205') and also quinine in test tube investigation show only a very slight action against micro-organisms, but in the living organism they are able to influence successfully the same disease producer by the use of relatively small doses. Therefore in chemotherapy it is not a matter of a disinfecting process in the usual sense of the word, that is, not a reaction which takes place between the chemical agent and the exciters of disease, but of a process in which the cells of the infected body play an important role. Likewise Dale found, for instance, that the benzidine dye, trypan red, has an effect upon *mal de Caderas* (*trypanosoma equinum*) only in the mouse, while it has no effect in guinea pigs, rats and dogs which have been infected with this parasite, and emetine produced a healing effect of amebic dysentery in the human body but not in experimental infection of cats with *endamoeba histolytica*, which can only be explained by the participation of the infected organism in the healing process. For this reason, as already mentioned, in the search for chemotherapeutic remedies, it is naturally not possible to decide through preliminary test tube experiments whether the chemical preparation in question will be suitable for therapeutic influence of an infectious process in the human body and the chemotherapeutic effectiveness of a substance can be determined infallibly through a test of healing first on the artificially infected animal and then upon the naturally diseased body."³²

ANTIMONY.—In order to conserve space merely a brief notation of a few other chemotherapeutic specifics is given. The modern introduction of antimony seems to have resulted from the work of Plimmer and Thomson³³ in 1907. They found it useful in nagana and surra trypanosome infections. Noguchi³⁴ and Smyly³⁵ found it would kill *Leishmania* in a concentration of 1:100. Stibosan used in the treatment of the same disease is not effective in a dilution of 1:20;³⁶ however, berberine sulphate which is not particularly useful kills the parasite in a dilution of 1:200 and depresses development in a concentration of 1:80,000.

How antimony was discovered is unknown, but the oldest medical documents extant mention it as a cosmetic and apparently it was employed in trachoma in prehistoric times in Egypt. Likewise its use in infectious diseases, for example smallpox, dates back about 1000 years; in fact, it was once regarded as a panacea. On the other hand few substances are able to produce pustular eruptions, very similar to that of smallpox, with the regularity of antimony. A variety of other involvements of the skin are also known.

In the bismuth treatment of syphilis, the earliest and most

dreaded sign of intoxication is the involvement of the mouth and throat. Is it not peculiar that Masucci introduced the bismuth treatment (in the form of bismuth protoiodide) of syphilis for syphilitic throat involvement?³⁷

Few pharmacologists would be willing to assert that the effectiveness of bismuth compounds in the treatment of syphilis depends upon a direct action. The failure of bismuth salts in strong concentrations (1-2%) to affect the spirochete, whereas the same preparations become effective in the presence of organ extracts is suggestive. One may also wonder about "concentration" when it is recalled that bismuth, in the commonly injected poorly soluble form, is transported by means of the white blood cell. If the attitude of Kadisch is correct organ extracts such as liver antolysate are capable of killing the spirochetes and perhaps bismuth stimulates body cells to the formation of substances capable of killing the spirochete. This view finds suggestive support when it is recalled that in the Levaditi-Lepine-Howard experiment it was found that the older the syphiloma, the less bismuth is necessary to induce cure. Kolle, proceeding from the slowness with which bismuth acts, concluded that bismuth was protoplasmic activating and catalytically active.

IODINE.—Reference to a substance which is widely and successfully employed as an external antiseptic permits allusion to another aspect of the problem. The discovery of iodine as an antiseptic is likewise lost in the darkness of antiquity. Plant forms of iodine were employed for this purpose by Hippocrates, Dioscorides, Galen, Celsus, etc. Incidentally the Chinese employed iodine in the treatment of goiter at a very early time.³⁸ Two brief citations may serve to emphasize an oft-neglected point.

"Even the best wound antiseptics never act through their 'anti-mycotic' action alone but always together with the 'cytophylactic' action of the tissues."³⁹

"In the healing of wounds we have to differentiate between the direct action of the disinfecting substance and the indirect action when, by this, the organic defense powers are first mobilized. And the latter is probably greater and more important in the healing effect of the wound antiseptics approved in practice."⁴⁰

The discovery of iodine as a direct antiseptic would probably not occur under simile thinking; the same holds for remedies for the various animal parasitic infestations of the intestinal tract which would probably not have been discovered by this method of thinking. Whenever the parasiticidal agent can be directly applied to the infectious agent in sufficient concentration to cause death by a direct influence, the simile does not come in question. For example,

the direct removal of tapeworms is not a simile problem. However the two citations introduced above suggest that this viewpoint of chemotherapy is changing.

Perhaps it is permissible to digress momentarily and indicate another aspect of the iodine problem. Kotschau has had occasion to observe a series of 272 "nervous and mildly hyperthyroid" women. Fifty-one were used as controls. All patients were subjected to the same regimen. However some were given sugar of milk tablets identical with medicated tablets and the periods of medication and non-medication were concealed from the patients.

Administration of iodine did not induce the well known toxic actions of iodine in every case. In addition to more or less individual coloring some women displayed cardiovascular symptoms, others gastro-intestinal phenomena, still others skin symptoms. This suggests varying susceptibility of different organ systems.

The patients may be divided into two groups: those in whom the typical iodine picture was displayed and those showing therapeutic responses. In other words a group in which existing symptoms were aggravated and a group in which the existing symptoms were improved or removed. The results can be tabulated as follows:

	Improved	Aggravated	Biphasic Effects	Unaffected
Nasopharyngeal symptoms.	19	41	16	3
Tendency to perspire	57	26	15	30
G. I. symptoms	43	25	14	21
Skin phenomena	28	48	19	16
Weakness and lassitude	92	4	17	66
Internal unrest	72	14	14	36
Tremor	60	14	16	25
Palpitation	65	34	35	30
Anxiety, oppression	42	26	18	21
Headache	86	12	22	23
Insomnia	59	17	25	23
Rheumatoid complaints	32	26	20	18

From this one perceives that drug action is extremely complex. On the one side five drops of Lugol's solution three times a day may be given for months without producing iodine intoxication; on the other side a fraction of a drop may produce cardio-vascular or gastro-intestinal symptoms within a few days. Between these extremes are innumerable transitions. One will also note that iodine does not act upon a single symptom but rather a group of symptoms, all of which are common to hyperthyroidism. With the larger amounts of iodine an increased incidence of aggravation was noted. Even with reduction of dosage, initial aggravation and subsequent improvement was encountered. In amounts which re-

semble the dosage of tuberculin, aggravations were no longer encountered.

Iodine medication is adapted to individually present iodine sensitivity. It is commonly held that iodine is contraindicated in the presence of iodine idiosyncrasy; however these observations suggest that on the whole the insensitive organism does not react to iodine, whereas the sensitive organism responded, not simply by aggravation with larger amounts, but by improvement with smaller doses. This suggestion ought not to seem unusual because sensitivity to tuberculin is the presumption and basis for the employment of tuberculin where aggravation and improvement may also be noted. Thus, in this instance iodine sensitivity is the presumption for iodine therapy according to simile thinking, and moreover, this sensitivity was observed only when symptoms resembling those of iodine intoxication were present prior to iodine medication. When the entire complex of iodine intoxication was present, not only, as a rule was iodine sensitivity present but the increased therapeutic response. It should also be noted in passing that thyreiodin proved even more satisfactory than iodine, a fact which ought not to be surprising because it is obviously a better simile than iodine. Space does not permit further analysis of this question here, but reference to the section on Kotschau's rule of typical effects will reveal how well Plummer's justly advocated "large" dose of iodine and the rapid temporary improvement is adjusted to the "B" curve. However to return to chemotherapy.

The basis of the conception of Ehrlich is that a remedy comes into consideration as a chemotherapeutic agent only if it has a direct damaging effect on the exciter of the disease. Parasitotropic remedies were sought in this way. If the remedy did not act *in vitro* but did *in vivo* it was supposed that de- or re-composition had occurred in the body, whereby a parasitotropic substance was produced out of the medicament. For example Ehrlich and Shiga⁴¹ found that trypan red in a 0.5 per cent solution does not kill the trypanosome of mal de Caderas even after two hours, whereas in mice experiments, in far smaller concentrations, it acts prophylactically when the infection is introduced two days after its injection. Ehrlich and Shiga were forced to assume that the action is due to dye, which freely circulating in the blood and unattached to cells, would damage the trypanosomes so that they would be unable to multiply. In the citations above there is the foreshadowing, not of a direct chemotherapy but one in which the host and its defensive "mechanisms" are given primary consideration.

It is commonly known that potassium iodide is a specific in tertiary syphilis and that the causative spirochete can be grown in

concentrations of this substance unattainable in the body, so that a direct chemotherapeutic action does not come into question.

A discussion of the origin of all the chemotherapeutic specifics would require an encyclopedia, since in the substances mentioned only a small fragment of their story has been presented and again it is obvious that all medicinal substances are chemotherapeutic substances. It must suffice here to note that the history is essentially the same regardless of what illustrations are selected; chaulmoogra derivatives in leprosy, the ipecacuanha derivatives in amoebic dysentery, etc., were treasures of folk medicines. On the other hand it is evident that digitalis, for example, not only frequently cures auricular fibrillation but also produces it as Edens⁴² has recently reiterated. That simile thinking is not confined to chemotherapeutic substances but is also applicable to forms of energy will be recalled by the fact that x-ray not only remains (outside of surgery) one of the best agencies in the treatment of cancer, but also produces it.

It will be apparent to anyone perusing an encyclopedia of pharmacology or who reads current literature that a large number of pharmacologists diligently looking for remedies, erect their experimental set-up upon the hypothesis of direct destruction of the "cause." For this reason the term *school of chemotherapy* was employed elsewhere in the text. It is highly probable that given time and further developments, this finding principle may be of use and will certainly furnish valid and interesting material. However it must be recalled that in each instance of success up to the present, the essential has been a refinement of some method already known to folk medicine or to medicine operating upon the basis of some other finding principles. Excluding infections of the skin and intestinal parasites, instances are exceedingly rare where the body cells permit this direct method and evidence is increasing that this direct action does not occur in the "systemic" diseases and that "internal antiseptis" is not accomplished. While it is dangerous to utter prophecies, it would seem that the continued interest of chemical structures and neglect of the host will continue to be met by failure.

More recently pharmacology has adopted another ancient principle with great success, namely, treatment by substitution. While it is not curative in most instances, it should not be belittled because of its symptomatic nature. In most instances such substances would probably not have been found by simile thinking; one thinks of the vitamins, the endocrine products, the liver and gastric substances in pernicious anemia, etc. There is strong reason for be-

lieving that hundreds of such substances exist and that the methods in vogue for their discovery are proper and finally that medicine will make spectacular advances in this domain in the next few years.

But it would be a great mistake to believe that the substances discovered in this manner cannot be utilized in simile thinking. If the action of massive doses of x-ray in the treatment of malignancy is a "contrarium" effect, this does not exclude a large domain application of the "simile," for instance, the employment of smaller doses of x-ray in the treatment of some anemias. The vitamins find discussion elsewhere. However, it must be noted here that in many cases the theory of substitution is not entirely clear. For example, it is generally agreed that iron was found useful in the treatment of "anemia" when it was noted that water in which swords had been allowed to rust, had beneficial properties. It is also known that the more active forms of iron are hemolytic; iron could have been found by simile thinking. How iron acts in anemia is unknown, but it may not be a simple "substitution" for a deficiency in iron in hemoglobin. For example, Burgi has recently secured excellent results in this group of cases with iron-free products.

Another point may be suggested at this juncture. A large number of medicinal substances, formerly widely and gladly employed by physicians, have been discarded, perhaps prematurely by medicine. When alkaloids were discovered and responsibility for therapeutic action in many instances was assigned to them, plants previously in vogue for centuries were consigned to, at least, a temporary oblivion on the basis that they contained no alkaloids, thereby overlooking the fact that other substances present might be responsible for the action, for example, resins, minerals, etc. The case of cod liver oil represents an interesting analogy. After centuries of successful lay and professional use, largely on the basis of "caloric" studies, it was held that any other oil could replace cod liver oil. After a period of unsuccessful replacement, vitamins were discovered. At present numerous attempts are being made to add the vitamin to some palatable medium in order to replace cod liver oil. Thereby the iodine content of the oil is forgotten entirely, and it is not impossible that the results obtained, for example in tuberculosis, with cod liver oil may be attributed in part to the iodine content rather than solely to the vitamin.

Another factor contributing to the discard of many remedies long enjoyed by medicine was the laudable determination voiced by Kobert among others, namely, to disregard tradition and experience and to re-study all known medicinal substances by the newer labora-

tory methods of science. Unfortunately this program was hardly under way when the brilliant work of Ehrlich, the development of endocrinology, the discovery of vitamins, etc., together with an attitude of physico-chemical mechanism turned attention almost exclusively away from the old toward the new. One great source of danger of neglect of the accumulated knowledge of the past becomes apparent when it is recalled that unawareness may become equivalent to unimportance.

In conclusion another factor underlying the disregard of the therapeutic properties of many medicinal substances used in the past involves the idea of specificity, or better perhaps nosology. History teaches that no remedy can be expected to act in every instance of disease (if one omits those diseases due to a deficiency in some extrinsic factor which may be supplied, for example, vitamins); for example, quinine will not cure every case of malaria, nor salvarsan every case of syphilis. This contention is supported by the fact that a large number of remedies, for example, salvarsan, plasmochin, etc., have been introduced in the treatment of malaria and an even greater number of substitutes for salvarsan. This ever changing attitude in itself is evidence that these remedies are not "specific" in a strict sense. This emphasis on the limitations of these substances should not be construed as an attempt to discount their value. Undoubtedly they represent some of the most spectacular advances made in the health of mankind in the annals of history. But the protean nature of syphilis immediately implies that not one, but many different remedies will be necessary for its eradication. Before this was generally appreciated, when experimental pharmacology was young, when nosology was still primitive, many substances were slated for discard. It ought to be re-emphasized in order to avoid misunderstanding that with no guide except experience, which was frequently fallacious, during the centuries undoubtedly more chaff than grain had accumulated. The ruthless determination to begin anew, to work with only a few remedies whose action was well attested, was a decision which called for the highest type of scientific courage and honesty. Moreover, this accomplished excellent results in several directions and those emphasizing the simile would do well to emulate their colleagues in the hereulean task of sweeping pharmacologic stables clean. Nevertheless they serve a distinct function in retaining the old until pharmacology gains time to direct its attention once again to applied pharmacologic history. And unless the accumulated wisdom of centuries is based upon faulty premises, that re-survey will be fruitful if rule investigation is pursued.

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A NOTE ON THE ACTION OF SULPHUR.—The writer is thoroughly conscious of many obvious defects evident in the preceding section. Perhaps overemphasis has been placed upon certain infectious diseases; but it is exactly in this field that medicine has made its most important advances in the field of chemotherapy (in the narrow sense of the word). Perhaps it has been unintentionally implied that "drugs" form the most essential feature of therapy. Perhaps the important field of palliation has received too little attention. At times the limit between palliative therapy and curative therapy is difficult to draw. For example, the statement has been made that substitutive therapy is usually palliative. As a matter of fact there is no evidence to support the contention that thyroid substance will cause regeneration of the thyroid gland. On the other hand, it is highly probable that if the "strain" on the islands of Langerhans can be relieved by insulin, those islands as yet not involved by any lesion beyond cloudy swelling may revert to normal or relatively normal structures, and in these instances the diabetes mellitus may be clinically cured, providing no undue strain is subsequently placed upon the pancreas. Moreover it has not been the intention to imply that the simile has at present anything to offer parallel in palliative value, for example, to insulin or thyroxin, nor for the regeneration of a dead cell of any organ of the body.

One intentional defect in the preceding section, and incidentally equally true of many others, is that the remarks are so general that they are vague and hardly susceptible of application. In order to minimize the potency of this perfectly valid objection it has seemed advisable to supplement the above generalities with a more detailed, but not exhaustive discussion of a specific example. In the preceding section the use of oil of chenopodium in intestinal infestation,

the question of the merits of gentian violet in the treatment of diphtheria carriers, etc., were not discussed because these things, though extremely valuable, have nothing to do with the subject under discussion. On the other hand, no one doubts the remarkable efficacy of quinine in malaria, salvarsan and mercury in the treatment of syphilis. These and a few others were, perhaps, insufficiently discussed since they represented the clearest examples of so-called specific chemotherapy, in the usual meaning of this phrase. It was suggested that the most accredited workers in this field now seriously doubt any "direct" action of these substances and increasing evidence emphasizing the participation of the body minimizes the possibility of a "causal" therapy in "systemic" diseases; this casts grave suspicion on the real validity of research prosecuted on the almost exclusive basis of structural chemistry. Unless theories on the effect of introduction of chemical radicles are employed as finding principles (and there are surprisingly few generalizations in this respect), the plan of investigation consists in the elaboration of this or that compound with the hope that something will be accidentally discovered. While not discounting the value of "trial and error" investigation, attention was directed to the existence of another finding principle. It is realized, of course, that the presentation in its generalities smacked strongly of "stretching the facts to fit the theory."

For this reason it seemed advisable to supplement the discussion by a note on the action of sulphur. The use of this illustration was prompted, not by its special adaptability to the ideas advanced here, but because it seemed to possess a majority of disadvantages. Some of these may be recounted.

Reference to practically any standard text book of pharmacology will reveal that the use of sulphur is advised principally for the treatment of local parasitic infestations, for example, in scabies where it is employed as a 10-15% ointment. Preparations of similar strength are at times used when keratolysis seems desirable although the alkali sulphides may be preferred here. Further study of these standard texts will indicate that sulphur is occasionally employed in doses of 20-60 grains as a mild laxative with no particular special properties which differentiate it from numerous other mild laxatives. Inquiry among those who consciously utilize the simile will reveal that the substance is employed in a wide variety of conditions, some of which involve the skin. If questioned on how they arrived at the conclusion that sulphur might be useful in certain skin diseases, and among these the skin diseases characterized by pustular eruptions or at least a tendency to sup-
puration, they would invariably respond that when sulphur is

administered to healthy human provers, it produces pustular eruptions or a tendency of the skin to suppurate. The remedy was "found" in this manner. If the inquiry is carried farther it becomes evident that they further allege that such eruptions were produced, not by sulphur applied externally in strong ointments, but by very small amounts administered by mouth; for example, 1/1000th of a grain of sulphur administered by mouth three times a day. In the first place one is confronted by the fact that 40 grains by mouth usually result in no further phenomena than the evacuation of a soft mushy stool, and the claim that a dose amounting to 1/40,000th of this amount, given a few times a day will alter the entire body economy, in this particular case, provoke remote phenomena in the skin. It is usually pointed out that much more sulphur than 1/40,000th of a grain three times a day is administered daily in the food, although obviously in the form of sulphur containing proteins. Many other queries may be raised, some of which will become evident as the discussion proceeds. The pertinent literature on sulphur has reached such dimensions that only a relatively small amount can be introduced here, and that presented is limited to the most part to the reports about the skin. The writings of Bier¹ are particularly interesting and may be consulted by those interested.

The medicinal uses of sulphur are recorded in the writings of Dioscurides² and Galen, so that sulphur may be truly regarded as an extremely old therapeutic agent. For centuries the drug was considered applicable in a large number of conditions, an alterative capable of effecting profound alterations throughout the entire body. It was supposed to purify the body, to cause the excretion of all kinds of products of disease, to rid the skin of many diseases and to change the status of disease in other organs. Likewise sulphur springs throughout the world were esteemed in the treatment of diseases which failed to react to other forms of therapy: bone fistula, chronic joint disease, anemia, syphilis, diabetes and other metabolic diseases, intractable neuralgias, etc. In many respects these and other conditions are still treated by sulphur by those employing simile thinking.

Late in the last century the medical viewpoint under the prevailing quantitative view began to change. The remarks of Leichtenstern are typical:³

"Since the materia medica has become freed from the former ballast and is based upon physiologic experiment and the careful critical observation at the bedside, the application of sulphur in therapy has become limited, except in a few instances. The belief in a powerful sulphur action of theiopegen (sulphur) springs has

given way to a much greater soberness since the relentless chemical analysis has discovered the minimal content of sulphur springs.

"As far as the therapeutic indications of the sulphur spring are concerned, they fail, since we are not able to credit sulphur either as an internal or external application with any significance, except with the indication of warm baths and the plentiful drinking of water."

Schmiedeberg,⁴ Köhler,⁵ Nothnagel and Rossback⁶ have similar statements. Penzoldt⁷ thought sulphur had manifold effects, none of which are significant. As Bier notes the German Drug Commission has nothing to say about sulphur in 1925 except the internal use as a cathartic,⁸ although in 1930 it takes cognizance of sulphur compounds as sulfrogel, etc., as parenteral stimulants for intramuscular injection.

Thus a naturalistic medicine swept aside the accumulated experience of centuries, the innumerable results of sulphur cures at spas on the basis of a theory and a quantitative analysis of spring waters. As Bier states: "This medicine which considers itself very scientific and efficient, not only believes to have exhausted the nature and value of mineral springs analytically but it also believes with the aid of this analysis to reproduce synthetically these natural waters with all their effects." The same situation held for a long time in respect to iodine but newer studies⁹ and experience with iodine prophylaxis of goiter have suggested to medicine the error of this type of thinking.

In short, then, one finds the great Hufeland esteeming the use of sulphur,¹⁰ and even Vogt¹¹ thirty-five years later was of the same opinion, and then again in less than fifteen years Oesterlen¹² doubted its value. To the historically minded reader the differences in opinions 1832 and 1845 clearly indicate the influence of the nihilistically directed school of Vienna.

Throughout these changes simile thinkers retained the symptomatology and indications of sulphur as gained through human provings.¹³ Between the two over-enthusiastic groups only the clear-sighted Hugo Schulz seems to have studied the question without bias.¹⁴

If one departs from mere argumentation and reviews the general facts available on the question, the following items may seem suggestive.

Is it not strange since sulphur is an essential constituent of every protein of the body, apart from protamines, that sulphur should not have greater physiologic significance than is indicated pharmacologically by its occasional employment as a mild laxative? Liebig's minimum law in metabolism states: "when an indispensa-

ble substance is lacking, the development of the cell, of the organ, is disturbed and its function made impossible." It is generally agreed that normal cell function is conditioned by the absolute necessity of presence of the mineral substances (Schulz, Emmerich and Loew). Moreover, it is generally agreed that the sulphhydryl group of cystin plays an important role in metabolism; here one may recall chondroitin-sulphuric acid in the joint cartilage, the sulphocyanates of the saliva, etc. The reversible actions playing between cystein and cystin should be mentioned in passing. The fact that cystin can adsorb ultra-violet rays should not be overlooked.¹⁵ Of considerable physiologic interest is the combination with glutaminic acid with these acids to form the quite universal glutathion.

The hydrogen atom of the SH group is very labile so that the compounds play important roles in cell oxidations. Ingested sulphur is ultimately oxidized largely to sulphates and finally excreted in the bile (taurin), urine, feces and sweat. Sulphur upon administration is said to be changed to hydrogen sulphide in the intestine; if the amount is large the irritant action upon the bowel causes diarrhoea and the dose is passed out of the body without systemic effects; amounts insufficient to produce diarrhoea may produce profound changes (see below). Absorbed sulphur is excreted through the skin, lungs, urine, and feces. The course of sulphur in the body has been followed by Krause,¹⁶ Regensburger,¹⁷ Heffter,¹⁸ Sabbatani,¹⁹ Salkowski,²⁰ Kojo,²¹ Heubner and Meyer-Bisch,²² Gürber,²³ Falta,²⁴ Haemaetainen and Helme,²⁵ Munk,²⁶ Bischoff and Voit,²⁷ Gross,²⁸ Hele,²⁹ Beck and Benedict³⁰ and many others. The conception of conversion into hydrogen sulphide for absorption arises from Rossing,³¹ Nasse³² and Heffter and is supported by Rey-Pailhade yeast investigations.³³ Other studies on this question are those of Wieland,³⁴ Spiro.³⁵

The cystein form is found in some proteins, the cystin in others. Particularly interesting is that the sulphur rich keratin in the upper layers of the skin contains the cystin form, while the lower layers which are concerned with cell division show the more active cystein form.

The sulphur containing protein compounds play important roles in cell oxidation and reduction processes. Normally ingested proteins are split to be re-synthesized to cystein or glutathion fractions of cell proteins. On the other side, most of the total sulphur metabolism is carried out to complete oxidation of sulphates which are excreted as alkali sulphates, earthy alkali sulphates or ethereal-sulphuric acid compounds. Taurin represents an intermediate phase of cystin splitting and of course is again resorbed and

utilized. Some sulphur appears as neutral sulphur in the urine. The skin excretion of sulphur is of interest in reference to the still to be discussed skin phenomena. The sulphocyanates in the saliva are of interest in the possible detoxication of CN.

Not only the keratin of the skin contains sulphur but also the skin pigments; the joint cartilage and synovial content of sulphur is interesting in respect to a possible relationship to joint symptoms. The major sulphur metabolism takes place in the liver, a subject which is mentioned later. The adrenals are supposed to be regulatory of sulphur metabolism³⁶ and contain neutral sulphur.³⁷

Turning now from general problems to specific phases of the subject, one may study the action of hydrogen sulphide which is formed from orally administered sulphur, either from bacterial action in the intestine or by intestinal cells³⁸ so that finally a mixture of hydrogen sulphide, polysulphides and sulphur reaches the intestines.³⁹ Wherever finely divided sulphur meets cystein in the body, the same general process occurs so that the results are probably similar from either oral or parenteral administration.

The acute toxic action of hydrogen sulphide which resembles other catalytic poisons as hydrocyanic acid needs no discussion. Likewise milder non-fatal chronic hydrogen sulphide intoxications are known.⁴⁰

The milder symptoms are headache, stupefaction, tendency to sleep, irregularity of intestinal evacuations. More severe symptoms are vertigo, excitation, intoxication, narcosis, etc.

The purgative action of larger amounts of sulphur is universally known and likewise needs no detailed discussion. Bokay⁴¹ has shown the stimulation of peristalsis by hydrogen sulphide formed from sulphur. One result is that no opportunity is given for absorption of the intestinal fluids.⁴² Van Leersum⁴³ has shown the stimulating effect of surviving guinea pig intestine when sulphur is present in a concentration of 1:4,000,000. Gordonoff⁴⁴ studied the action of water containing H_2S and found actions in a concentration of 1:10 million, these effects consisting of stimulation, whereas 1:200 caused depression in accordance with the Arndt-Schulz rule which is mentioned later.

Likewise the heart is affected by hydrogen sulphide⁴⁵ although the effects of weaker solutions have not been studied. In addition the general systemic action of sulphur from small doses has been experimentally reviewed and confirmed by Schulz, and more recently by Riesser and Simonson⁴⁶ and Zimmer.⁴⁷

In the recent re-proving by Riesser and Simonson and Richter different doses were employed, the saturated alcoholic solution in

amounts equivalent to the 4th decimal dilution (1-10,000) and again with twice as much.

In order to reduce results to objective determinations, pulmonary ventilation was measured by the Zuntz-Geppert method and a distinct increase in respiratory ventilation shown. It becomes distinct after about 2 weeks, is greatest in the 3-4th weeks, and less again in the 5th week even though larger doses are administered. Respiration may become irregular and the frequency may be doubled. With increased ventilation the basal metabolism tends to become higher with each increased dose of sulphur; if the dosage remains constant, the metabolism falls. The capacity for restitution as measured by the performance of definite work was distinctly decreased. The fact that the investigations of Siegfried⁴⁸ are opposite in direction, are not important as his experiments were too brief, etc. Lowering of basal metabolism, however, was also noted. A similar effect on metabolism is reported by Gordonoff and Misushina.⁴⁹ Studies of the action on the intestine and metabolism have been supplemented by others on the blood pressure.⁵⁰

The effect on sugar metabolism has also been fairly well studied by Bürgi⁵¹ and Gordonoff.⁵² They found histologically and chemically in rabbits and rats, an increased deposit of glycogen in the liver from the prolonged use of sulphur spring water. The same occurred after the intramuscular injection of colloidal sulphur.

Recently interest has been directed to the hypoglycemic effect of sulphur, in which hypoglycemic actions were reported after the use of 1 mg. by mouth, 1/100,000 mg. intravenously and 1/1000 mg. per kilogram body weight.⁵³ Larger doses did not increase the effect but lessened and even reversed it. Abel and Geiling's⁵⁴ purified insulin was not as active. It is possible that sulphur is to insulin what iodine is to thyroxin and the recently described bromine is to some pituitary secretions. While the hypoglycemic effect has been denied,⁵⁵ it has been repeatedly confirmed.^{56, 57} Space prohibits a discussion of other metabolic actions of sulphur.^{58, 59} In general, the work suggests that sulphur may act like a foreign protein.^{60, 61, 62} Not only is sulphur now employed in the treatment of some joint diseases, but also in disturbances of blood pressure.^{63, 64}

Particularly important for our purpose is the question of the action of sulphur on the skin. Here one is not concerned with dipilatory effects,^{65, 66} nor the so-called keratinizing effect,⁶⁷ nor increased vascularization,⁶⁸ for it is generally agreed all these effects are reversible in the sense of the Arndt-Schulz rule.⁶⁹ The theory of sulphur actions on the skin will be found summarized in the writings mentioned in the bibliography.⁷⁰⁻⁷⁶

The question to be raised here is a simple one: Hahnemann states that sulphur produces skin eruptions,⁷⁷ a statement confirmed by Schulz and more recently by Bier⁷⁸ and Abegg.⁷⁹ On the other hand Heubner denies that the use of sulphur in "boils" involves the simile on the grounds that sulphur will not produce skin eruptions.⁸⁰ He does not seem to base this statement on any personal experience and incidentally overlooks the observations of Lewin.⁸¹

It ought to be obvious that questions of this nature can be examined only by properly arranged experiments and never by utterance of belief. Although the writer has heretofore refrained from citation of personally conducted work, it seems absolutely necessary to mention one series of experiments. The question is not simply whether or not sulphur has the ability to produce skin eruptions, but whether sulphur administered by mouth in small amounts (1/1000th of a grain) is capable of producing skin lesions which may be ascribed to the ingestion of sulphur. The fact that Schulz and Bier, among others, make this assertion on the basis of observations under their direction or upon their own persons may be dismissed here.

The writer attempted to solve this question in the following manner. He secured the co-operation of 114 medical students who agreed to take one tablet containing 1/1000th of a grain of triturated sulphur in sugar of milk, three times a day, one half hour before meals. The volunteers placed the tablets under the tongue and allowed them to dissolve.

At various times the writer has conducted similar tests with a variety of substances with smaller groups. In such cases there are usually a number of volunteers who react with a wide variety of subjective symptoms, the inevitable result of taking "something." For this reason substances are given as "unknowns" and often a few weeks of administration of blank tablets interposed without knowledge of the volunteer. In the present case the procedure varied. The volunteers were informed that the test would be concerned with sulphur; that the amount would be 1/1000th of a grain; that the usual dose of sulphur by mouth (as a laxative) was 20-60 grains, on an average 40,000 times the dose to be administered; the students were permitted to secure the tablets personally from any pharmacy they desired; they were informed that the writer had grave doubts that any symptoms would develop and that no volunteers would be accepted that would not agree to participate at least six months in the experiment; it was stated that undoubtedly a "neurotic" group would develop some symptoms but that this would be more suggestive of their emotional instability rather than evidence of an action of sulphur. In short everything possible

was done to minimize the possibility of securing sulphur effects. Naturally there was no reward for participation in the experiment.

It is interesting to note that of the group of 114, 24 students developed no findings whatsoever, and there are many reasons for assuming that they conducted the experiment honestly. However, 27 did develop skin eruptions which varied from a diffuse erythema to furunculosis (16 instances), and in one case the development of 16 furuncles necessitated discontinuing temporarily the services of one volunteer. A few of the provers with acne were improved, some temporarily improved, others aggravated. This is mentioned because acneiform eruptions were quite frequent. Other skin effects consisted in sweating (localized or generalized), an occasional instance of tendency to falling of hair, etc. Eighteen provers had diarrhoea; several instances of epistaxis, acute rhinitis, etc., were observed in regard to the respiratory system. The experiment was continued for about two months, although in most instances the phenomena noted above occurred within a month.⁵²

It would seem from these experiments that small doses of sulphur administered by mouth can produce skin eruptions, at least in a percentage of cases, more than 20% in this study. The writer has no intention of generalizing from this experiment, nor is it intended to imply that all symptoms ascribed to this or other drugs are actually drug effects.

On the basis of the above experiment, which had been previously performed with smaller groups by others, it is suggested that sulphur may be of use in the treatment of certain skin diseases. Naturally the question is raised whether or not this application of the finding principle has proven valuable clinically. For a partial answer reference may be made to the study of Bier⁵³ who has reported 586 cases of chronic furunculosis treated with sulphur, in amounts equivalent or smaller than those employed in the experiment mentioned above. The details of the results obtained by this authoritative worker in a reputable institution (University of Berlin) can be found in his publications in an easily accessible journal and need not be detailed here.

The work of Bier is particularly interesting since the question was raised as to possible psychologic effect rather than actual drug effect. In order to decide this question Joachimoglu prepared some powders containing 1/1000th of a grain of sulphur iodide, others merely with sugar of milk. The attending physician did not know which contained drug and which sugar of milk alone. The cases receiving the drug reacted successfully, those receiving sugar of milk did not, but when this aspect of the experiment was over the latter were placed upon the drug and reacted favorably. This has

been acknowledged by Joachimoglu⁸⁴ who has no interest in the simile problem. Sulphur has also been used successfully in other staphylococcic pyodermias⁸⁵; the results are not so distinct in streptococcus infections,⁸⁶ although better in prophylaxis of erysipelas.⁸⁷ Sulphur has likewise been employed in sepsis⁸⁸ and purulent bronchitis⁸⁹ but as yet the data are quantitatively insufficient for an opinion.

The ancient use of sulphur in connection with heavy metal poisoning, advanced in this country by Wilms, has been emphasized by Spiethoff in Germany.⁹⁰

However it would still not be worthwhile to discuss sulphur on the basis of the above material, were it not for the fact that sulphur represents an opportunity to suggest what may be termed the constitutional aspect of drug therapy.

Beginning from the old observation⁹¹ that some provers had a hydrogen sulphide odor to the excretions after taking sulphur,⁹² Bier attempted to investigate this problem. He presumed that some individuals have a disturbed sulphur metabolism whereby the small dose of sulphur acts as an excitant provoking changes in the stored body sulphur. This idea was based upon the fact that the odor of sulphur compounds was not common to all patients taking the drug. Moreover, some individuals felt much better after taking sulphur, others not, some developed furuncles, others did not. Investigations of sulphur metabolism⁹³ have yielded uncertain and variable results possibly because of differences in the subjects.

Bier's study may be summarized as follows: Tablets of sulphur were carefully prepared so that they contained equal amounts of the drug. Outside of minute traces of sulphuric acid they contained nothing but elementary sulphur.

Quantitative tests were performed to determine the limit of visibility at which the precipitation of mercury or silver occurs. It was found that blackening of silver and mercury will not occur with amounts less than 1/100th of a milligram of sulphur. The limit for detection of hydrogen sulphide by smell varies with the sensitivity of the nose but is greater than the amount contained in many tablets containing sulphur 1:1,000,000. A patient would have to take such tablets of sulphur daily for a month and then excrete all the sulphur at one time to equal 1/100th of a milligram.

Tests were made to determine the normal excretion of sulphur through the skin. A silver plate 200 cm.² was attached to the chest of a patient. The patients proceeded to follow their usual mode of life. The clean plate was weighed exactly before the experiment. After it had been carried for exactly 10 days it was again cleansed with 1% NaCl, alcohol, water, distilled water and again weighed

exactly. The increase in weight showed the amount of sulphur adherent to the plate. Calculated for the total skin surface it was found that this amounted to about 10 milligrams of sulphur excretion per day through the skin.

Tests were also carried out to determine the sulphur excretion through the lungs. With the method used none was found in 9 normals.

A small series were then examined after they had been given sulphur in the third decimal trituration (1:1000). They showed an excretion of 24.6, 27.4, 27.9, 33.4 milligrams, that is, an average of more than three times the usual amount. Likewise a few were tested with the sixth decimal (1:1,000,000) and approximately the same figures obtained so that no difference was noted after the administration of the two different amounts.

Patients with furunculosis or seborrhoea were then examined by the same method, this group being comprised of cases which did not develop the odor of hydrogen sulphide when treated with the third or sixth decimal trituration of sulphur. Two excreted too little (8 mgs.), four too much (18, 23, 28, 12) with the third, and with the sixth, 6, 1, 12 milligrams respectively.

One patient was found who developed the sulphide odor when taking sulphur 1:1000. The odor developed on the second day and his excretion of sulphur for the period was 576 milligrams, that is, 60 times normal. After discontinuing the sulphur he continued to excrete 117 milligrams or eleven times normal on the next day, then averaged 54 milligrams for 10 days, and after thirty days was excreting about twice normal. The seborrhoea about which the patient had complained was markedly improved and general well-being decidedly better than before the experiment. The patient was located two years later and agreed for the sake of experiment to make a retrial, although he considered himself cured. After taking sulphur D 6 for 10 days, the plate was hardly darkened and there was no sulphur odor to the secretions.

Thus it is seen that there may be individuals whose sulphur metabolism is disturbed in disease, here, in disease involving the skin. In them very small amounts of sulphur provoke a transformation or a remobilization of sulphur in the body. The diarrhoea produced in many cases receiving small doses may well be due to the excretion of tissue sulphur.

Incidentally it may be remarked, though it is not particularly important, that these same doses of sulphur were of value in experimental staphylococcus infections of rabbits.⁹¹

Extremely interesting experiments have been carried out by Baader⁹⁵ at Bier's request. They concern chronic lead poisoning

in the human. Remarkable remobilization of stored lead in the tissue resulted from the use of the third and sixth decimal trituration, requiring discontinuance of the experiments. The results are of general interest because the provocation of symptoms from these small amounts in patients with lead poisoning strongly suggests a sensitization to lead. This might account for the rapid recurrence of symptoms of lead poisoning in those who have once been poisoned, when they attempt to return to their former occupation.

This must be deemed sufficient for the present purpose. The discussion with sulphur strongly suggests that: 1) sulphur is capable of acting upon the skin when the drug is given in small doses by mouth; 2) it produces eruptions which closely resemble the usual staphylococcus skin infections; 3) it has proven unusually valuable in the treatment of such cases; 4) sulphur excretion may be enormously increased through the skin in certain individuals who may have disturbance of sulphur metabolism, suggesting a "sulphur" type of patient.

Naturally no attempt is made here to justify other applications of sulphur in therapy, but sufficient has been said to show that very small doses given by mouth have been effective in the treatment of resistant skin and gland (sweat gland abscesses of the axilla) infections. It is needless to add that greater improvement in the clinical results may be expected from the further inclusion of symptomatic indications.

It is generally known but often forgotten that acute intoxications with large amounts of medicinal substances yield an essentially different picture than smaller amounts administered over a longer period of time. In many cases the first procedure yields relatively little information beyond the fact that the experimental subject dies a cardiac or respiratory death. By the second method the gradual and sequential involvement of organs and tissues can be followed. Although no mention has been made of the fact here, it is also obvious that with human provings alone, the subjective aspect of the situation can be studied. Finally, in reference to this particular study, it will be noted that there is a vast difference between studying the skin of the human and the skin on the usual laboratory experimental animals.

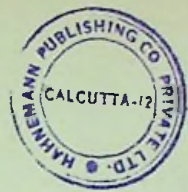
The above seems to suggest that the simile in the case of sulphur has been a valuable finding principle. Some evidence has been advanced to indicate that sulphur not only produces, but also cures certain types of skin infections. The example may also serve to show that drugs may have a more indirect mode of action than is often considered, moreover, that substances considered more or less "inert" in small doses, may actually have effects.

The writer does not intend to generalize from this experiment which is interesting with respect to one drug and one group of conditions, but it is suggestive that with simile thinking remedies are suggested in a wide variety of fields. For example, (without any pretense of priority) the writer remarked several years ago that the symptomatology of ergot poisoning resembled that of several forms of "vascular" disease akin to Raynaud's disease and Buerger's disease. It is interesting to note that recently this remedy has been tried in the treatment of thrombo-angiitis obliterans. Gerlach⁹⁶ had occasion to treat a patient with gangrene of the toes resulting from ergot (gynergen) poisoning. Because of other symptoms (cramps, nausea, vomiting) and as the result of interest in the pharmacology of histamine, this drug was administered with the result that the spastic attacks disappeared, moreover, that the gangrene appeared to improve. Since histamine is allied pharmacologically with ergot, he decided to treat six cases of thrombo-angiitis obliterans with small doses (1:100-1:1,000,000) of ergot. The usual dose was five drops of 1:1000 solution three times a day, followed after some days by 1:100. If there is any aggravation he suggests 1:10,000-1:1,000,000. Six cases have now been under observation for five years, with striking improvement. Some symptomatic improvement was noted in some other forms of gangrene. Knowledge of the depilatory effect of thallium acetate led Bier to employ this remedy in certain forms of alopecia with interesting results. The well-known fact that several snake venoms produce hemorrhagic states ought to suggest its utility in some of the hemorrhagic diseases. Apparently this has not been tried on a large scale. Numerous other suggestions will occur to the reader; some are mentioned later.

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ORGANTHERAPY.—Several years ago (1922) the writer suggested the employment of the venom of the spider, *Latrodectus mactans*, in the treatment of certain forms of angina pectoris, on the basis that the bite of this animal often results in a syndrome not unlike angina pectoris. Current literature would seem to suggest that the idea was not without merit. Non-critical consideration might lead one to think that a mere symptomatic comparison was the essential in finding remedies by the simile or in suggestions of this kind. But the fact that anacardium produces vesicular eruptions is not a sufficient reason for thinking that it would be useful in all types of skin diseases with vesicular eruptions.

It is generally conceded that the spirocheta pallida is responsible for syphilis. The existence of certain strains with an elective tendency to involve particular tissues has been postulated but the evidence supporting this contention is fragile; on the other hand, there is strong basis for the suspicion that the host is highly responsible for the varying manifestations of the disease. Since "direct" disinfection does not appear to take place, the question arises as to whether consideration ought to be given the particular organs involved and their types of response. Reference is not made here to the contradictory statements made about the penetration of arsphenamines into the central nervous system, but for therapeutic plans based on sites and types of involvement. For example, knowing the tendency of sulphur and arsenic to involve the skin, would sulpharsphenamine be preferable to bismuth in this instance or not? Conversely knowing the tendency of bismuth to affect the mucous membranes of the gastro-intestinal canal would bismuth compounds be superior here or not?

As the word is employed here, organotherapy is an attempt by

means of drugs to assist the diseased organs to carry out the healing process to a greater extent through their own power. It is assumed that healing must be conducted by the diseased organ or organism providing proper conditions are obtained. For example, bone is not formed by calcium salts, but by living cells. In this restricted sense organtherapy assumes that if the intrinsic powers of the tissue or organ are insufficient for accomplishing cure, it is the task of the physician to supply such powers as far as he is able. Naturally this can be accomplished in various ways which do not necessarily exclude each other; for example, rest may be combined with forms of stimulation and among the available forms of stimulation the "drugs" are available.

It should be obvious that organtherapy is quite distinct from symptomatic measures which may accomplish certain important objects as the relief of pain by morphine, the removal of poison in the stomach by an emetic, a transfusion in hemorrhage and countless other valuable symptomatic procedures. Organtherapy refers, for example, to the stimulation of healing of a peptic ulcer at times by silver nitrate without any reference to the merits of alkalis which may neutralize acid and thus remove an obstacle to healing. A long quotation from a work by Hugo Schulz¹ may illustrate this problem; although the quotation is lengthy, it summarizes the entire situation well.

"The great thinker Paracelsus has compared the processes which occur in the course of human life with those of the environment, the human organism as a microcosm as opposed to the macrocosm. As the result of far reaching training and development of our methods of investigation, more and more we see realized what Paracelsus suspected. What we already know of the origin, further development and also the therapy of the infectious diseases can be considered in this respect almost as a paradigm. If anywhere it is here that the value of biologic research appears clear and distinct. The same processes which the careful observer finds over and over again in living nature are met, *mutatis mutandis*, with distinct clarity in the forms of disease which must be traced to infection with organized living matter. I shall illustrate this by example. It is sufficiently well known that for the normal development of certain plants, a definite composition and condition of the soil is an absolute requirement. Reversely we can draw conclusions from the flora surrounding us on the type of terrain that is necessary for their development. If we consider a well developed meadow, we know that the ground under it is not made up purely of sand and that its content of moisture should not exceed a certain limit. Only a soil under the proper conditions permits the proper quantitative

and qualitative growth of grass, as the owner intended to have it. Thereby it is a matter of course that the ground may contain the seeds of many different plants. It is certain, bacteriologically speaking, that it is anything but sterile. And as a matter of fact, here and there we see other types of plants springing up. Here blossoms of ranunculus and there a dandelion, but they need little attention in regard to the value of the meadow. All else which otherwise could grow from the innumerable seeds which are carried by the winds and finally come to rest upon the soil, either do not grow or at least do not reach any height. The conditions necessary for their development are either absent or insufficient so that they scarcely develop beyond their initial stage. We have also, to summarize the matter briefly, completely normal conditions before us. Let us now take a case in which for some reason a disturbance in the moisture content of the soil occurs, for example, an insufficient drainage of an excessive rain so that normal conditions cannot prevail for some time. One finds an entirely different situation when he now looks at the meadow. Grasses are found which we are accustomed to see only in swampy and moist areas. From the standpoint of normal conditions, they are all pathologic signs. If the process continues, then the good feeding grass disappears more and more and the meadow becomes useless for its intended purpose. And if everything remains as it is, then after some time we find a more or less swampy territory covered with sour grass and sedge, where formerly we had good feeding grass. For the botanist, it is of course of much greater interest but the owner thinks differently about it. And yet during the entire time nothing has altered except that the water content of the ground has become abnormal and so remained. Nothing has changed in its characteristic composition since the first. Only after some time the results of the effect of water on the building materials in the soil were brought about slowly but constantly. If in time, while there is still enough sufficiently healthy grass remaining, the excess water is removed, then the entire picture changes again. Rushes, sedges and reeds and all that do not belong here gradually disappear. The good pasturage now again finds the possibility of developing powerfully and again gains the upper hand. The meadow is now 'healthy' again. The excess of water and nothing else brought about the damage of the meadow. With its removal the normal condition is again restored.

"I have treated this example in some detail intentionally. Many similar ones could be cited, but one will be sufficient. Those who would not limit themselves merely to investigation of the theory of life in the laboratory and in the study room and for whom the

surrounding manifestation and processes in the external world are viewed with an open eye and the opportunities realized, to them the subject of Paracelsus's thoughts and considerations will run parallel with ours.

“We shall now turn from the macrocosm to the microcosm. How are the conditions in the human organism? That a tissue absolutely normally nourished and standing in complete physiologic equilibrium, for example, as the mucous membrane, does not form a suitable soil for the microorganisms coming into consideration as causes of infection, I have already mentioned.² The discoveries of recent times have confirmed those opinions. Today we are certain that there are people who go through life as the carriers of diphtheria. They may harbor diphtheria bacilli in their throat or typhoid bacilli in their intestines without having any disturbance. For other people whose organs are not in a favorable condition, they are a great danger.

“We now see—to remain with diphtheria—that under certain conditions, a mild, ordinarily insignificant, angina may be the occasion for the development of a severe diphtheritic disease with all its consequences. The beginning is very simple. It is merely concerned with a disturbance in the circulation within the pharyngeal mucous membrane and the vessels supplying its vicinity. A slight swelling and increased reddening of the mucous membrane is the first sign that we observe. Every disturbance of this nature, no matter how unimportant it may seem at the beginning, conceals a number of factors which may become very dangerous. The blood supply of the tissues is insufficient, the metabolic products which should be carried away by the venous drainage compete with it. For the maintenance of normal tissue life, one is just as unsuitable as the other. Insufficient supply of oxygen in the arterial blood makes the necessary complete physiologic oxidation of tissue constituents incomplete. In addition to the results of normal metabolism, pathologic ones add themselves. The drainage through the venous system is incomplete. The material remains, accumulates and acts as a further cause of endangering the normal life in its vicinity.

“The general nutritional disturbance which must develop under the conditions depicted above, has a further result that the functions of the individual constituents of the tissues must change. Only a completely normal mucous gland is able to furnish a physiologically efficient product. Only a completely nourished epithelial cell is able to fulfill its tasks in an adequate manner which undoubtedly extends beyond acting as a mere cover for the tissues below it.³ But it is also certain that the disturbances of which we speak

here may be so slight that we are not able to prove them by the finest existing means and yet they are sufficient for furnishing a nutrient soil suitable for the correct development of the lowest organisms. If this condition is fulfilled then these living organisms can liberate their poisons to the fullest amounts. The entrance of these poisons into the tissues conditions a new severe damage and certainly does not assist their resistance against the impending danger. To the contrary. Now comes what must come and what pathology has taught us as the necessary consequences of every inflammatory process in which infection by microorganisms comes into question and where the morbid processes may develop further undisturbed.

“Now I ask the reader to compare with this description of the development and progress of an infectious disease, the example I have previously chosen from the macrocosm. There the steadily mounting decrease of utilization value, here the endangering of human existence. In both cases great effects developed from small causes, here as well as there conditioned through far reaching changes in the original nutrient soil.

“How do we now find the task which therapy must fulfill under these conditions? The closely related thought is certain: remove and render harmless the micro-organisms bringing damage. But experience has proven that this way is the one which brings the least result. The attempt to render microorganisms harmless cannot occur without the substance affecting the surrounding tissues at the same time. Furthermore, one must consider the absorption of the antiseptic substance used, which, as unfortunately experience has also taught us, under some conditions is much more endangering than the original malady for which it was applied with more or less justification, moreover, without previous consideration with respect to the possible consequences. I have already said that in this way nothing sure is attained. Much more promising is the thought of increasing the resistance of the organism in that it is treated with substances which seem able either directly to destroy the invading poison or to increase the reaction of certain constituents of the organism against the action of the poison or the activity of its producer.

“But there still remains a further possibility of suitably treating infectious diseases when united with the above mentioned endeavors to approach the danger. I refer to direct organotherapy of the nutrient soil of the infection by means of suitable medicinal substances. And I will attempt to prove on this occasion that this method of therapy can be easily carried out and is successful.

“Does there exist any way to influence the total nutrition medic-

nally and with this the totality of living conditions of the diseased tissue or organ so that we accomplish nothing more than physiologic balance? In other words: in an infectious disease are we able to accomplish by means of drugs that which has to happen unaided in the natural healing process, but which for some reason cannot be brought about without some additional assistance?

"In order to answer this question sufficiently, it is necessary that we consider the individual processes which are of importance for realization of the intent just mentioned.

"If I subject an organ to the influence of a drug substance which is in any way able to change the behavior of the organ, then I thereby allow a stimulus to act upon the organ and its individual constituents. Everything which brings about a change in the behavior of an organ is a stimulus no matter whether the altering factor approaches the organ and its cells from without or is produced by the living tissues from within.

"And in order to remain here with the concrete case: we know that mercury has a very intense stimulant action on the mucous membrane of the throat . . ." (Schulz then shows the identity of the lesions of cyanide of mercury and diphtheria so far as the throat is concerned).

". . . How can it be explained that a poisoning with mercury can produce a morbid picture which can give occasion for confusion with diphtheria? And how is it possible that corresponding events are brought about in other parts of the body? Why was Virchow able to stress with right that at autopsy, one could not determine from the start whether a severe dysentery or a sublimate poisoning had existed during life?

"I have repeatedly stressed that the expression of reaction of every tissue, every organ to any stimulus, therefore also medicinal stimuli, must always be the same, if the same substance of the organ is involved by equal intensities of the stimulus. If I stimulate the motor nerve of a muscle, then the result is either a stronger contraction of the muscle, or in case the stimulus surpasses a certain grade, paralysis of the muscle. What holds for skeletal muscle, also holds for smooth muscle, for instance of vessels. If I stimulate the gland cells, then the result must be a change in the amount and constitution of the glandular secretion. If in some way I stimulate the total metabolism, then it must become more intense or weaker. A third possibility does not exist, providing, under certain conditions, that there is not a balance between the intensity of the stimulus and the resistance of the stimulated parts. But this does not concern us now. This is what counts and what must be maintained: every organ, every organism can react only to stimuli by

virtue of its anatomical structure and its physiologic function. These two factors are so well known that we can include them as full values in our calculations. But the result which such a stimulant action may have for general health as well as for life, we can determine from experience as probable, but not with certainty for every case. After all one mucous membrane catarrh is like another. But its consequences direct themselves in each individual case according to the significance of the mucous membrane for the total activity. The accompanying symptoms and consequences of a catarrh of the mucous membrane are entirely different from the same affection of the bladder mucous membrane. The original affection is always the same, though it may have the most different causes. Almost always we are concerned with changes in nutrition which deviate from normal and thereby in the entire living activity of the stimulated tissue or organ. Without them further conditions can be created which promote the vital activities of the lowest organisms which are already present in or on the diseased organs or have reached it during the morbid state. Herein lies the important point for our conception of the significance of the 'nutrient soil.'

"The fact that drug substances and organized and unorganized producers of disease, produce effect pictures which have a great similarity to each other is a well-known fact. I have attempted in the preceding to demonstrate its basis. Nothing special is found in this fact. It does not require much thinking to come to the conclusion which, after all, could hardly be otherwise.

"If now in a previously healthy person under the influence of a certain drug we see how characteristic changes are brought about in the behavior of any organ, then we are justified in the conclusion that some closer relation exists between the drug substance and the altered organ. This relation may be an immediate one, based upon the direct influence of the medicinal substance on the elements of the organs, but under certain conditions, it may have developed after starting in some other location. It will then be our task to trace out this other site so that we do not err in considering a secondary event as a primary one.

"A further question: provided the intensity of the stimulus is known, can we state in advance, how the reaction of the organ must behave in response to the stimulus? Today we may answer this question with yes. The first who recognized the lawfulness in this action and who answered it as a far reaching sign for all living manifestations in nature was the Griefswald psychiatrist, Rudolf Arndt.⁴ The basic biologic law formulated by him reads as follows: 'Weak stimuli kindle living activity, moderate promote,

strong depress and the strongest remove it. But it is entirely individual what displays itself as a weak, moderate, strong, or so-called strongest stimulus.'

"If Arndt's law is correct then the following experiment must come out positively: (Schulz here includes experiments showing small doses of antiseptics stimulate activity of yeast). . . .

"In conjunction with this law I have shown that under certain conditions there is still something else which holds and which is of importance for therapy: diseased organs react more sensitively to the same stimulus than do normal ones. We can release drug reactions in sick organs with stimuli which would not produce a reaction in healthy organs. . . . But from this still something happens which I would like to stress here particularly, even though it is self understood. I am able to make an organ sick with a drug if I employ it in excess. And this disease process may be very similar to the one against which the drug is being employed. The reason for this has been given above. A strong stimulus must damage. The type of damage is conditioned by the organ itself. It is positively individual, stated Arndt, what is to be considered a weak, strong, or strongest stimulus in the individual case. And what behaves as a weak stimulus for the healthy organ, may, on the contrary, be the opposite for the diseased organ."

Many problems raised by Schulz cannot be discussed here although two must be mentioned in passing. It will be perceived by reference with the thoughts expressed earlier that the Arndt-Schulz formulation is not a "law" but a rule of rather broad application. There is also no inevitability of "hypersensitivity" to drug stimuli in disease even though this is very often observed. Other questions will also occur to the reader. However, the point to which attention is directed may be stressed again. In thinking of this kind, therapy is guided by the phenomena presented by the particular patient and not solely at the obligative factor. While the etiology, in the usual sense of the word, plays an important role, it is not exclusively important. For example, in the illustration employed, cyanide of mercury is used in tonsillar and pharyngeal diphtheria, not because of the presence of the Klebs-Loeffler bacillus, but upon the assumption that the tonsil is involved and has reacted, more or less efficiently, in a particular manner. The remedy is found by the simile. On the other hand, this type of thinking implies that cyanide of mercury will also be useful in some other ulcerative and pseudo-membranous diseases not due to the Klebs-Loeffler bacillus. It is interesting in this connection that Lebourg and Prunet⁵ have recently reported that the cure of bismuth stomatitis is markedly accelerated by the intravenous administration of cyanide of mer-

cury. They add that this confirms the theory of their master Millian: "Le meme medicament susceptible de declancher une stomatite par biotropisme se montre employe de la meme maniere, un excellent agent de guerison des stomatites." It should not be forgotten in this connection that the employment of cyanide of mercury in diphtheria does not contain any implication that diphtheria antitoxin should be omitted nor that it is superfluous. Similarly while the percentage of successful results varies, digitalis finds extensive application in auricular fibrillation due to other factors than rheumatic heart disease.

Another point deserving emphasis is the following. Pathologists use the term etiology in a much broader sense than do clinicians when they are acting as therapists. The alterations of the blood vessels in the nasal mucosa are as "causal" in the etiology of acute rhinitis as some micro-organisms recovered in the discharge. The clinician is prone to speak of chronic irritation as the "cause" of cancer while pathologists almost invariably add some "intrinsic" factor.

Omitting from consideration prophylaxis, the real field of causal therapy, the opportunity for the application of causal therapy is limited if the necessity of concurrence of several "etiological" factors is conceded to hold in the vast majority of diseases with which the internist is confronted. If one adds to this the further restrictions imposed by inability to directly attack the "causes," an obstacle which increases with the duration of the syndrome, the possibility of a causal approach suffers further limitations. On the contrary, when less consideration is given to some one precipitating factor and more devoted to organotherapy, the opportunities for applying "causal therapy" are extended.

Another field is suggested by simile thinking although at present it is in such a primitive state of development that perhaps it ought not to be mentioned. However it opens an extensive field for investigation. A corollary to organotherapy is: organs carry in themselves the means for their own restoration. Extrinsic factors may augment or diminish intrinsic "powers," but no new ones are added. For example, if the gall bladder contains within its cells the "hormones(?)" necessary for the constant replacement of gall bladder cells, these, in combination with "organ specific" remedies, offer great possibilities in fields as yet quite unworked by medical investigators. The writer would prefer to have the suggestion called Utopian, than to have the statement be the signal for the inconsiderate introduction of all kinds of "cell foods." The thought, although submitted here without supportive evidence, has been introduced merely to indicate the potential fruitfulness of

combining simile thinking with physico-chemical mechanistic investigation as they are not mutually exclusive.

A division between organotherapy and constitutional therapy is artificial although the second term may have some value in emphasizing a broader conception than "focal-specific."

The numerous classifications of constitution need not be reviewed in this place, but allusion must be made to one striking defect of all those examined. They are all artificial since in nature there are individuals rather than constitutions. But in addition, all those examined seem designed to emphasize some particular panel. In one the classification is anthropologic, in another, some part of the nervous system is selected as "vagotonia"; again emphasis is placed upon the endocrine system as exemplified by the "Basedowoid" type. Without attempting to enumerate the almost countless varieties it will be recognized that any arrangement which fails to embrace simultaneously the somatic, neuro-chemical, and psychologic panels will tend to be one-sided.

Proving of drugs conducted on the healthy human would appear to furnish occasion for a minimum number of "as-ifs" in pharmacology. On one side there is the substance to be tested, on the other the actual human individual. The results obtained by this procedure would furnish information in all panels simultaneously, and the information would be obtained upon a higher level of approximation to reality than is obtainable by any other method of pharmacologic investigation. It will be noted that this method would not displace the various "constitutional" types which have been devised, but would be superimposed upon them, a supplement for therapeutic purposes. It is also obvious that the results of this method remain upon a descriptive level and do not involve any speculation. On the other hand it would not obviate the necessity for the various pharmacologic methods now in vogue, nor minimize their importance.

This is not the place to discuss structure versus function. However, in many diseases functional changes are manifested before structural alterations are demonstrable with the technic now available.

It has been unfortunate, in the opinion of the writer, that two equally valid methods of investigation which ought to supplement each other, have been regarded as mutually exclusive. The fruitfulness of each has tended to magnify the importance of one or the other according to the position adopted by the worker.

In conclusion it may be said that simile thinking in therapeutics is not confined to a similarity or identity of the releasing factors. For correct application it demands attention to organotherapeutic

requirements. To return to the example of anacardium and vesicular eruptions. A vesicular eruption may be encountered, among others, in certain diseases of the posterior root ganglia and again in some allergic syndromes, and finally from a large number of irritants acting upon the skin. To expect that anacardium will prove as effective in allergic diseases as in herpes zoster not only overlooks the actual situation but disregards all the advances made by pathology in the last century. But it would seem equally naive to regard some disturbance of the secretion of acid in the stomach as the cause of peptic ulcer and denominate neutralization of acid by alkali "causal therapy." Without commenting upon its symptomatic value, scientists today tend to regard it on the level of a rather primitive dermatology.

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A NOTE ON SYMPTOMATOLOGY.—In one of the preceding sections attention was directed to a viewpoint of etiology. Emphasis was placed upon the importance of the "conditions" in simile thinking and the suggestion was made that appreciation of the multiplicity of co-operating factors in simile thinking more nearly approximated the modern viewpoint of pathology than is otherwise common in therapeutics. For example it is known that in experiments with aconite, the subject evidences loss of thermal regulation. The body temperature of the homothermal animal tends to approximate that of its environment. For many decades aconite has been employed in certain syndromes induced by exposure. Within the limits of the field of utility of aconite, these syndromes tend to be manifested in the respiratory system after exposure to cold. In a similar manner, not simply infectious agents, but all of the extrinsic factors of disease, play an important role in the selection of the remedy in simile thinking. The situation is not particularly altered by the fact that in some diseases, as syphilis, the releasing factor (spirochete) is so dominant that other conditions may not be prominent. In these cases the etiologic problem is merely simplified.

In the second instance attention was directed to the level of organs. To remain with the example of aconite, the disturbances of thermo-regulation are general and when, for example, the syn-

drome following exposure to cold manifests itself as an acute rhinitis, the possibility of successfully employing aconite is over for the most part and agents with particular organ actions are said to be indicated. For example, when the capillaries of the mucous membrane of the nose are "paralyzed" and the patient manifests a profuse thin acrid watery nasal discharge which excoriates the lip, and when he complains of a frontal headache due to concomitant involvement of the mucous membranes of the frontal sinus, photophobia and lachrymation from involvement of the conjunctival mucous membrane, etc., aconite would be useless in this "cold" and probably arsenic would be indicated. Between these two stages, when systemic manifestations were still present, when the face was hot and flushed, the temperature rather high, the carotids throbbing, pupils dilated, the nasal mucosa congested but dry, a remedy of the belladonna type would be indicated. Late in the treatment of acute rhinitis, when the discharge is thick, stringy, etc., and the systemic manifestations slight or absent, a remedy of the type of potassium bichromate might be indicated. The same situation obtains in the treatment of most diseases. The etiologic diagnosis does not furnish the sole indication for treatment, for careful consideration must be given to the anatomic-pathologic diagnosis and the pathologic-physiology presenting. It does not seem necessary to discuss at length the fact that two individuals may be exposed to the same stimulus, for example cold, with entirely different responses. In one the syndrome presented may resemble the manifestations mentioned in connection with belladonna, while the other may react with general aching, profound prostration, soft compressible pulse, drowsiness and chilliness as is noted in gelsemium intoxications. Nor would it seem highly speculative to presume, in view of the different responses, that different therapeutic regimes are in order. Parenthetically it may be remarked here that nothing in the above should be construed as providing reasons for not ordering the patient to bed, for not prescribing a suitable dietary regime, nor is it intended to imply that numerous other measures ought to be neglected, nor that they are useless. The discussion is intended to emphasize that the therapeutic diagnosis in simile thinking includes etiologic, anatomico-pathologic (structural), pathologico-physiologic (functional), and prognostic indications.

There is no necessity for reviewing here a large amount of nonsense that has been written on each of the various indications. For example, the writer has had occasion to show that bryonia, like a number of other substances, when injected subcutaneously in guinea pigs often produces, among other phenomena, rupture of the stomach, peritonitis and death of the animal. It would be

ridiculous to state that bryonia is a remedy for perforation of the stomach. Here prognostic indications alone demand that primary consideration be given to surgery. It is likewise obvious, as emphasized earlier, that an attempt at exactitude is responsible for a record of innumerable incidental findings. For example there is no evidence that one salt of mercury affects the right tonsil and another affects the left tonsil. It may be said in general that the evidence for an exclusive or even preferential involvement of one organ in comparison with the other of a pair is more than problematical. In some instances this last statement is probably not entirely valid. For example there is ample reason for believing a lymphatic connection exists between the caecum and right kidney, whereas such a connection is less obvious or unproven between the large intestine and left kidney. Omitting from consideration other anatomical differences which exist between the two kidneys, it may be said that in some cases a pyelitis of the right kidney is associated with a caecal stasis, whereas the role of constipation may not be so prominent in a pyelitis of the left kidney. No discussion is required to show the importance of symptoms on one side or the other in connection with unpaired organs. Naturally none of these subjects cannot find discussion here. The following remarks, designed to show how some factors influence the choice of a remedy, may likewise serve to emphasize some aspects of symptomatology as well as to reflect the possible usefulness of human provings.

To apply the simile correctly there should be available a complete history of the disease in the individual, not simply designed to secure data on the development of the phenomena, but also the evolution in the particular patient. Here one is concerned with the history of the person. The history of the individual constitution is a related topic. For example, in a case of "duodenal ulcer" one is not concerned solely with a present and past history in order to abstract a syndrome consisting of the symptoms and signs of ulcer; in addition one intends to secure the manifestations in the particular patient; has he pain, when does he have it, what aggravates it, what relieves it, etc.? All this data is not secured for the purpose of deducing the status of gastric secretion or gastric motility but the expression of ulcer in the given individual. The same holds for the determination of the individual constitution.

Again age and sex play important parts in the therapeutic prescription. Age may be a very decisive feature in the selection of a remedy. For example, a vertigo in an old person presumably associated with a cerebral arteriosclerosis might suggest barium carbonate; barium is practically never employed in the vertigos of adolescence. The low sacral backache for which helonias is em-

ployed at times is "sex limited," that is, it is employed only in women. Constitutional build frequently plays an important role in the selection of remedies, for example the use of phosphorus in chest disorders, particularly in those with an asthenic habitus; the calcium salts are employed particularly in the lymphatic type of child. Then too, certain remedies have indications from the state of nutrition, state of strength, the general anthropologic panel of constitution.

In this same total impression of the patient is the status of the autonomic nervous system, particularly the vagotonic or sympathicotonic trends. The child who slept poorly, who showed a tendency to gastric hypersecretion, polyuria, etc., and later in life complains of bradycardia, irregularity in breathing, persistent constipation, gastric hypersecretion, etc., may present the vagotonic trend and thus offer important indications for therapy. A study of the symptoms recorded under different drugs strongly suggests involvement of the vagus by many substances not as yet investigated in this connection. The same holds for patients who show tachycardia, elevation of blood pressure, flushing, trembling and hyperglycemia, in the sympathicotonic sense. The reactions of such patients to adrenalin and pilocarpine are suggestive of the merit of correctly including such etiologic factors. It is unnecessary to indicate the extent to which this functional testing may and often must be carried out. Necessarily these tests offer indications of partial constitutions only, unless the totality is considered.

Peculiar to simile thinking is the inclusion of factors dealing with physiological variations. The aggravations with time of day find support in the experience of therapists and balneologists. The relatively great resistance of patients early in the morning, the relative lability in afternoon, is reflected in the afternoon temperatures, etc., in some patients, and in the so-called inverse types of temperatures in others. Nowadays one appreciates more fully than formerly that there is a more or less definite daily rhythm of temperature, pulse, blood pressure, oxygen consumption, carbon dioxide excretion from the lungs and nitrogen excretion through the kidneys which reach their lowest level from 4-6 in the morning and which increase to the high point in the afternoon. Since these curves remain constant for the individual, not simply when forced to remain in bed but when working nights and sleeping days, undoubtedly such time factors attain importance in the individualization of the patient. It is not improbable that they are connected with variations in activity of the autonomic nervous system, for the nocturnal aggravation of the vagotonic is well known.

The digestive factors and the type of food habitually eaten are

likewise included. As it is generally appreciated that animals fed with a base rich diet are relatively resistant to inflammatory stimuli and narcotics, hyposensitive to adrenalin and hypersensitive to insulin, whereas animals fed with acid foods react quite the opposite, inclusions of this kind should not excite surprise. The relationship of these items to acid base equilibrium is obvious. The relationship of meat diets to calcium deficiencies and to increased oxygen utilization are well known from experiences with low protein diets in hyperthyroidism.

The effect of rest needs no discussion, but in relation to motion, to work, fatigue may seem strange to those who do not recall the relation of some of these factors to blood lactic acid, and this in turn to capillary vaso-dilatation, to pulse rates, blood pressure, etc.

Closely connected with the relation to rest are the physiologic variations in sleep with changes in blood carbon dioxide and the shifting of the acid-base, the reduction of respiratory irritability, pulse slowing, narrowing of pupils, fall of temperature, tendency to sweating, etc. That many of the effects of psychic excitation are in the opposite direction need not be emphasized here.

Again attention is devoted to longer lasting variations of a physiologic nature; here the menstrual period, the pre- and post-menstrual period is scrutinized. The increasing pulse rate, blood pressure and temperature in the premenstrual period, the change in blood magnesium, the change in coagulability of the blood, the frequent appearance of the Rumpel-Leede phenomena, suggest the general nature of changes in the premenstrual period. Again one may recall the hypersensitivity of the tuberculous patient to tuberculin in the premenstrual period. The profound alterations in gravidity are too well appreciated to be detailed here.

Seasonal variations are likewise included. The seasonal variations in the blood, blood vessels of the skin are now generally known. The same applies to the tendency to miliary tuberculosis in the Spring, to the tendency to tetany, etc.

Climate, the influence of the sun, rain, cold, etc., are also included. Thus one approaches the Hippocratic conception of "etiology."

Not much more need be added on the second trend, the anatomico-pathologic, since this has been discussed above.

While it is difficult to make comparative statements the anatomico-pathologic trend usually provides the most important indications in practical therapeutics. Considerable confusion arises in the mind of the student when first confronted by the innumerable symptoms in the textbooks of materia medica, but separation of these pictures into anatomico-pathologic trends greatly simplifies the procedure. For example, sharp stitching pain in the chest.

worse upon deep breathing, will be found under bryonia as well as under numerous other drugs. But bryonia is indicated only when the pain finds its chief origin in a dry pleurisy, associated with some intercostal muscle spasm and when both are sequential to pathology in the smaller bronchi and alveoli. The picture is that of a respiratory infection in which apparently the pleura is involved by lymphatic extension rather than by contiguity, although the remedy is used in lobar pneumonia with pleural involvement. Sharp stitching pains due to so-called intercostal neuralgia, herpes zoster, etc., will not react to bryonia.

The anatomico-pathologic trend may be exemplified in tonsillar inflammations. Difficulty in swallowing is common to many drugs; differentiating is the chronic lymphoid hyperplasia in barium, acute congestion in belladonna, mild congestion with extensive oedema in apis, exudate in the crypts and fetor ex ore in mercury, peritonsillar abscess in hepar sulphur, etc.

To merely compare symptoms is undoubtedly one of the most unsatisfactory methods of applying the materia medica. A swelling of the leg is quite meaningless and found under many drugs; differentiation arises from the fact that in case A, there is an erysipelas of the skin which might react to belladonna, a neuro-myositis, which might be susceptible to Rhus toxicodendron in case B. Case C presents an old thrombophlebitis in which calcarea fluorica may be indicated, case D is due to congestive cardiac failure in which digitalis may be valuable, case E presents the symptom in the course of pernicious anemia where arsenic would possibly be indicated, while case F has a nephrosis in which uranium nitrate might be tried. Naturally the above is intended to be illustrative and does not even begin to exhaust the possibilities.

Every laboratory test yields indications for therapeutics, according to the simile. The albuminuria of terebinthina is associated with acute hemorrhagic nephritis, that of berberis with pyelitis, that of the snake venoms is found in multiple embolization of the glomeruli, etc.

The same might be said of the blood count, the low white counts in gelsemium, the potassium salts, particularly the bichromate in acute infections, the lymphocytosis of barium salts, the polymorphonucleus leucocytosis of hepar sulphur. It seems unnecessary and furthermore impossible to mention here all or even many of the indications derived from pathologico-physiologic indications. But the important point is that an x-ray picture of the chest showing a chronic fibroid tuberculosis often yields in practice more therapeutic indications for silicea than many symptomatic expressions. Still here the other indications cannot be overlooked. Pneumo-

coniosis will not react to silicea so that the so-called etiology is important; likewise the symptomatic picture may assist in the differentiation of remedies. However, the important feature must not be overlooked, namely, the paramount importance of the anatomico-pathologic and pathologico-physiologic trend.

Naturally such indications will have different values. Whereas increased knee reflexes, Babinski's sign, ankle clonus, and the absence of atrophy in the lower extremity will form an extremely important group of indications for *Lathyrus sativa* in lateral column involvement of the cord, and from which considerable improvement may be obtained at times, still the remedy is not useful in the sequella of hemiplegia.

The extreme simplicity with which provings are recorded has led to a criticism that they are unscientific, but obviously a true description of what was observed is at least as valid as an explanation of what happened. There is, however, no evidence to support the contention that some rare, unusual subjective symptoms equal in value objective common phenomena. A red swollen, smoothly glazed tonsil without exudation on the surface, associated with streptococci, and associated with involvement of the Eustachian tube is relatively more important than whether the patient complains of a splinter-like or a burning pain. On the other hand, when burning pain has been repeatedly recorded in the provings and is found to be a useful symptom clinically, it attains importance. In the final analysis the problem is not one of objective versus subjective, but the inclusion of both when they have attained certainty, through quantitatively sufficient experimental and clinical experience.

The last trend of the materia medica to be mentioned here is the prognostic indication. Only a few of these problems can be mentioned. Not rarely in chronic diseases remedies apparently well selected fail to act. Then one may "interpolate" a remedy such as sulphur and then return to the indicated drug if necessary. This is not unlike the rather common procedure of employing digitalis in congestive heart failure. Should the digitalis fail to act, when it is apparently well indicated and administered in proper dose, one at times prescribes the iodide of arsenic and mercury, and then returns to digitalis with considerable success. Another aspect of the prognostic indications is reflected in the clinical observation that certain groups of remedies supplement each other well. Thus arnica is often employed in acute sprains and is followed by rhus toxicodendron in the subacute stage; aconite, spongia and hepar sulphur form a frequent sequence in some upper respiratory disorders.

In conclusion it should be obvious that the simile can be practiced correctly only by the well trained physician. The most careful mechanical registration of symptoms would not differentiate between some forms of cerebral glioma, vascular crises, and meningismus which require different procedures, the first of which, for example, is not susceptible to internal medication. The swollen, painful scrotum may contain a hydrocele, a tuberculous or syphilitic testes or epididymis, a teratoma, etc. The prognostic elements mentioned earlier are, therefore, extremely important.

Regardless of how obscure this subject may seem when compressed by brief discussion, a few observations emerge with striking clarity. By the very fact that the simile is alleged to be a biologic rule, cognizance must be taken of the totality of the conditions under which the drug must operate. In the preceding discussion these have been classified under several headings as etiologic (extrinsic and intrinsic factors), anatomico-pathologic (structural factors), pathologico-physiologic (functional including objective and subjective symptoms) and prognostic indications. In the present primitive state of medical knowledge this represents a programmatic ideal rather than an accomplishment frequently performed, for, as yet, medicine must confine itself to a relatively simple surface zone of the actual phenomena. On the other hand, the fact that this highly desirable information is often lacking does not furnish an excuse for not utilizing it when it is available. If observations were confined to the primitive level of records of symptoms, the simile would indeed be the grave of science. The mere mechanical comparison of symptoms not only fails in a large percentage of cases, but is actually dangerous in that it may be utilized in instances where the simile is not applicable or when better procedures are available. There are certain remedies which may be indicated in decreased visual acuity. However the patient may need glasses, he may have a cerebral glioma, he may be diabetic or display evidence of an advanced nephritis, a leukemia, a detachment of the retina, a cataract, etc. It is, of course, indisputable that results are obtained at times by exclusive recourse to symptoms in some types of cases. This is suggestive of the possibilities of a method when it is occasionally successful even when applied crudely, but this is certainly not a valid argument for persisting in this primitive stage. From this it is evident that the simile can be rationally applied not only by the physician, but by one who is fully conscious of the continued advances in all the branches of science allied to medicine. Finally it should be clear that the correct application of the simile involves more strict individualization of the patient than is customary in general medicine at present.

THE ARNDT-SCHULZ RULE.—The problem of posology is extremely important in the practical application of simile thinking in medicine so that some reference to this subject may be made at this point. A brief review of the first modern explanation of the "small" dose, so often associated with the simile, may serve as an introduction.

Hugo Schulz of Griefswald was the first investigator to devote careful attention to this problem, and as the simile became a finding rule for drugs, the Arndt-Schulz rule became one for finding doses. The point worthy of note in the following discussion is that drugs have more than one effect. Many investigators believe that drug effects are quantitative, that is, the effect is directed in the same direction (stimulation or depression) with a given drug, with large or small doses, the result differing only in respect to the amount of response. On the other hand, the Arndt-Schulz rule states that the effects of drugs are qualitatively different according to dose, for example, that small doses stimulate while large doses of the same substance depress. The work of Arndt, who arrived at the same conclusion independently, is not discussed here.

The earliest work of Schulz on this subject begins with the memorable statement,¹ "the alterations which a medicament provokes in the activity of an organ, can present effect pictures under definite conditions which are entirely opposite to one another. We see one and the same organ perform either with an outspoken increase of physiologic function, or, on the other hand, with decisively decreased energy and distinctly lessened activity. . . ."

Thirty years before Boecker² had stated: "We are accustomed to expect from small doses, small, from large doses, more distinct actions of drugs but it must be recalled that there are circumstances under which small doses of drugs can bring about the reverse of large." However, the idea was forgotten until rediscovered by Arndt and Schulz.

Schulz reasoned as follows: the alterations are the expression of a stimulus action which acts on the fundamental constituents of the body, the cells. The reacting cells give a type of response which is qualitatively fixed by the anatomic or histologic structure of the cell, but it varies quantitatively with the strength of the stimulus. Pflüger's law of muscle contraction had proven that one and the same cause, an electric current, could produce opposite effects on the muscle according to the strength of the current. Moreover, Schulz considered that when the nerve is in a pathologic state, its irritability is altered characteristically, whereby a current of the "same" strength is now equivalent to the strong current on normal

nerve, so that with "pathologic" nerves a much weaker current would be necessary to demonstrate reversible actions. After discussing elective affinities of drugs, Schulz proceeded to formulate his idea: "every stimulus conditions in a cell or cells which compose an organ, either an increase or a diminution of its physiologic function corresponding to the smallness or greatness of intensity of the stimulus."

In proof of the above assertion he cited the reversible effect of sodium chloride on salivary fermentation,³ the stimulation of fermentation of yeast by small doses of formic acid and depression by large,⁴ as confirmed by Thol,⁵ similar stimulation and depression with thallium,⁶ the stimulation and depression of the movements of spermatozoa by small and large doses of quinine.⁷ He called attention to the relation of his statement to the so-called primary actions of drugs, the well-known stimulation from small quantities of alcohol, the stimulation and depression by camphor,⁸ the stimulation and depression of the nervous system by physostigmine, the little known stimulative phase of conine and the well-known depressive phase,⁹ the reversible action of small and large doses of digitalis on the heart,¹⁰ as well as Nothnagel's report on the reversible actions of the morphine,¹¹ particularly in reference to the nervous system. Schulz reported similar results with juniper and copaiva, which stimulate diuresis in small doses and cause anuria in large amounts. Turning to the infectious diseases he cites among others the treatment of diphtheria with cyanide of mercury,¹² tartar emetic in pneumonia, emetine in dysentery, veratrum in cholera,¹³ all of which he regarded as measures for increasing the defense of the organism by small doses of substances capable of producing, when given in large doses, symptoms similar to those of the disease for which they are administered.

He concludes the work with the following thoughts: the activity of a drug depends upon the existence of a connection between it and the tissues on which it acts; the action is in accord with the Pflüger law; under pathologic conditions the sensitivity is increased so that what is "weak" and what is "strong" depend upon the individual case.

In his next work¹⁴ he introduced experimental evidence. Working with yeasts at 21° he used the best known antiseptics of the period and showed that with small doses, in place of killing the yeast cell, they increased the activity as measured by fermentation. This appeared with 1:500,000-700,000 bichloride of mercury, iodine 1:600,000, potassium iodide 1:10,000, bromine 1:300,000, chromic acid 1:3000-6000, salicylic acid 1:4000, arsenious acid

1:40,000, and he also confirmed the previous work on formic acid. He emphasized that the figures obtained by him with the strain of yeasts with which he had worked would undoubtedly vary from the figures secured by other writers. Incidentally the stimulating action of arsenic had been foreshadowed by Johannsohn.¹⁵

In modern times the stimulating action of the sublimate has been confirmed by Supfle,¹⁶ Euler,¹⁷ Biernacki,¹⁸ Walbum,¹⁹ Zeller,²⁰ Kötschau,²¹ the stimulating action of arsenic by Supfle, Biernacki, Kötschau and Meier,²² Harden and Young.²³ To these may be added similar studies with other substances in which the stimulating action of phenol was observed by Cassel,²⁴ Abderhalden,²⁵ quinine by Biernacki, Kötschau, Rona and Grassheim,²⁶ potassium ferrocyanide by Kötschau, iron chloride by Neuberg,²⁷ insulin by Ahlberg,²⁸ Zeller and Abderhalden, potassium permanganate by Biernacki and Zeller, strychnine by Popoff,²⁹ Kötschau, Leibig,³⁰ electroferrol by Kötschau, silver nitrate by Supfle, Walbum, toluol by Abderhalden as well as by Euler and Lowenbaum.³¹ Zeller also observed stimulation with lysol (1:2000), naphthalin (1:60,000), alpha and beta naphthol (1:240,000), sodium nitrite and amyl nitrite (1:16,000), oil of turpentine (1:16,000), formalin (1:80,000), hexeton (1:4000), foramide (1:40,000), eserine (1:400,000), morphine (1:16,000), blood charcoal (1:400).

If attention is directed to the metals which are so widely used as antiseptics, one will find reports on substances which are stimulating although they are commonly supposed to have but one action, depression and death of the microorganism. Studies showing stimulation are largely accidental, except in the case of plant physiologists who at times are concerned with possible increases in crop yield. It is therefore surprising that such stimulative effects have been found at all since no particular search has been made for them.

A rapid survey of the metals which have been studied in this respect shows that stimulating actions have been reported from uranium,^{32, 33, 34, 35} vanadium and thorium,³⁶ cadmium,³⁷ zinc,³⁸ manganese,^{39, 40, 41} lead,³⁸ tin,⁴² nickel,⁴³ iron,^{44, 45, 46} gold,⁴⁵ copper,^{47, 48, 49} platinum,⁴⁵ silver, platinum, thorium, barium, cobalt, vanadium, lithium, tellurium.⁴⁹ The lethal properties of chlorine as well as its indispensability for life are generally known, and Schulz has reported on iodine, and bromine. The stimulative effect of fluorine on bones is also generally appreciated. Sulphur has also been shown to be stimulating.^{50, 51, 52} Orlowski confirmed the stimulating action of arsenic⁵⁴ and Frouin has shown the stimulating effects of the rare metals of the cerium group, lathanum, neodymium,

samarium. The stimulating action of beryllium is likewise generally known.

The effect of small doses of substance on plants has been extensively treated in the masterly work of Czapek⁵⁵ so that it needs no detailed discussion here, and the action of drugs on bacteria is discussed by Buchanan and Fullmer as far as they have been reported.⁵⁶ Czapek introduces his discussion of the chemical effects on plants with the following noteworthy words: "in the field of biochemistry we must also include those actions of chemicals which are often designated as 'releasing actions,' in the physiologic sense, and which join entirely with the stimulus actions of physical physiology. We must separate such events sharply from catalytic processes in that in chemical stimulus action, generally nothing can be said of an increase of the stimulus effect proportionate to the concentration of the stimulus material. On the other hand, as we shall soon see, very small quantities of materials can result in significant increase in the vital processes, while somewhat greater quantities have a decisively depressing influence." Near the end of the section on stimulation of growth Buchanan and Fullmer state (p. 214) Hueppe's law but without comment. The law reads: "every substance which in a definite concentration kills protoplasm, will inhibit development in smaller amounts, and in still greater dilution will act as a stimulant."

When one considers that little attempt has been made to observe stimulating actions of metals and the so-called antiseptic substances in respect to their effects upon yeasts and micro-organisms, when further one recalls that such observations are for the most part accidental, it is actually surprising that so many have been discovered. Attention should not be directed to omissions in the list because such stimulative actions have not been generally sought and may be difficult to secure with some substances.

However some other examples of reversible actions may be cited in order to show that they are not obtained only on unicellular organisms. A few of these are cited here, others will be found later:

Rona and Bloeh⁵⁷ and Rona and Grassheim⁵⁸ noted reversible effects of quinine on oxygen respiration of chicken blood and yeast cells. Resnitschenko observed stimulation and then depression of respiration of *Ascaris*.⁵⁹ Matthaei has reported a similar reversibility of nervous reflexes,⁶⁰ Platz⁶¹ has reported a double phase effect of atropine on the pulse, small doses causing bradycardia and large doses tachycardia. Sand⁶² has reported stimulating and depressing actions of arsenic. The well-known primary stimulating and secondary depressing actions of chloroform, ether, and nitrous oxide

are known to every physician. Irving⁶³ has reported that small doses of chloroform stimulate plant respiration, larger doses causing depression. Warburg has had similar results with urethane derivatives.⁶⁴ Blume⁶⁵ has reported increased salivation with small amounts of atropine. Yet Cushny in his well-known pharmacology implies atropine is an exception to drugs having reversible effects.⁶⁶ Bowing reports the "irritating effects of small doses of nicotine, lead, atropine on the myenteric plexus,"⁶⁷ and the depressing effects of large doses. Barrath⁶⁸ calls atropine a double phasic substance and Petsctakis⁶⁹ has proven the double phasic effect to be dependent upon dosage. Zondek and Ueko have shown the double phase effect of hormones.⁷⁰ Lang and Vas have reported reversible effects of small and large doses on blood sugar,⁷¹ Franzen, the reversible effects of alcohol on pepsin splitting of egg white⁷² and Poulssen,⁷³ the reversible effects of alcohol on work performance. Weber has reported the pyretic and antipyretic effects of quinine on different species⁷⁴ and Stuhlinger the pyretic effect of salicylic acid⁷⁵ which is used as an antipyretic in larger doses. The well-known stimulating effect of iodine in hypothyroidism is, perhaps, used no more often than the metabolism decreasing effect in Graves' disease. Knipping⁷⁶ has shown the same to be true of arsenic. Schubel and Gehlen reported the stimulating effect of small doses of quinine on the uterus and the depressing effect of large doses.⁷⁷ Mainzer and Joffe⁷⁸ have shown that the acidosis produced by ammonium chloride is followed by an alkalosis. Anatol and Gomori⁷⁹ reported the phase effects of lobeline on intestinal movements; Arndt et al.,⁸⁰ that the sugar reducing synthalin may also produce an increase in blood sugar, which was confirmed by Basel and Staub.⁸¹

Gellhorn⁸² observed stimulating and depressing effects of ultra-violet rays on ciliary movements, Grinberg⁸³ confirming the biphasic effect. Zeller⁸⁴ showed the stimulating effect of x-ray as well as depressive effects on yeasts. Groedel and Schneider⁸⁵ have studied the stimulative effect of x-ray on paramecium, and Halberstadter and Simons on plant growth.⁸⁶ Sierp and Robbins made similar observations.⁸⁷ Ivens⁸⁸ concluded that all seedlings are stimulated by moderate doses of x-ray. Gutzeit et al.⁸⁹ reported an increase in the movement of flagella in typhoid bacilli from small doses of x-ray. Gassul⁹⁰ observed reversible effects of x-ray on tadpole growth according to dose, small, stimulating and large, depressing.⁹¹ Miescher⁹² showed stimulating effects on gastric secretion from small doses of x-ray and depressing from large.

These examples have been introduced to suggest that reversible effects occur with all types of stimuli and not merely from "drugs."

as well as to indicate briefly the frequency with which the phenomena are observed. The well-known textbook of pharmacology written by Sollmann mentions in passing about one hundred and twenty-five instances of reversal of action. Thus it may be said that there is considerable experimental evidence supporting the Arndt-Schulz rule which is usually stated as follows: *small doses kindle vital activities, moderate increase them, large depress them and largest remove them; but it is entirely individual what shall be considered, small, moderate, large or largest.*

A review of the entire literature dealing with substances displaying reversal of action from large and small doses would be extremely interesting in this connection, but such a statement would require a monograph larger than this entire study. As the subject receives further attention later, no additional literature need be cited here and attention may be directed to a more pressing problem.

Handovsky⁹³ recently studied the Arndt-Schulz rule. Working with histamin in various concentrations he found that large doses killed a certain percentage of the protozoa employed as a test object. Using size as a measure he noted that organisms treated with smaller doses of histamin showed an increase in comparison to untreated controls. Small doses of histamin stimulated growth, large doses abolished it and killed the organism. However, according to this investigator the small doses of histamin also killed a few protozoa, and he concluded that their bodies acted as "nutrient" stimuli or as food and thus increased the growth of the survivors. In other words small doses of histamin killed a few organisms, large doses killed more. Since this offers nothing new, the Arndt-Schulz rule is superfluous. In this manner Handovsky reduced the generalization to an absurdity. Kötschau⁹⁴ working in the writer's laboratory showed by means of yeast experiments that Handovsky's explanation was not inevitable and moreover did not obtain in many cases. Outside of the fact that most of the literature on parthogenesis tends to repudiate Handovsky's conclusion the following experiments are also indicative of its unreliability.⁹⁵

Studies were carried out with eggs of *Asterias Forbesii*, and with various concentrations of butyric acid. For thirty-eight minutes after removal from the ovary, the eggs were placed in sea water. Next they were placed in varying strengths of butyric acid for eight minutes, after which they were returned to sea water. In the following table the first column represents the strength of the butyric acid solution, the second (PTC) the percentage of eggs cleaving regardless of whether or not the cleavage was normal. The third column (PNC) is the percentage of normal divisions

among the eggs which cleaved and the last column (PCYT) is the percentage of eggs showing cytolysis.

	PTC	PNC	PCYT
n/390.....	0	0	0
n/364.....	3	82	0
n/338.....	13	74	0
n/312.....	17	74	0
n/286.....	32	58	0
n/260.....	58	40	0
n/244.....	73	31	5
n/218.....	77	12	16
n/192.....	68	11	34
n/166.....	48	5	54
n/140.....	34	4	65
n/114.....	8	0	92

In another series of experiments, similar eggs were employed thirty-eight minutes after removal from the ovary, but the concentration of butyric acid (50 ccm. sea water plus 2 ccm. n/10 butyric acid) remained constant while the duration of exposure varied. The first column represents the duration of exposure in minutes, the other symbols as above.

	PTC	PNC	PCYT
1.....	0	0	0
2.....	9	73	0
3.....	13	65	0
4.....	19	67	0
5.....	24	60	0
6.....	41	59	0
7.....	52	49	4
8.....	57	46	8
9.....	71	32	15
10.....	79	7	16
11.....	56	0	28
12.....	8	0	92
13.....	4	0	96
14.....	0	0	100

Comparable results were obtained with other chemical substances—hypertonic sea water, mechanical, thermal, and electrical stimuli, etc. In the above experiments it is obvious that “small” doses lying near the minimum effective stimulus gave the highest percentage of normal divisions, whereas “larger” doses yielded more spectacular results but increasing percentages of abnormal divisions and cytolysis.

In reference to the Handovsky explanation, it is important to recall that the experiments just reported never required more than five hours, whereas according to the literature, the egg does not take nourishment for at least 50 hours. Finally experiments with

single eggs yielded results which are entirely comparable with the above, and thereby all "nutritive" stimuli are excluded. Other details will be found in the original publication.

More recently Heubner⁶⁵ has published some interesting observations which are particularly suitable for brief discussion at this point since they provide a connection with a subject still to be discussed.

Heubner denied (what no one asserted) that cells in general are not subject merely to one rule. Therefore he questions whether or not substances which are not simply nutriments, but which evoke a true "kindling of vital activity" are not exceptions rather than the rule. "I think we may say today that the promulgation of the Arndt-Schulz law was an error from which we must liberate ourselves, if we are to make progress in discovery. One may recognize the rule as a necessity in nerves, because there each damage releases an excitation. . . ."

Heubner introduces a series of personal studies, largely on tissue cultures and particularly on fibroblasts, and cites some studies of others, among which are the extensive investigations of R. Meier on yeast cultures and avian blood corpuscles.

He states: "occasionally but only exceptionally and never to be reproduced with certainty" a fibroblastic culture seemed to grow somewhat better under minimal doses of poisons than the untreated controls. "However more frequently an acceleration of 'out-wandering' was demonstrated in leucocytes by arsenious acid, oil of turpentine, and strophanthin in concentrations of 10^{-7} - 10^{-8} ." "The results of these investigations with chemically defined substances also indicate that stimulation effects were predominantly on the motile leucocytic form and here also brought about only by some of the substances tested."

It will be noticed that Heubner's assertion that the Arndt-Schulz rule is an error must be qualified by the results of his own work, for at times he observed effects in agreement with the formulation. It so happens that rule does not hold in the form which Heubner has interpreted it but his interpretation is unusual. The accepted interpretation is as follows: there is no "kindling and promoting" stimulus (in small and moderate doses) of vital activity which will not depress and remove vital activity in large and largest doses. The reverse of this statement is not true unless other factors are introduced, for example: a stimulus which damages a living structure and impairs its activity when administered in a large dose, is not always biologically useful when weaker, except under very definite and special conditions.

The effects of a large number of substances on the isolated cat

intestine perfused in oxygenated Ringer's solution have been noted by the writer in the course of investigation of the simile problem. With rare exceptions the substances mentioned below have not been previously reported in the literature, so that the results may not be without general pharmacologic interest. To describe the experiments completely would require a fairly large volume so that allusion is made simply to the effect of small and large doses on normal cat intestine. The substances are listed alphabetically to facilitate reference. No substance is included which did not produce some effect in a dilution of 1:1000, although in practically every instance some action was noted in a dilution of 1:2000. This figure refers to the final concentration of the substance (as chemically pure substance or 10% tincture from which the alcohol had been removed) and is called the "small dose." The results obtained are listed in the first column as stimulation (S) or depression (D). The second column contains the results obtained with a "large dose," almost invariably a 1:100 dilution; ? means inconstant results.

Abies Canadensis	D	D	Arum Tri.	S	D
Acetic Acid	S	D	Asafoetida	D	D
Actaea Spicata	S	D	Asimina Tri.	?	D
Agave Americana	D	D	Asparagus Off.	S	S
Agnus Castus	D	D	Athamanta	S	S
Agrostemma	D	D	Avena Sat.	D	D
Aletris Far.	S	D	Azadirachta Ind.	S	D
Allium Sativa	D	D	Barosma Cren.	S	D
Allium Cepa	D	S	Bellis Per.	D	D
Alnus Rubra	D	D	Benzoic Acid	S	S
Aloes	S	D	Berberis Aquia.	D	D
Alstonia	S	D	Bovista	D	D
Althaea	S	D	Brucea Ant.	S	D
Amelopsis Quin.	S	D	Bufo Cin.	D	D
Anacardium	?	D	Cactus Grand.	D	D
Anatherum	D	D	Cahinea	S	D
Anagallis Arv.	D	D	Caladium	D	D
Angustura Cor.	S	D	Calendula Off.	D	D
Anthemis	S	D	Calotropis	S	S
Anthoxanthum Odor.	S	D	Caltha Pal.	S	D
Apis Mel.	S	S	Cantcharis	D	D
Apocynum Can.	S	D	Carbolic Acid	D	D
Apocynum And.	S	D	Carduus Ben.	D	D
Aralia Quin.	S	D	Carduus Mar.	D	D
Aralia Rac.	S	D	Cascarilla	S	D
Araena	S	D	Castanea	D	D
Aristolochia Muhl.	D	S	Castoreum	?	D
Aristolochia Serp.	S	D	Caulophyllum	D	S
Arnica Mont.	S	D	Cedron	S	D
Artemisia Vulg.	D	D	Cereus	D	D
Arum Canadensis	S	D	Chamomilla	D	D
Arum Drac.	D	S	Cheiranthus	D	S
Arum Mac.	S	D	Chelone Glab.	D	S

Chenopodium	D	D	Eucalyptus Lab.	S	S
Chimaphila Umb.	D	D	Euonymus Atrop.	S	S
Chimaphila Mac.	D	D	Euonymus Europ.	S	D
China Off.	D	D	Eupatorium Arom.	D	D
Chin. Ars.	D	D	Eupatorium Perf.	D	D
Citravia I.	D	S	Eugenia Vulg.	D	D
Cicuta Mac.	D	D	Euphorbia Amyg.	S	S
Cicuta Vir.	D	D	Euphorbia Cor.	S	D
Cichorium	S	D	Euphorbia Hyper.	S	D
Cina	S	D	Euphorbia Lathyr.	S	S
Cinnamomum	S	D	Euphorbia Off.	S	D
Cistus Can.	S	D	Euphrasia	D	D
Clematis	D	D	Eupion	D	D
Coccinella	D	D	Fagopyron	D	D
Coccus Caeti	D	D	Felix Mas.	D	D
Cocculus Ind.	D	S	Formica Ruf.	D	D
Colchicum	S	S	Franciscea Uniflora	D	D
Collinsonia	S	D	Fraximus Amer.	S	D
Colocynth	S	S	Fucus Vesc.	D	D
Commoeladia Dent.	S	D	Galium	S	D
Conium Mac.	D	D	Gambogia	D	D
Condurango	D	S	Gaultheria	S	D
Convallaria Maj.	S	D	Gelsemium	S	D
Convolvulus Arv.	S	D	Genista	D	D
Convolvulus Duart.	D	D	Gentian Crue.	S	D
Coravia Off.	D	D	Gentian Lutea	S	D
Cornus Alter.	D	D	Gentian Quin.	S	D
Corydalis Form.	S	D	Geranium Mac.	S	D
Cotyledon Umb.	S	?	Gnaphalium Poly.	D	D
Creosotum	D	D	Gossypium	S	S
Cucurbita Pepo.	D	S	Gratiola Off.	D	D
Cuphea	D	D	Grindelia Rob.	D	S
Cupressus Lanc.	S	D	Guana Aust.	D	D
Crataegus	S	S	Guaco	D	D
Crocus Sat.	S	D	Guaiacum	D	D
Cyclamen	D	D	Gymnocladius	D	D
Datura Arbor.	S	D	Hamamelis Virg.	D	D
Dictamnus Alb.	D	D	Hedeoma Pul.	S	D
Dioscorea Vill.	D	D	Helleborus Foet.	S	S
Dirca Pal.	D	D	Helleborus Nig.	S	S
Drosera	S	S	Helonias	S	D
Dulcamara	S	S	Hepar Sulph.	S	D
Echinacea	S	S	Hepatica Tri.	D	D
Elatarium	S	S	Hydrangea Arbor.	S	S
Ephedra Vulg.	S	S	Hypericum	S	S
Epilobium	S	S	Hydrastis	S	D
Epiphegus	S	D	Hydrophyllum	D	D
Equisetum	D	D	Iberis	D	D
Erechthites Lier.	S	D	Ictodes	S	D
Eriodyction Cal.	D	D	Ignatia	D	D
Erodion	D	D	Illicium Anis.	S	D
Eryngeum Aquat.	S	D	Ipecac.	S	D
Eryngeum Mar.	S	D	Iris Vers.	S	D
Erythrinum	S	D	Jatropha	D	D

Jequirity.....	D	D	Magnolia Glauca.....	S	D
Juglans C.....	D	S	Mellilotus Alba.....	S	D
Juglans Regia.....	D	D	Mercurialis Per.....	S	D
Lactic Acid.....	D	D	Mezereunn.....	S	D
Lappa.....	D	D	Monotropa Uni.....	?	?
Laurocerasus.....	D	D	Nabulus Serp.....	S	D
Leptandra.....	D	D	Oleum Cajapat.....	D	D
Linaria Vulg.....	D	D	Oxalic Acid.....	D	D
Lobelia Inf.....	D	D	Oenanthe.....	S	S
Lolium T.....	D	D	Oenothera Bien.....	D	D
Lycopersicon.....	D	D	Pieric Acid.....	S	S
Lycopodium.....	S	D	Salicylic Acid.....	S	D
Lycopus.....	S	D	Thlaspi Burs.....	S	D

Brief reference should be made to these results. At first glance the studies would seem to minimize the importance of the Arndt-Schulz rule because only 36% of the drugs appeared to stimulate in the small dose and depress in the large. As a matter of fact the results very strongly emphasize the validity of the Arndt-Schulz rule, since the reversal was produced within a relatively small variation of concentration. As a matter of fact experiments with larger doses (1:50 or more) frequently produced depression with substances listed above as exclusively stimulating, and in all instances sufficiently large doses caused paralysis. Adding these cases to the group mentioned above and including the few which at times produced stimulation at 1:2000, it will be noted that 50% of the substances fall within the Arndt-Schulz formulation.

Just as the list contains comparatively weakly acting drugs, so many are relatively strong in their intestinal effect. For example, chenopodium is listed above as a depressant, whereas, in other experiments with isolated cat intestine, a concentration of 1:50,000 is definitely stimulating. In other cases dilutions to 1:4,000,000 or less (as with sulphur) are required to bring out stimulation effects. From experiences with these higher dilutions, with similar studies on isolated rabbit intestine, it may be said that there is ample reason for asserting that more than 80% of the above substances will show a reversal of action by variation of dose alone.

In order to increase the figure beyond this point it is necessary to complicate the experiment by the introduction of some other factor, such as the use of fatigued rather than normal intestine, variations in the concentration of salts in the perfusing fluid, decrease in oxygenation, etc. It is not impossible that some substances may be found which may not "stimulate" in small doses and "depress" in large, but there is very little reason for assuming that they represent a frequently encountered phenomenon, and still less occasion for presuming that the Arndt-Schulz rule is the exception rather than the rule. It should be equally apparent that the

formulation is incomplete, since other factors besides posology play roles in drug action. Some of these receive consideration elsewhere. It is not overlooked in the above experiments that "depression" was encountered with "small" doses and "stimulation" with large. The criteria employed for "stimulation" consisted of an increase in number or amplitude of the intestinal contractions or a decided shortening of the intestinal strip. Whether or not "stimulation" of inhibitors might produce the opposite to these, whether or not relaxation is an active phenomenon, is left untouched here and the substances have been left in the "depressant" class although many do not belong there.

Naturally the subject is far more complicated than the above discussion might imply. For example, one substance was encountered which yielded no apparent action after small or large doses, yet stimulation was shown on washing the drug out of the tissues. Again in 75 instances where depression is reported above as occurring after small and large doses, 28 drugs showed stimulation on washing out. Likewise in 26 cases where stimulation is recorded from small and large doses, washing out produced depression in 9 cases. Other combinations of reversed actions were also observed. As the details of these experiments will find publication elsewhere it is not necessary to dwell upon them here, except it may be noted in passing that investigation of 165 substances in regard to the effect on isolated rabbit intestine perfused in Tyrode's solution also harmonizes with the conception of the widespread validity of the Arndt-Schulz rule.

In order to indicate that intestinal muscle does not represent an exceptional situation, the following results obtained in studies of the heart, blood pressure and respiration may be mentioned. The studies were conducted on cats under urethane anesthesia. Stimulation is defined here as a rise in blood pressure, an increase in the amplitude of contractions or an increase in cardiac rate as shown by the carotid tracing. The effect on the respiration has been omitted in order to simplify presentation here. The drugs are listed alphabetically. The first column headed "S" reflects the instances in which stimulation was observed, the second "D," depression, the third column "SD," stimulation followed by depression, the fourth column "DS," depression followed by stimulation. It should be emphasized that these combinations were observed after different doses; moreover in many instances the dosage was so large that it is doubtful that many substances listed here have significance for cardio-vascular therapy. In another place the study will be described in detail, although this preliminary statement may not be without interest for those concerned with the lesser known drugs. "x" means the particular action was observed.

	S	D	SD	DS		S	D	SD	DS
Abies Canadensis.....	x	x		x	Azadirachta Ind.....	x			
Abies Nigra.....	x			x	Barosma Ind.....	x			x
Abrotanum.....			x	x	Bellis Per.....				x
Acalypha Indica.....	x				Berberis Aquil.....		x		x
Acidum Aceticum.....	x			x	Berberis Vulgaris.....	x		x	
Acidum Hydrochloricum	x				Bovista.....	x			
Acidum Lacticum.....	x				Brucea Antidy.....	x			x
Acidum Nitricum.....	x				Bryonia Alba.....		x		x
Acidum Sulphuricum....	x			x	Bufo Ciner.....		x		
Actea Racemosa.....	x	x	x	x	Cactus Grand.....		x		
Aesculus Glabra.....		x		x	Cahinea.....	x			
Aesculus Hippocastanum	x			x	Caladium Seg.....	x			
Aethusa Cynapium.....	x			x	Calendula Off.....	x			x
Agave Americana.....	x	x		x	Calotropis.....	x		x	
Agnus Castus.....	x	x		x	Caltha Pal.....	x			x
Agrostemma Gith.....		x		x	Capsicum Ann.....		x		x
Ailanthus Gland.....	x			x	Carduus Ben.....	x			x
Aletris Farinosa.....	x			x	Carduus Mar.....	x	x		
Allium Cepa.....	x			x	Cascarilla.....				x
Allium Sativa.....	x	x	x	x	Castanea Vosca.....				x
Alnus Rubra.....	x	x	x	x	Castoreum.....	x			x
Aloe Soc.....	x	x	x	x	Caulophyllum.....	x			x
Alstonia Scholaris.....	x			x	Cedron.....		x		
Althaea Off.....		x			Chamomilla.....	x			x
Ambrosia Artem.....				x	Cheiranthus.....	x	x		
Ampelopsis Quin.....		x		x	Chelidonium Maj.....	x			x
Amygdala Amara.....				x	Chelone Glab.....				x
Anacardium Orientale...		x		x	Chenopodium An.....				x
Anagallis Arv.....	x			x	Chimaphila Mac.....				x
Anatherum.....	x			x	Chimaphila Umb.....	x			
Angustora Cor.....		x			Chin. Ars.....				x
Anthemis Nob.....		x			China Off.....			x	
Anthoxanthum Odor....		x			Chionanthus Virg.....				x
Apocynum And.....	x				Cichorium Int.....	x			
Apocynum Cannab.....	x			x	Cicuta Mac.....		x		
Aralia Racemosa.....		x		x	Cicuta Vir.....	x			
Aranea Diadema.....	x			x	Cina.....				x
Aristolochia Muhl.....				x	Cinnamonum.....				x
Aristolochia Serp.....	x				Cistus Cana.....		x		
Arnica Mon.....				x	Clematis Erecta.....				x
Artemisia Abrot.....	x			x	Coccinella Sept.....				x
Artemisia Vulg.....		x		x	Coeculus Ind.....				x
Arum Draconis.....		x			Coccus Cacti.....				x
Arum Mac.....	x			x	Colchicum Aut.....	x			
Arum Tri.....	x			x	Collinsonia.....	x			
Asafoetida.....	x			x	Colocynthis.....				x
Asarum Can.....	x			x	Commoeladia Dent.....	x	x		x
Asclepias Cor.....	x	x		x	Condurango.....				x
Asclepias Tub.....	x			x	Conium Mac.....				x
Asimina Tri.....	x			x	Convallaria Maj.....	x		x	
Asparagus Off.....	x				Convolvulus Arv.....				x
Athamanta Oreo.....	x				Convolvulus Duart.....		x		
Avena Sativa.....	x			x	Copaiva.....		x		x

	S	D	SD	DS		S	D	SD	DS
Lathyrus S.	x		x		Lippia Mex.	x	x		x
Laurocerasus	x	x			Lobelia Card.		x	x	x
Ledum Pal.	x	x	x		Lobelia Erin.		x		x
Lemma Min.	x	x	x		Lobelia Inf.		x		
Leonurus Car.	x	x	x		Lupulin		x		x
Leptandra	x		x		Lycopodium		x	x	
Liatris S.	x		x		Lycopus Vir.		x		x

The above list is intentionally incomplete in many respects. The reader will note that only the first half of the alphabet is represented, and it would have been possible to cite an equal number of instances from the last half. Likewise specific reference to posology is lacking although it may be said in passing that relatively large doses were employed. For example, the alcohol was removed from 10% plant tinctures, the original volume restored with normal salt solution, and usually doses began with 0.1 cc. of a 1:100 preparation of the preparation whose volume had been restored to the original. Doses were increased by reducing the dilution rather than increasing the amount of fluid injected in order to minimize the possibility of changes in blood volume. The inclusion of these details, which would be indispensable in a report of the pharmacology of the substances mentioned, would carry the discussion of this aspect far beyond the limits set for the entire work. The substances are merely mentioned in order to stress the frequency with which reversal of action is encountered.

Incidentally it may be said, although no evidence is introduced here, that studies with these drugs on the isolated rabbit heart (Langendorf's method), on the normal and pregnant uterus, and on bladder muscle yield similar observations, the last mentioned structure providing the poorest results.

In studies carried out with some of the lesser known drugs some observations were made which may not be without interest in connection with reversal of action. The studies were made on rabbits under paraldehyde anesthesia. The first column represents broadly three types of doses, small (S), moderate (M) and large (L). In most cases they do not represent the minimum effective nor the maximum tolerated, but amounts comparable to those mentioned in the experiments on the intact heart, blood pressure. The procedure here differed in that the chest was opened, the left lung collapsed and levers were attached to the auricle and ventricle in order to study the effect of the drugs on rate and amplitude of these structures. Respiration was recorded from the trachea as usual. BP is the blood pressure. "D" is depression and "S" stimulation.

THE ARNDT-SCHULZ RULE

	Dose	BP	Respiration		Left Ventricle		Left Auricle	
			Rate	Ampl.	Rate	Ampl.	Rate	Ampl.
Abrotanum	S							
	M	DS	S	S	D	D	D	D
	L	D	SD	DS	D	D	D	D
Absinthium	S	DSD	S	D	D	D	D	D
	M	D	S	D	DS	DS	DS	DS
	L	D	S	D	SD	SD	SD	SD
Aconitum N.	S	DS	DS	S	DS	D	DS	D
	M	D	S	S	D	S	D	S
Aesculus	S	D	S	D	D	SD	D	
	M	D		D	D	D	D	D
	L	D		D	D	DSD	D	DSD
Agaricus	S	S	D	S	D	D	D	DS
	M	D	D	SD	D	D	D	D
	L	D	D	D	D	D	D	D
Anacardium	S	D	SD		SD	DSD	SD	D
	M	D	D	S	SD	D	SD	D
	L	D	D	S	D	S	D	D
Ant. Tart.	S	SD		S	DS	DS	DS	DS
	M	S	S	S	DS	SD	DS	DS
	L	D	D	D	D	D	D	DS
Apis Mell.	S	S	D		D	S	D	S
	M	S	D	S	D	S	D	S
	L	S	D	SD	D	S	D	S
Arnica Mont.	M	D	SD	DS	SDS	D	D	D
	L	D	D	SD	D	D	D	D
Arsenic (As ₂ O ₃)	S	D	S	S	D	S	D	S
	M	D	S	D	D	D	D	S
	L	D	S	D	D	D	D	D
Asafoetida	S	D	SD	D	D	D	D	D
	L	Heart showed fibrillation						
Asclepias	S	SD	S	S	D		D	
	M	S	D	S	D		D	D
	L	DS	S	S	DS		D	DS
Baptisia	S	DS	S	D	D	DSD	D	DSD
	M	DS	S	D	D	DS	D	D
	L	D	D	D	D	D	D	D
Barium Cit.	S	S	S	DS	D	SD	D	SD
	M	S	D	D	D	DSD	D	D
	L	D	D	D	D	D	D	D

	Dose	BP	Respiration Rate	Ampl.	Left Ventricle Rate	Ampl.	Left Auricle Rate	Ampl.
Belladonna	S	S	S		S	S	S	
	M	D			D	SD	D	
	L	D	S	D	D		D	DSD
Berberis V.	S	S	DS	D	D	D	D	D
	L	Respiration stopped						
Bovista	S	S	D			S		
	M	S	D	S	D		D	
	L	D	D	D	D	D	D	D
Capsicum	S	S			DS	D	DS	D
	M	D	D	S	D	SD	D	D
	L	D	D	D	D	S	D	D
Causticum	S	S			D	D	D	
	M	SD	D	S	D	D	D	D
	L	D	D	D	D	D	D	D
Chelidonium	S	D	SD		S	S	S	D
	M	D	D	D	D	D	D	D
	L	D	D	D	D	D	D	D
Cicuta Vir.	S	D	S			D		
	M	D	D		D	D	D	D
	L	D			D	D	D	D
Cimicifuga	M	D	S		D	D	D	
	L	D	D	D	D	D	D	D
Cina	S	D	S	D	D	D	D	D
	M	D	S	D	D	D	D	D
	L	D	SD	D	D	D	D	D
Cinchona	S	S			D	D	D	
	M	D	D	D	D	SD	D	D
	L	D	D	D	D	D	D	D
Clematis	S	S	D		S	S	S	D
	M	DS	D	S		S		S
	L	DSD	D	S	S	DSD	S	DSD
Cocculus	S	S	S		D		D	D
	M	S	S	D	D	D	D	SD
	L	S	S	D	D	SD	D	DS
Colichicum	M	S		S	D	D	D	D
	L	D	D		D	D	D	D
Colocynth	S				S	D	S	D
	M	D	D	D	D	D	D	D
	L	D	D	D	D	D	D	D

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	Dose	BP	Respiration		Left Ventricle		Left Auricle	
			Rate	Ampl.	Rate	Ampl.	Rate	Ampl.
Collinsonia	S	S	S	—	D	D	D	D
	M	DS	D	—	D	DS	D	D
	L	DS	D	—	D	D	D	D
Dulcamara	S	SD	D		D	D	D	DS
	M	D	D	D	D	S	D	D
	L	D	D	D	D	D	D	D
Gelsemium	S	D	S	D	D		D	DS
	M	SDS	S	S	D	DS	D	DS
	L	D	D	D	D	D		D
Hepar Sulph.	S	SD	S	D	D	D	D	DS
	M	SD	S	D	DS	DS	DS	DS
	L	SD	SD	D	D	D	D	DS
Hydrastis	S	D	S	S				S
	M	SD	D	DS	D	D	D	D
	L	D	D	D	D	D	D	D
Ignatia	S	D	S	D	D	D	D	D
	M	D	S	D	D	DS	D	D
	L	D	D	D	D	D	D	D
Ipecac	S				D		D	
	M	S	D		D	D	D	D
	L	D	D	D	D	D	D	D
Iris	S	D	S	D	D		D	S
	M	S	S	S	D	D	D	D
	L	DS		S	D	D	D	DSD
Kalmia	S	DS	D	SD	D	DSD	D	DSD
	S	DS	D	SD	D	D	D	D
	S	D	D	D	D	D	D	D
Ledum	S	D						S
	M	D	D		D	D	D	D
	L	D	D	D	D	D	D	D
Lycopodium	S	D	D	D	D	D	D	D
Phosphorus	M	D	SD	DS	D	D	D	D
Podophyllum	S	D	S			D		
	M	DS		D	D		D	
	L	SD	D	D	D	D	D	D
Pulsatilla	S	S	S	D	D	DS	D	DS
	M	SDS	S	D	D	DS	D	DS
	L	D	D	DS	D	D	D	D

	Dose	BP	Respiration		Left Ventricle		Left Auricle	
			Rate	Ampl.	Rate	Ampl.	Rate	Ampl.
Rheum	S	DS	S	D	D	DS	D	DS
	M	D	S	D	D	D	D	DS
	L	D	D	D	D	D	D	D
Rhus Tox	S	DS			D	D	D	
	M	DS		D	D	D	D	D
	L	D	D	D	D	D	D	D
Rumex	S	S	S	D	D	DS	D	DS
	M	S	S	DS	S	D	S	S
	L	DSD	S	DS	S	DSD	S	DSD
Sambucus	S	SD		D	D	S	D	DS
	M	D	SD	D	D	D	D	DSD
Sanguinaria	S	S	S	D	D	D	D	D
	M	S	S	D	D	D	D	D
	L	D	D	D	D	D	D	D
Senecio	S	DS	D		D	DS	D	DS
	M	S	D	D	D	DS	D	DS
	L	DS	D	D	D	DSD	D	DSD
Potassium	S	D	S	S	S	D	SD	D
	M	S	D	DSD	D	D	D	D
Bichromate	L	D	D	D	D	D	D	D
Staphisagria	S	S	S	D		S	D	DS
	M	S			D	D	D	DS
	L	D	D	D	D	DSD	D	DSD
Terebinthina	S	S	D		D	S		S
	M	S	D	S	D	DSD	D	SDS
	L	D	D	D	D	D	D	D
Veratrum album	L	D	D	SD	D	D	D	D
Veratrum viride	S	S			D	DS	D	
	M	DS	D	D	D	DS	D	DSD
	L	D	D	D	D	D	D	D

On the basis of experiments briefly reported above, an experience with an equal number of substances not mentioned, together with an extensive literature, some of which is noted later, it may be said that the Arndt-Schulz rule is fundamentally correct. This statement is not to be interpreted to mean that it formulates the entire situation. No substance has been encountered, which, if it stimulates in small and moderate doses, will not depress or abolish the vital activity involved after larger doses. Likewise no substance has been

encountered, which, though damaging in larger doses, may not be biologically useful in smaller doses under very definite and special conditions. Naturally "small" and "large" are relative conceptions, varying not only with different substances, but with the same substance under different conditions.

The relationship of this to the simile is readily discerned. Large doses of ether produce depression; small doses produce stimulation. When it has been determined ("found") that ether in large doses produces depression, according to simile thinking, ether in small doses is a possible remedy for "depression" under certain conditions.

For reasons which will become increasingly clear the writer does not believe the above situation depicts the entire event of disease. To mention only one item, the phenomena of disease are not all "depressant" in nature. However, there is little doubt that the Arndt-Schulz rule is an important guide in posology.

It should also be noted in passing that the ether example indicates quite clearly how the simile and the contrarium methods of thinking supplement each other. Both the "stimulating" as well as the "depressing" phases of ether can be utilized therapeutically.

Finally it should not be presumed that the above interpretation of the Arndt-Schulz as a finding principle is the only possible interpretation. Another will be advanced later.

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THE WILDER ORIGINAL VALUE RULE.—As indicated above it is often difficult to confirm the Arndt-Schulz rule with some of the substances commonly known as depressants. So much emphasis is usually placed upon "large" and "small" doses that the investigator may forget that these terms are comprehensible only in relation to other factors. One of these factors is the state of the tissue at the moment the stimulus is applied. Passing over an important development which is considered subsequently one may briefly present the so-called Wilder rule. Unfortunately it also is one-sided. Whereas in the Arndt-Schulz stress is placed almost entirely upon dose, here the varying state of the tissue alone receives emphasis.

For several years Wilder¹ was engaged in a clinical-experimental investigation of the vegetative nervous system. He admits the value of the contributions of Eppinger and Hess and Pötzl. Eppinger and Hess so far as the conceptions of sympatheticotonia and vagotonia are useful in understanding organ neuroses and somatic symptoms in neuroses; still their contributions to pharmacology, whereby the sympatheticotonic and vagotonic drugs are supposed to be a basis for diagnosis and therapy, have not been substantiated. Wilder ascribes the failure to confirm as due to:

1. "It is incorrect that in the usual investigation there is one characteristic reaction of an individual with atropine, adrenalin,

pilocarpine, and indeed one is not concerned here simply with a difference in amount but also with a difference in quality (type) in one and the same individual.

2. "With the strictest maintenance of conditions in a series of studies, with a fixation of conditions more rigidly than has previously been attempted according to the literature, one cannot obtain individually constant reactions."

The doses of the drugs employed were 1 mg. of atropine and adrenalin and 1 eg. of pilocarpine. In the report under discussion quantitative studies in the pulse and blood pressure curves were obtained. The values obtained after resting are considered as 0 values, above or below plus or minus respectively. Duration of an effect is attaining more significance in pharmacology and the duration of action has the same significance as the amount. It was noted that different curves could be obtained and these results could be formulated in a rule: "The higher the initial value, the slighter the tendency to an increase and the more marked the tendency to a fall and reverse" so that with all three drugs (adrenalin, pilocarpine, atropine) with a high initial value there were slight increases and marked falls, that is, vagotonic curves; with low initial values sharp increases and only slight falls predominated. These results were obtained in 75% of 128 cases investigated. Furthermore, he was able to demonstrate the following tendency: If two individuals are studied and one has a lower initial value than the other, not only will the first reach the maximum point sooner, but will tend to go beyond it. A search of the literature failed to reveal similar studies except a report by J. Bauer with similar results. Although results are not reported for other parts of the vegetative nervous system, Wilder believes that the rule holds in general. With this he formulates his rule more broadly: "The outcome of a vegetative reaction in any field is—as others have tended to express it—dependent upon the 'state of the organ.' The initial value law now yields a closer approximation of this dependence in that the outcome of a vegetative reaction is primarily dependent upon the already existing state of excitation of the vegetative nerves, that is, the grade of activity of the vegetative organs in the following sense: the higher the grade of activity present before the introduction of the stimulus, the less the stimulating and the more the depressing aspects of the reaction. But if the state of excitation reaches a high grade, then in consequence to the existence of an antagonistically acting system, with stimulating agents, 'paradox' reactions occur and when there is only slight activity, paradoxical reactions are noted with depressing agents." As Wilder stresses, this "lawfulness" is not constant since there are other laws of which this one is

but a part. Wilder makes the following suggestions: from clinical experience there are individuals with bradycardia and low blood pressure in which the vagus is found stimulated and the condition considered vagotonia in the sense of Eppinger and Hess. In this instance adrenalin gives (opposite to the idea of Eppinger and Hess) not a vagotonic reaction but a strong sympatheticotonic reaction. That is, a man presents the symptoms of vagotonia, or at least the bradycardia may be interpreted as vagus excitation, and although he should have a vagotonic curve a sympatheticotonic is found. Furthermore, that the moment a normal pulse is obtained, adrenalin will then produce a vagotonic in place of sympatheticotonic reaction in him. He likewise suggests a difference between the excitation of a nerve and the excitability. In other words: the higher the state of excitation of a nerve, the less its sensitivity to stimulating and the greater its sensitivity to depressing stimuli.

This discussion naturally turns back to the old Pflüger law of electrotonus: if an electrical current flows through a nerve and a chemical stimulus is interpolated, an interference point is formed between the anode and cathode. Toward the anode the excitability is reduced, toward the cathode increased.

Wilder hopes to explain many things by his rule. Obviously here is an explanation for the fact that one and the same individual may react differently to the same dose of a drug in successive studies. It will also help to explain the "independence from dose" in vascular reflexes, the law of vasoneurosis. It will also assist in understanding the effect of "small doses," whereby adrenalin lowers increased blood pressure. It will assist in explaining biphasic effects which are so common in vegetative reactions. Thus: 1 mg. adrenalin provokes in time unit A an increase in blood pressure of x_1 above the original value. Adrenalin now present in the body will now find a higher initial value (original + x_1) and its action will be weaker. This will be repeated from time unit to time unit until a maximum is reached and then the adrenalin begins to act paradoxically. Now in place of rise in blood pressure, a fall occurs. These thoughts lead to a further consideration of so-called cumulative effect. Thus atropine is commonly employed in the treatment of vagotonia. It is supposed to depress the vagus endings. If the case is treated with 1 mg. of atropine daily, the vagus may be stimulated more and more through a summation of atropine action. Atropine will stimulate or depress the vagus according to the status of the tissue. This rule would also explain why an adrenalectomized animal reacts more strongly to adrenalin than a normal animal since the blood pressure is lower in the first. If vessels are narrowed by adrenalin, atropine

dilates. The rule may explain why pituitrin raises the blood pressure particularly in Addison's disease. The cardiac slowing in paroxysmal tachycardia and Basedow's are also to be explained in a similar way. Pituitrin increases the blood sugar, but lowers adrenalin hyperglycemia; the same holds for caffeine, paraldehyde, antipyrin, quinine, etc., in place of pituitrin. The work of Bang has shown the ease with which a starved rabbit reacts with hyperglycemia, and Staub and associates have shown the same for man. Adrenalin, which increases the blood sugar of normals, has no effect or decreases it in diabetics. Insulin acts more strongly in diabetics than in normals, and Pollak has shown that successive doses of insulin within 120 minutes act increasingly weaker. Wilder was able to secure "paradox" effects of adrenalin on the blood sugar in diabetics. The same holds in regard to calcium metabolism. It is well known that parathormone injections raise the level of calcium in the blood. If parathormone is used to elevate the amount of calcium, the lower the original value, the greater the rise; more accurately, parathormone raises calcium more when calcium is lower than normal and parathormone lowers high blood calcium. Furthermore if the amount of calcium is high after parathormone, the injection of more will lower the calcium value. Likewise parathormone after calcium injections lowers blood calcium.

The same general observations can be made in regard to diuresis. Pituitrin, which so markedly depresses the output of urine in diabetes insipidus, is a diuretic in reflex anuria. It depresses diuresis in animals given fluid, and increases it in thirsty animals. Gaisböck has shown that adrenalin acts like pituitrin on urine excretion. Trendelenburg has reported the same effects from pituitrin on chloride metabolism. Moreover, it is well known that the antipyretics lower temperature more in the febrile than in the normal. On the other hand, hot air apparatus does not affect temperature or lowers it. Thyreiodin increases temperature in the hibernating hedgehog when the temperature has been lowered. The example of iodine is especially instructive. Several writers have shown that thyroxin can increase the metabolism up to 60%. Beyond this it often lowers metabolism. Further thyroxin which so markedly raises lowered metabolisms has little effect upon normal values. It may increase it slightly and temporarily and then acts no further. In this way the so-called paradox effect of thyreiodin in Basedow's disease is to be explained. Iodine, which markedly helps cretins, has little effect upon the normal and also helps in Basedow's disease. Then too it is clear that Lugol's solution is an excellent preoperative measure (for about one week)

but later may lead to an aggravation. Exact estimations of the metabolism as performed by Thomson, suggested the correctness of Wilder's conclusions: Iodine acts favorably as long as the metabolism is considerably increased. If the metabolism reaches a certain grade which is individually different, then iodine effect is reversed and the metabolism is increased. Also in this way Wilder would explain why minimal doses of iodine may provoke thyreotoxic symptoms while other cases with cardio-vascular symptoms show no aggravation.

Passing to the consideration of single organs, the heart is an excellent example of parasympathetic-sympathetic antagonism. In paroxysmal tachycardia, atropine and adrenalin which should increase the pulse rate, actually cause a reduction thereof. Digitalis works, as is well known, on the previously weakened heart and camphor reduces the pulse rate only in auricular fibrillation. In this way paroxysmal tachycardia and auricular fibrillation can be considered as high grade tachycardias, whereby drugs which should increase the pulse rate act paradoxically. The same holds for the pupil. After section of the sympathetic, adrenalin works more strongly instead of more weakly. Both adrenalin and ergotoxin affect tonic contraction of the uterus. But if one gives the first agent and follows with the second, the second has no effect or acts paradoxically. The same holds for yohimbin, quinine, hydrastin, etc. The same also holds for the stomach. In a case of hemihydrosis an interesting effect was reported. On the side which was not perspiring pilocarpine acted strongly, on the sweating side weakly. Bronchial asthma is supposed to be classical example of a vagal neurosis. Pharmacologic reactions here as a rule show a vagotonia. The cases which react sympatheticotonic are those with low original values of the blood pressure. Furthermore adrenalin scarcely affects normal bronchi, but markedly widens the contracted tubes. Essential hypertension is also supposed to be due to vagus irritation, according to the adrenalin blood pressure curves. But why should vagus irritation lead to hypertension, except on the basis of the initial value rule? The same rule has been observed in the actions of surviving organs. The isolated uterus is a more sensitive organ than the uterus in situ, because isolation involves section of the pre- and post ganglionic fibers, which increases irritability. Caffeine markedly accelerates the isolated heart, the isolated rabbit ear shows narrowing of the vessels in the smallest doses of adrenalin, and isolated vessel strips react to adrenalin in amounts of 0.00000000000000000001. Pituitrin is active only on the isolated frog kidney (Trendelenburg). Innumerable other examples could be cited. In summary then: "the

first part of the initial value law: the decrease of stimulating effects, the increase of depressing effects with a high initial value and the reverse is a property of the cell itself, a general biologic property."

As yet pharmacology has but little time to become acquainted with the Wilder rule. It implies one of the difficulties intrinsic to the application of the Arndt-Schulz principle, in that while dose is a very important factor, it is not the exclusive one.

After twenty years of investigation of the vegetative nervous system, Danielopolu² has recently reported his conclusions, many of which are related to the topic under discussion. For example, his "law" of predominance has many points of similarity with Wilder's initial value law. His experiments have convinced him that all substances and reflexes involving the vegetative nervous system are amphotropic. The law of predominance is concerned with the factors which determine the dominance of one action or the other. For example, a predominance of action on the sympathetic or parasympathetic will depend upon:

1. The intensity of action of the exciting factor. A small dose of adrenalin is amphotropic with predominance on the parasympathetic, a large dose is amphotropic with sympathetic predominance. A weak excitation of the carotid sinus produces a reflex which predominates on one group, while strong excitation produces a reflex predominating on the other. Although these results may be obtained in the healthy they are studied more easily in the presence of pathology.

2. The general vegetative tonus. The amphotropic factor predominates more on the sympathetic or the parasympathetic when the tonus of the first or second group is elevated. Example: if one injects a small dose of eserine, it is chiefly the parasympathetic tonus which is elevated. The amphotropic oculo-cardiac reflex will now produce more marked slowing of the heart than before the injection of eserine. An intermediate dose of adrenalin in a vagotonic will produce predominantly parasympathetic effects, in the sympathetonic, predominantly sympathetic effects.

3. According to the state of local tonus in the organ. The amphotropic factor will predominate more on the excitatory group when the local tonus is elevated, more on the inhibitory group when the local tonus is diminished. Example: a balloon connected with an apparatus for recording is introduced into the lower part of the esophagus. Pressure on the eyes produces what is known as the oculo-esophageal reflex. If the balloon is slightly distended so that it scarcely stimulates the wall of the esophagus, an oculo-esophageal reflex will reveal a marked phase of inhibition, followed

by a slight phase of excitation which is often lacking. If the esophageal balloon is strongly distended so that the wall of the esophagus is excited, then ocular compression does not produce the inhibitory phase, but that of excitation alone.

Limitations of space do not permit discussion of his laws of amphotropism, etc., but allusion should be made to his remarks on modifications of vegetative tonus. Eppinger and Hess have described syndromes of vagotonia and sympathicotonia, in short, predominance of one or the other divisions of the autonomic nervous system. Clinical and animal experimental investigations have served to convince Danielopolu that this division is not valid. He classifies the modifications as follows:

1. General Modifications.

Vegetative hypertonia

Amphotonia

Vagotonia

Sympathicotonia

Vegetative hypotonia

Hypoamphotonia

Hypovagotonia

Hyposympathicotonia

Mixed States

With hypertonia of one group and hypotonia of the antagonistic group.

2. Local Modifications

From lesions of the organ.

From lesions of the centrifugal vegetative pathways.

From lesions of the centripetal vegetative pathways.

From lesions of the centers.

Perhaps these remarks will be sufficient to emphasize the importance of the state of the tissue or organ in determining the drug effect. This should also make clear why the Arndt-Schulz rule does not formulate the entire situation, although many of these observations fall into line when it is recalled that Schulz emphasized: "but it is entirely individual as to what constitutes small and large." If the relativity of these conceptions is borne in mind the Wilder conception and the Danielopolu investigations harmonize with each other and with the Arndt-Schulz rule. However, as emphasized at the beginning, both viewpoints are somewhat one-sided, one emphasizing the importance of dose, the other the importance of the state of the tissue.

The work of Danielopolu is also interesting in regard to its emphasis on the need for investigation of the effects of various doses on the human organism. For example, it is generally held that atropine paralyzes the parasympathetic nerve endings and that stimulation has not been encountered in animal experimenta-

tion. Danielopolu reports (vol. I, p. 91) in regard to this drug: "investigations which we have made on man (heart, vessels, digestive canal, etc.) have shown us that small doses of atropine excite the two antagonistic groups and chiefly the parasympathetic, while large doses paralyze both groups, but chiefly the parasympathetic. Of the two actions on the parasympathetic and sympathetic, the action on the parasympathetic (excitation with small doses and paralysis with large) is the one which is important. The action on the sympathetic is negligible in the normal subject." He proceeds then to comment on how this viewpoint combined with a knowledge of the importance of organ variations will clarify atropine effects which are now very obscure. The same idea finds emphasis elsewhere (vol. II, p. 95).

In conclusion the dose is very important in determining the drug effect, as reversal of action in the sense of the Arndt-Schulz rule can be demonstrated quite easily with variation of dose alone. It is not the exclusively important factor, for the status of the tissue may determine whether a given dose is large or small. Again reversal of actions may be obtained by varying the state of the tissue while keeping the dose "constant."

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A NOTE ON PHASE EFFECTS.—Before turning to the conception which reflects the present status of the posology problem, it seems advisable to pause briefly for reference to a closely related subject, namely, phase effects. This discussion not only supplements some of the remarks previously made but also will serve as an introduction to the Kötschau rule of typical effects. At the same time stress will be placed upon the futility of speaking of the effect of a drug, as if the dose, the condition of the tissue, etc., had no importance in determining the response. As the writer has made a detailed account of phase effects available,¹ no exhaustive discussion is necessary here.

If the drugs belonging to the cocaine series are studied in reference to their action upon the blood vessels of the frog, the various members can be arranged in the series from the "vaso-dilating" stovaine to the biphasic (initial constriction and subsequent dilatation) cocaine and the "vaso-constricting" alypin.

The above arrangement has validity only when the drugs are employed in dilutions of 1:1000. With some members the action is quantitatively different with various dilutions, a solution of 1:20,000 producing a similar but weaker effect than 1:100. On the other hand some members, for example, eucaine, will display the constricting influence weakly in dilute solution; dilute solutions of psicaine are usually dilating but at times constriction may be observed.

When perfusion experiments are permitted to continue until the vessels return to their normal caliber and then the drug is washed out with Göthlin's solution, exactly reversed effects are noted. Alypin which was a "pure" constrictor now causes pure "dilatation"; psicaine which was a "pure dilator" now only produces constriction. The "release" vasodilatation effect of alypin is greater than its "entrance" vaso-constriction.

The importance of the state of the tissue is likewise evident from studies made with different concentrations of the same drug. For example, alypin 1:4000 applied to the normal vessel causes vaso-constriction. But if this concentration, applied after a solution of 1:2000 alypin, has produced vaso-constriction, then 1:4000 causes vaso-dilatation. These transient, often reversely directed effects, in spite of unaltered continuation of the stimulus, produced by various interferences, regardless of whether they are evoked by a poison, its washing out or otherwise are termed phase effects. A few points relative to phase action may be briefly mentioned.

Phase effects have been found in all isolated smooth muscle organs which have been studied for such responses. The following common objects of study have displayed them:

Rabbit heart ²	Cat heart ¹⁴
" kidney ³	" intestine ¹⁵
" mesenteric vessels ¹	" uterus ¹
" cutaneous muscles ⁴	Frog liver ¹⁶
" intestine ⁵	" lung ¹⁷
" ear ⁶	" vessels ¹⁸
" uterus ⁷	" heart ¹⁹
" coronary vessels ⁸	" stomach ²⁰
" brain vessels ⁹	Dog kidney ⁴
Beef subclavian ¹⁰	Pike brain vessels ²
" bronchial muscle ¹¹	Guinea pig uterus ²¹
" carotid ¹²	" " heart ²²
" adrenal ¹³	Toad heart ²³
Cat kidney ⁴	Turtle heart ²¹

It would be possible to compile a list containing innumerable examples of substances capable of producing phase actions on smooth muscle organs. The following list is suggestive:

Adrenalin ²⁵	Ephedrine ¹⁷	Potassium bromide ⁵⁹
Alcohol ²⁶	Ergotamine ⁴⁵	" chloride ⁶⁰
Ammonium salts ²⁷	Ether ¹⁶	" nitrate ⁵⁹
Aniline ²⁸	Guanidine ¹⁷	Pyrocatechin ⁶¹
Anions ²⁹	Hedonal ⁴⁸	Quinine ⁶²
Antipyrine ¹	Histamine ⁴⁹	Salicylic acid ³
Arecoline ³⁰	Histidine ⁵⁰	Sodium chloride ⁶¹
Atropine ²⁵	Hydrastis ⁴⁵	" succinate ⁶¹
Barium chloride ²	H-ion conc. ²⁹	" hydroxide ⁶⁵
Bitter substances ³¹	Lithium chloride ⁵¹	Sparteine ⁶⁶
Caffeine ³²	Lobeline ⁵²	Strophanthin ⁶⁷
Calcium ³³	Magnesium chloride ¹⁷	Strychnine ⁶⁸
Camphor ³¹	Mammary fluid ⁵³	Sugar ⁶⁹
Casein ³⁵	Mistletoe ⁵¹	Testicular ext. ⁷⁰
Cations ³⁶	Morphine ⁹	Thyroid ext. ⁷¹
Chloral hydrate ³⁷	Muscarine ²⁵	Tyramine ⁵
Chloroform ³⁵	Nicotine ⁹	Uranium nitrate ⁷²
Cholesterin ³⁹	Phloridizin ⁵⁵	Urea ⁷³
Choline, acetylcholine ¹⁰	Phyryn ²	Urethane ⁷⁴
Cocaine group ⁴¹	Physostigmine ⁵⁶	Ventricular ext. ⁷⁵
Convallamarin ⁴²	Pilocarpine ⁵⁷	Veratrin ⁷⁶
Digitalis group ⁴³	Pituglandol ¹	Veronal et al. ⁷⁷
Diphtheria toxin ⁴¹	Pituitrin ⁵⁸	

One may repeat, what another has said after prolonged study of this field: there are scarcely any materials left which have not been found to have phase effects.⁷⁸ As implied earlier phase effects may be secured only on washing out. "Every alteration in the caliber of a vessel by an agent, later on is followed by a distinct compensatory one in the opposite direction."⁷⁹ A substance with a known phase action on washing out, may not display it on a given organ with the present technique.⁷⁸

In regard to the explanations for phase effects, it may be said that many theories have been proposed, all of them unsatisfactory. Among the prominent are the "water changing effect theory"⁸⁰ and so-called "detoxification stimulation."⁸⁰ This subject has interested, up to the present, only a small number of investigators so that the results as yet available are not sufficient to formulate a final opinion as to the nature of these effects. For example, strophanthin constricts the ear vessels as well as those of the kidney. On washing out, the former are constricted still farther, the latter are dilated. The washing out effect may be as strong as, or stronger than, the initial effects,^{58, 77, 81, 82, 83} in fact, some drugs show effects only on washing out.^{65, 81, 83, 84, 85} The phases may be opposite to the original action⁸⁶ or the washing out effect may be a reversal.^{9, 38} The phase may last seconds,⁸⁷ minutes¹ or hours.⁸⁸

Usually only two phases are seen,⁸⁹ but there may be three,⁹⁰ four, five or more.⁹¹

Phases can be produced by suddenly changing the concentration of the drug⁹² or the initial concentration of the poison. *The improvement phases are produced with minute doses.* Many substances have a critical concentration at which the phase effect is produced.

It is possible to influence artificially phase effects by means of drugs.

As a summary of these observations the following general statements may be made: phase effects can be produced in a wide variety of smooth muscle organs. The phase may be similarly directed as the poison phase, or opposite; but is constant for given drugs on given organs. Among the conditions favorable for the production are the state of the tissue (fatigued organs showing them nicely), the kind of tissue, the time of year,⁹¹ the concentration of the poison, the suddenness of change. The effect of the phase may be momentary or permanent; there may be any number of phases.

It may be well to add that phase effects have been observed with practically every substance on practically every function of the body. The following is a list of some of the drugs or stimuli and some of the functions influenced.

Acids ⁹³	Ethyl chlor. ¹¹⁹	Picrotoxin ¹⁴⁵
Adrenalin ⁹¹	Fat ¹²⁰	Pilocarpine ¹⁴⁶
Alcohol ⁹⁵	Food intake ¹²¹	Potassium cyanide ¹⁴⁷
Alkalies ⁹⁶	Guaiacol ¹²²	Psychic influences ¹⁴⁸
Amyl nitrite ⁹⁷	Guanidine ¹²³	Purin deriv. ¹⁴⁹
Apomorphine ⁹⁸	Hunger ¹²⁴	Quinine ¹⁵⁰
Atropine ⁹⁹	Hypophysis ¹²⁵	Roentgen rays ¹⁵¹
Atmospheric press. ¹⁰⁰	Hydrocyanic acid ¹²⁶	Salmiac ¹⁵²
Bile ¹⁰¹	Infections ¹²⁷	Sera ¹⁵³
Bitter substances ¹⁰²	Iron saccharate ¹²⁸	Sodium chloride ¹⁵⁴
Bleeding ¹⁰³	Insulin ¹²⁹	Sodium iodide ¹⁵⁵
Calcium chloride ¹⁰⁴	Light ¹³⁰	Sodium citrate ¹⁵⁶
Camphor ¹⁰⁵	Lipoids ¹³¹	Solaesthin ¹⁵⁷
Carbon dioxide ¹⁰⁶	Lobeline ¹³²	Somnifen ¹⁵⁸
Carbon monoxide ³⁸	Luminal ¹⁰⁸	Strontium ¹⁵⁹
Chloral hydrate ¹⁰⁷	Meat ext. ¹³³	Strophanthin ¹⁶⁰
Chloretone ¹⁰⁸	Mechanical stim. ¹³¹	Suffocation ¹⁶¹
Chloroform ¹⁰⁹	Mineral water ¹³⁵	Sugar ¹⁶²
Choline ¹¹⁰	Mistletoe ¹³⁶	Temperature ¹⁷³
Cocaine group ¹¹¹	Morphine ¹³⁷	Thyroxin ¹⁶⁴
Collargol ¹¹²	Nicotine ¹³⁸	Tear gland ¹⁶⁵
Digitalis group ¹¹³	Novasurol ¹³⁹	Trypsin ¹⁶⁶
Eel poison ¹¹⁴	Organ ext. ¹⁴⁰	Urethane ¹⁶⁷
Ektebin ¹¹⁵	Papaverine ¹⁴¹	Urea ¹⁶⁸
Electrical Stim. ¹¹⁶	Phenol ¹⁴²	Venesection ¹⁶⁹
Ephedrine ¹¹⁷	Phosphates ¹⁴³	War gases ¹⁷⁰
Ether ¹¹⁸	Physostigmine ¹⁴⁴	Work ¹⁷¹

Acid-base ¹⁷⁰	Hemoglobin ¹⁷⁹
Agglutination time ¹⁸¹	Kidney volume ²¹⁰
Autonomic nerv. sys. ¹⁸⁹	" excretions ²⁰²
Basal metabolism ²⁰⁰	Labyrinthine reflexes ²²¹
Bile output ²¹⁰	Leucocytes ¹⁸⁰
Blood calcium ¹⁷⁴	Muscle dehydration ¹⁹⁹
" catalase ²¹⁸	" permeability ¹⁷⁷
" chlorides ¹⁸⁴	" phosphoric acid exc. ¹⁷⁷
" cholesterol ²⁰¹	" water intake ²⁰⁷
" coagulation ²¹²	Narcosis ¹⁹⁸
" dilution ¹⁸³	Nerve muscle irrit. ²⁰³
" globulins ²²³	Ocular-cardiac and solar reflexes ²²²
" phosphates ¹⁷⁴	" fluid product ²⁰⁵
" potassium ²⁰⁹	" pressure ¹⁹³
" pressure ¹⁰¹	Pancreatic secretion ¹⁷³
" sedimentation ²²⁴	Process of recognition ²⁰¹
" sugar ¹⁷⁸	Pulse ¹⁹³
" urea ¹⁸²	Pupils ¹⁹²
" uric acid ¹⁸²	Respiration ¹⁹¹
Caecal chronaxie ¹⁹⁷	Respiratory exc. ¹⁷⁵
Carbon dioxide product ²⁰⁸	Reticulo-endothelial sys. ²¹⁴
Cardiac conduction ²⁰⁶	Skin chromatophores ¹⁹⁶
Chorda tympani irrit. ²¹⁵	Taste ²¹³
Co-ordinated movements ²²⁰	Temperature ¹⁹⁵
Erythrocytes ¹⁷⁹	Urinary output ¹⁸⁵
Gastric movements ¹⁸⁷	" solids ¹⁸⁶
" muscles ¹⁸⁸	Vision ²¹⁹
Glandular secretions ²¹¹	

From the above partial list, to which may be added several hundred previously noted, it should appear that there is hardly any poison or other type of stimulus which is not able to produce phase effects, not only upon isolated organs but also upon every function of the organism or the totality of the organism. With this fragmentary survey which is designed merely to show the extent of phase effects and phase producing substances one may pass to the summarizing conception of Kötschau. Then perhaps the problem of the dose may be clearer.

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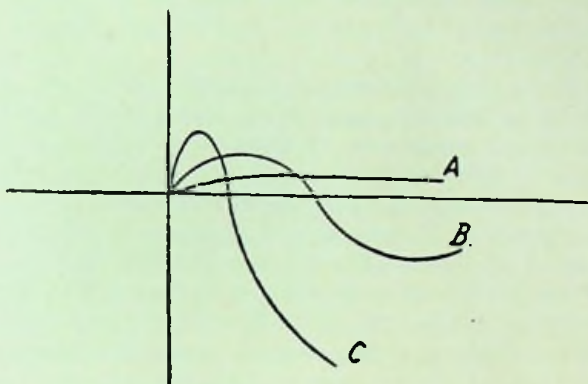
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THE KÖTSCHAU RULE OF TYPICAL EFFECTS.—In his first publication Kötschau depicted the three typical effects of drugs in the following fashion:



In explanation he added;¹ "It has long been known to pharmacology that the effect of every substance upon the organism is determined by two different doses, the minimal doses which begin to have an effect at the threshold of irritability and the maximal dose which is at the upper limit. Nevertheless the minimal dose has not attained any significance to this day. Practical therapeutics recognizes maximal doses almost exclusively and considers its object to be the destruction of disease. For this purpose only the maximal dose can have any significance. This dose is the highest allowable limit for the therapist, for in greater amounts than these, irreversible reactions may take place in the organism. Although there was no practical necessity for a knowledge of minimal doses, this by no means indicates that we do not know anything about them. Looking through textbooks of pharmacology we find them frequently determined in animal experiments. We read that in many cases the effect of small doses differs from that of large doses, not only quantitatively, but qualitatively as well. . . . If therefore the origin of biologic phenomena and particularly those shown on the diagram is dependent upon certain conditions,

it is necessary for us to become acquainted with the latter. The fact that they have not been emphasized as much as they should may be explained by the preference for large doses and their independence from any conditions at all. But the smaller the dose, the more specific its effect and the more its dependence on all possible factors which I shall summarize as follows in so far as they are known:

1. The dose, one of the most essential conditions.

2. The effective agent employed. Most substances have a specific effect, e.g. pilocarpine has a different effect from epinephrine. Heuber and Meier distinguish three types of toxic effects for an organism as primitive as yeast: a) prussic acid type, b) fluoride type, c) silver type.

3. The object upon which the experiment is performed. A uterus is differently affected from an intestine and a gravid uterus differently from a non-gravid one. Organs of a rabbit react in a different manner from those of a guinea pig, to cite only a few examples from among the warm blooded animals.

4. The irritability of the organ or organism in reference to the effective agent employed. The question of irritability is a chapter in itself. It depends upon endogenous and exogenous factors, or constitutional or conditional ones. To one working with isolated organs, it is striking that by means of repeated treatment with a substance, they can become more or less irritable. By this means the effect of the same dose differs fundamentally, not only quantitatively but also qualitatively. Similar changes are known in anaphylaxis and idiosyncrasy. Meyer Gottlieb reports idiosyncrasies with chloral hydrate in which stimulation occurred in place of hypnosis.

5. The medium in which the organ or organisms are contained. Thus Ringer's solution deficient in calcium can fundamentally alter the effect of a substance. Likewise the addition of substances which are more active on surfaces can change the effect of a drug. I recall among other things the reversal of atropine and ergotamine effect on the autonomic nervous system under the influence of substances affecting the capillaries (as described by Ascher and Scheinfinkel).

6. The functional state of the organ or organism at the moment of conducting the experiment, this functional state being studied in relation to whatever exogenous and endogenous factors influence it."

In discussion of the Arndt-Schulz rule Kötschau adds: "Even if it is proved that the Arndt-Schulz law in its widest generaliza-

tion is not valid and therefore had better be designated as a very valuable hypothesis or rule, still it is worthy of note that not even one pharmacologic substance can be found which under some conditions does not have a stimulating effect." As Riesser has said:² "It seems that there is a non-specific increase of muscular irritability which can be evoked by all sorts of substances in small and minimal doses. Apparently the first reaction of every cell to minimal disturbances of its equilibrium is an increase in irritability. Such disturbances can be produced more or less definitely by any given substance, if it is administered in a suitable dose."

There are many important differences in the Arndt-Schulz rule and the Kötschau rule. The most important is the observation of the one factor which is inevitably present in every biologic phenomenon, namely, time. The Arndt-Schulz rule is static, the latter is kinetic. The Arndt-Schulz rule implies a neutral point which must be exceedingly rare if it exists at all, whereas the Kötschau rule eliminates this highly improbable feature. The Arndt-Schulz postulates one effect, the Kötschau rule several. The Arndt-Schulz rule is a rule of dose similar to the Loewe formulation which is mentioned later. The Wilder rule is essentially one concerned with the status of the organ. On the other hand, long before Loewe and Wilder, Kötschau perceived the importance of dose and the status of the tissue, but logically considered them as mere conditions, not deserving exclusive emphasis.

In the explanation of the curves Kötschau adds:³ "If the time element of the course of an effect is represented by an abscissa and the height of the biologic effect by the ordinate, a small dose will produce a weak monophasic effect or irritation (Curve A), a medium dose a double phasic curve with a stronger stimulation at the beginning followed by a reversible depression (Curve B), a strong dose causes a short intensive stimulation (at times absent) and then an irreversible injury or paralysis."

Kötschau fully appreciated that the curves merely represented a schematic representation of the biologic effect, for he added:⁴ "The whole subject is in reality much more complex. From the fact that exactly opposite curves can be obtained in which Curve A appears as a depression, one may conclude that there is also an opposite scheme in which the ordinates give the degree of depression. Besides there are surely more than two phases, and indeed there appear to be later weaker phase fluctuations." This suggestion found confirmation in the work of Rentz.

In regard to the status of the tissue at the moment the stimulus is applied the following remarks are pertinent: "Finally another point which has great significance, namely, the importance of the

condition of the organ at the time the stimulus is applied. If my intestinal preparations were fresh, I was never able to obtain monophasic stimulation of the A type with narcotics, but if the preparation was old or artificially weakened, for instance, by the extraction of oxygen or by a light treatment with urethane, I was able to increase the tonus and waves in the sense of the hypothesis of typical effects by the use of opium alkaloids, as well as by many other narcotics, as alcohol, ether, chloral hydrate, etc."

In another place he has written: "A strongly contracted muscle tends to go into relaxation much sooner than one which is already relaxed and vice versa. And indeed I have observed that an organ or organism reacts more readily according to Curve A the more the observed function has deviated from the normal in the direction which corresponds to the characteristic effects of the drug under consideration. To use a typical example, the stimulating effect of papaverine on the intestine or leech muscle can be most convincingly demonstrated if the organ has been previously fatigued either through asphyxiation, exhaustion or by adrenalin or urethane; all measures which parallel the characteristically inhibitory action of papaverine. Similarly the depression of the tonus of the leech muscle by morphine can be best demonstrated when the tonus of the muscle is originally high, which corresponds to the characteristic stimulating action of morphine on smooth muscle. Zih reported a similar observation at the Congress of physiologists at Frankfurt in 1927. He found that spleen extract in small doses produced an increase in the erythrocytes and large doses a decrease. Nevertheless in the case of animals, with less than six million erythrocytes per cubic millimeter, he almost always noted an increase in their number; while in animals with more than six million he always noted a decrease. Rona and Grassheim,⁵ observed that the respiration of yeast can be increased by small doses of quinine only when the yeasts have been depressed by unfavorable conditions of life. We see therefore that a change in the normal functional state is one of the preliminary conditions which are standard although not absolutely necessary for the performance of an effect according to my diagram. Consequently I believe that I will be shortly able to establish the following: *under suitable conditions the possibility exists of causing a not irreversible functional change to return to normal (in the sense of Curve A) by means of small doses of those substances particularly those whose characteristic and chief effect in large doses would have aggravated the already changed functional state.*" In a footnote he adds: "R. Gottlieb states: 'Experience with other smooth muscles leads us to conjecture that the effect of stimuli which promote

and inhibit contraction depends in a large measure upon the state of the organ involved, i.e., upon the tonus prevalent in its musculature.⁶ Saito has also shown that the effect of HCl on the leech muscle preparation depends upon the tone of the muscle. If it is high to begin with, then the acid regularly causes relaxation; while if it is low, it causes contraction.⁷

Thus according to Kötschau's views: medicine is concerned with the question of bringing a function which is no longer working at its optimum back to normal. The agreement of this view with the writer's definition of the simile is clearly recognizable. One also will perceive that with his rule the entire question of small doses is changed to the question of adequate and physiologic effects.

It is important to note that the Kötschau rule is a description of observations and comparisons, and thus arrangement into a formulation. It merely states what happens under the conditions of the experiment. It represents a so-called "what" question in biology. It explains nothing and has nothing to do with causal analysis. In causal analysis one leaves biology because partial causes which are known are substituted for the total causes or total conditions. By consideration of isolated single factors, one neglects the totality of the event, for unity is not formed by a summation of the single factors.

Kötschau considers that the defense reaction of the organism leads the changed functional state directly back to normal. This is an A curve. If the defense reaction of the body is too weak, either because of reduction in power of resistance of the organism from internal conditions, or too strong influence of the external factors, then a B curve may arise, the first phase corresponding to the defense of the organism, the second to its defeat. Under certain conditions, for instance in negative energy, the defense is absent (1st phase).⁸ The work of Louros and Scheyer⁹ exemplifies such biologic processes in the reticulo-endothelial system and the study of Lehner and Rajak¹⁰ illustrates them in the field of allergy. The entire question of allergy could be restudied profitably in connection with this rule.

The simile is adapted primarily to A curve therapy and probably operates largely through it. While the "contrarium" usually is employed in connection with the second phase of the B curve or the C curve, it may operate also through the A curve, for example, in the digitalis therapy of some cardiac diseases. In certain forms of heart failure the administration of digitalis is followed by remarkable initial improvement and then in spite of continued therapy there is a change for the worse; instead of considering the possibility that the A curve has been surpassed and

that the B curve is being presented, larger amounts of digitalis or some other agent are added to the therapeutic scheme. Not rarely at this stage cessation of all therapy may result in success, whereas further therapy can easily result in injury.

In surgical anesthesia one operates with the second phase of the B curve of ether. Sufficient amounts of ether are given to produce the contrarium of consciousness. On the other hand, patients who have fainted are often revived by means of small doses of ether in the form of Hoffmann's drops. Here one operates through the first phase of the B or the A curve. The same situation operated to a great extent in the introduction of harmin for the treatment of "lethargic encephalitis." It was introduced on the basis that it lessened the tremor and rigidity of the Parkinsonian syndrome, and there seemed to be little question about the therapeutic efficacy. But Fischl and Schaefer¹¹ state that "certain still to be investigated analogies in the effect of harmin with the encephalitic symptoms in the rabbit on the one hand, on the successful application of harmin alkaloids in the sequels of encephalitis lethargica on the other (suggest that one can) . . . assume an influence on the same function of the central nervous system through the encephalitic virus and the plant bases mentioned." Here again one finds the symptom similarity and the organotropy of the simile of importance. But the most important observation may be easily overlooked. If the simile operates through the first phase of the B curve and so-called contrarium through the second phase of the B curve, they become supplements of each other, parts of a united medicine, in short Hippocratic medicine.

In this way an understanding is gained for the application of many remedies. Calomel was once prescribed extensively for the purpose of disinfecting the intestine, a hope absolutely unjustified. Recently Burgi¹² wrote that intestinal catarrh is associated with increased peristalsis action and is treated with laxative agents. This in reality belongs to the field of the simile. Likewise it is generally acknowledged that the antipyretic treatment of disease has failed, whereas success has been attained with proteins, which produce, among other symptoms, fever. Haffner¹³ has said that here we are concerned with the simile since an infection is treated with an infection and allergy with allergy. The treatment of burns with heat and frozen toes with cold is a confirmed simile therapy, and it is generally appreciated that the contrarium is neither correct nor useful in these cases.

If the B curve were more generally appreciated many disagreements in pharmacology would disappear. Some state that camphor

in small doses has a stimulating effect;¹⁴ Stross and Wiechowski consider camphor as a narcotic; actually, camphor is both.¹⁵

A note may be inserted at this point on the vitamins. In the earlier period of their therapeutic employment, the results approximated A curve therapy. On the other hand, reports are beginning to appear in the literature on the damages produced by hypervitaminosis. Reyher¹⁶ has reported toxic effects from vitamin D on the basis of clinical as well as therapeutic tests. Others have noted with vitamin D that an acidosis is produced¹⁷ and the calcium balance becomes negative¹⁸ and loss of weight and finally death has been reported.¹⁹ These citations merely show that A curves can be converted into B and C curves with ease when the animal is already in a phase state, that is, diseased. However, when the animal is given relatively small doses, but still physiologically effective amounts, the acidosis is reduced and the calcium balance becomes normal with a typical A curve. The work of Reyher and Walkhoff²⁰ as well as that of Seel²¹ is very suggestive as to the ease with which a ricketic patient can reveal the curative first phase of the B curve and then pass into the damaging stage of aggravation and injury from large doses of vitamins.

In a recent publication Pfannenstiel²² has summarized the situation in regard to the significance of vitamins for health. "In the course of these investigations²³ it became evident that overdosage with irradiated ergosterin was able to produce the most severe phenomena of disease, indeed, even rapid death with the picture of cachexia. Apart from the weight disturbance observed by myself, others have demonstrated the calcification effect of larger doses as characteristic." "On the basis of our investigations the presumption gains in probability that vitamin D, which is able to regulate the level of blood phosphorus, when the vitamin is administered in excessive amounts, provokes a phosphorus poisoning. In any case the phosphorus content of the blood increases far above the normal after the administration of larger amounts of vitamin D and in consequence to the increased oxidation in the organism there follows a destruction of the physiologic fat deposits. Simultaneously there proceeds a deposition of calcium bound to phosphorus in the walls of vessels and in the various organs, so that the calcification depicted develops. The doses of vitamin D which act poisonously are approximately 3000 times greater than the doses effective against rickets. The therapeutic index, that is, the border between healing and toxic action, is likewise very large in the case of vitamin D. A danger of vitamin D poisoning exists then only when highly concentrated or pure vitamin D preparations are administered in too large doses or smaller amounts are

administered for too long a time. With the demonstration that the vitamins can be just as poisonous as any other pharmacologic agent which is given in excessive amounts, there is created a task for the pharmacologist, namely, to study in detail the toxic effects of the vitamins. Today where vitamin B₁, A and perhaps C are on their way to find application in medical practice in a highly concentrated form similar to that of D, it may be anticipated that hypervitaminosis will be observed and described with these vitamins."

Actually Drigalski²⁴ has already reported this in reference to vitamin A. "Too little as well as too much vitamin leads to considerable alterations in the organism and can lead to severe disturbances of the biologic equilibrium. It is not improbable that a one-sided heightened introduction of definite vitamins can also aggravate certain diseases. Excessive use of vitamin B complex with an exclusive raw vegetable diet seems, for example, to favor the growth of cancer." Collazo and Rodriguez²⁵ have mentioned bilateral exophthalmus and multiple fractures from fibrous osteodystrophy in conjunction with D hypervitaminosis.

It does not seem too much to say that widespread recognition of these curves can clarify many actions now considered paradoxical or obscure. The case of adrenalin is typical in this respect.

Among the "biphasic" actions of adrenalin the following may be noted: early increase of blood calcium and sugar, decrease in blood potassium and phosphates, later the reverse;^{26, 27} early acidotic, later alkalotic stage;²⁸ hypophosphatemia, then hyperphosphatemia;²⁹ hexophosphoric acid decreases and then increases;³⁰ increase of blood sugar followed by decrease;^{31, 32, 33} in tetanus^{32, 33} and in fever hyperglycemia decreased and second phase predominated; there are also subsequent additional blood sugar phases;³⁴ dilution of blood followed by overcompensation;^{35, 36} hypochloremic phase of blood followed by hyperchloremic stage;³⁵ decrease in blood urea and uric acid followed by an increase;³⁷ erythrocyte, hemoglobin, serum albumin increase followed by decrease;³⁸ lymphocytes increase, polymorphonuclears decrease, then the reverse;³⁹ initial leucocytosis, then leucopenia, then leucocytosis;⁴⁰ agglutination time of blood increased, then shortened, but with small amounts only shortening of time;⁴¹ increased then decreased excretion of phosphoric acid from muscles;⁴² respiratory exchange increased in starved rabbits and then decreased;⁴³ polyuria followed by retardation of salt excretion;⁴⁴ cessation of urinary secretion;⁴⁵ increased and then decreased excretion of urine;⁴⁶ increased sugar and decreased phosphates in thoracic duct lymph, then the reverse;⁴⁷

retardation then augmentation of gastric movements;^{48, 49} stimulation of dog stomach;⁵⁰ in sympatheticotonics it retards the gastric secretion, in vagotonics it augments;⁵¹ it accelerates, slows and then accelerates the dog heart;⁵² increase and then decrease of blood pressure;^{53, 54} decrease, increase and decrease of blood pressure from intravenous injection;⁵⁵ from small doses temporary decrease followed by increase in narcotized animals;⁵⁶ increase, decrease and increase of blood pressure;⁵⁷ paradox pulse and blood pressure effects in vagotonics;^{58, 59, 60} paradoxical effects in diabetes insipidus;⁶¹ constriction then dilatation of the pupils;⁶¹ decreased and then increased and finally decreased intra-ocular pressure;⁶² retardation and then improvement of respiration in warm blooded animals, increased movement and then apnoea in frogs;⁶³ dilute solutions cause rhythmic variations in plant cell respiration, large doses retard⁶⁴ or yield Cheyene-Stokes breathing;⁶⁵ increase and then decrease of the temperature of the brain and liver;⁶⁶ decrease and then increase in brain temperature;⁶⁷ peritoneal temperature decreases and then increases;⁶⁸ increase and then decrease in wheals on skin;⁶⁹ retraction and then expansion of chromatophores;⁷⁰ lengthens and then decreases chronaxie of the caecum;⁷¹ polyphasic actions.⁷²

Adrenalin effects are often dependent upon the tonus; for example, the amount of fall in blood pressure depends upon the tonus: the higher the tonus, the greater the fall,⁷³ adrenalin acts, tonus increasing or tonus decreasing according to the initial tonus of the turtle heart;⁷⁴ the same holds for the stomach of carnivori,⁷⁵ rabbit bladder,⁷⁶ frog blood vessels,^{77, 78} warm blooded heart,⁷⁹ warm blooded vessels,⁸⁰ and pigeon muscle.⁸¹

The effect of adrenalin is often dependent upon the irritability of the sympathetic nervous system, for example, in the eye,^{82, 83, 84} for frog vessels,^{85, 86} muscle of the penis and erector pilae,⁸⁷ uterus⁸⁸ and lid muscles.⁸⁹

Adrenalin effect is also variable according to the environment, for example, the cation and anion content: on the frog blood vessels there is a weakening or reversal according to the calcium content;^{90, 91, 92, 93} others perceive that calcium sensitizes the vessels for adrenalin.^{94, 95}

But the dependence of adrenalin action on calcium also varies with the tissue; an increase of calcium depresses adrenalin effect on the iris;^{96, 97, 98} an increase of calcium increases adrenalin effect on the intestine,^{99, 100, 101, 102} the same obtaining for the uterus.^{101, 102, 103} Calcium excess reverses certain depressing actions into stimulating effects.¹⁰⁴

An absence of potassium depresses adrenalin action on the frog heart, a slight increase promotes it.^{105, 106} A heart brought to standstill by an excess of potassium is revived by adrenalin; a heart brought to standstill by adrenalin is revived by potassium.¹⁰⁷ On the isolated uterus an excess of potassium converts the stimulating action of adrenalin into a depression, a depressing action to stimulating.¹⁰⁸ Barium promotes the stimulating actions of adrenalin on the heart¹⁰⁹ and on the blood vessels,¹¹⁰ but the depressing actions are antagonized on the intestines, bronchi and uterus.^{111, 112} Through metal salts as those of copper the depressing action of adrenalin on the excised intestine is reversed into a stimulation,¹¹³ and organs are made more sensitive to its effect by lead salts.¹¹⁴ Adrenalin effects are stronger in an alkaline medium than in a neutral, but absent in strong alkali or acid;⁹¹ shifting of the reaction from acid to alkaline may reverse the action of adrenalin so that doses which cause narrowing of the vessels now widen.^{75, 115}

Variations of action according to the particular tissues are exemplified by narrowing of the glomerular vessels in frogs,^{116, 117, 118, 119} widening of the vessels of frog adrenal,¹¹⁷ widening of vessels in frog liver,^{120, 121} but narrowing in mesentery.^{122, 123, 124} Strong solutions dilate the vessels of the tongue.^{125, 126, 127} The veins are narrowed.^{128, 129, 130, 131} Adrenalin acts as usual on inflamed vessels at first but the sensitivity decreases with the processes of inflammation.^{132, 133, 134}

Stimulation and depression of the vasomotor center has been reported;^{135, 136} variations of the dilator response of blood vessels is also known from experiments with dilute solutions, prolonged perfusion, and from changes in tonus;^{137, 138, 139} increase of temperature diminishes the constrictor response of vessels to adrenalin or reverses it into dilatation. Denervated ear vessels dilate from doses which constrict the vessels of normal ears;¹⁴⁰ skeletal muscle arteries are dilated by small doses and constricted by large;¹⁴¹ rings of coronary arteries are dilated in most animals but constricted in man;^{142, 143, 144} coronary blood flow is also increased in intact animals;¹⁴⁵ coronary vessel constriction from small doses which do not affect the heart muscle;¹⁴⁶ pulmonary vessels react differently according to the site from which they are taken;¹⁴² constriction¹⁴⁷ as well as dilatation has been reported;¹⁴⁸ in the lungs of reptiles adrenalin dilates vessels in small doses and constricts in large.¹⁴⁹ Cerebral vessels are narrowed and then dilated with small doses;¹⁵⁰ intestinal bleeding is increased and then decreased;¹⁵¹ coagulability of the blood is increased by small doses, retarded by large.¹⁵²

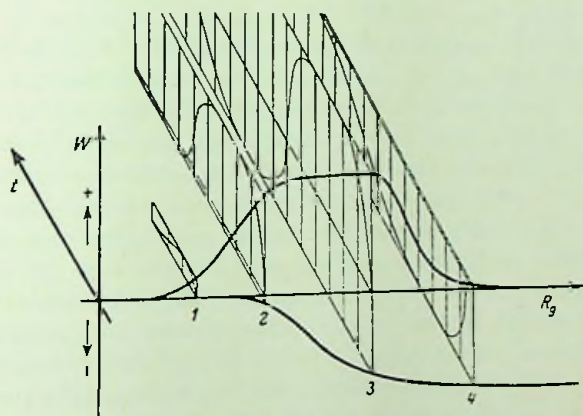
Very dilute solutions depress the heart, larger amounts stimulate,

still larger depress; stimulant concentrations remove the Luciani irregularity, lower concentrations increase it.¹⁵³

In pregnant cats adrenalin produces uterine contractions, in non-pregnant it causes relaxation;¹⁵⁴ pituitrin reverses some of the uterine actions of adrenalin.

Naturally all these results will be further complicated by washing out experiments. When adrenalin causes excitation of the rabbit heart, washing out causes depression;¹⁵⁵ vessel narrowing in rabbit kidney from adrenalin is followed by widening on washing out;¹⁵⁶ increase in tonus of beef subelavian from adrenalin, on the other hand, shows further increase on washing out;^{157, 158} cat intestine depressed by adrenalin, shows excitation or depression on washing out;¹⁵⁹ frog liver vessels widened by adrenalin are narrowed on washing out;¹⁶⁰ coronary vessels widened by adrenalin, show further widening or no effect on washing out;¹⁶¹ rabbit intestine depressed by adrenalin shows washing out excitation;^{162, 163} rabbit ear vessels narrowed by adrenalin show further narrowing on washing out;¹⁶⁴ lessened tonus of frog lung due to adrenalin often shows increased tonus on washing out.¹⁶⁵

The above review naturally represents only a small fraction of the enormous literature dealing with the pharmacology of adrenalin. But even these few citations are sufficient to indicate the need for some valid generalizing formulation, a requirement which seems more vital than the further accumulation of isolated facts. Recently Loewe has attempted to formulate a scheme which would eliminate some of the confusion.¹⁶⁶ His remarks deal with the question of dosage, and the conclusions are summarized in the accompanying bologram.



Skizze nach S. Loewe



He states: "We can now sharply formulate the basic question of the transition of stimulation to depression by means of a consideration of the total bologram surface. If we check the single effect picture from 0 value of the stimulus strength, so in the region of sub-threshold stimulus strength from the effect 0, the bologram surface in this region falls together with the R, t plane. If it is now permitted to increased excitation, in the first step of the bologram where the stimulus strength increases over the absolute stimulus threshold (for example plane 1), there is a monophasic single effect wave and exclusively positive action values may be expected. If we consider planes (for example 4) from the other end of the stimulus degree axis, so that the stimulus strength approaches infinity, then again a monophasic effect picture appears, however a purely depression effect. And indeed between these limits of pure stimulating effects and pure depressing effects lies the transition picture of bi-phasic effects. And it is indeed probable that by a slight stimulus strength only a small wave of depression follows a large stimulation wave (plane 2). Then with increasing C the depression wave can become ever greater (for example plane 3). Then also under conditions the excitation wave can grow still further and by a further increase of C can then diminish. But finally it lessens entirely and at the highest value of C gives way to pure depression."

It will be observed that the curves reported by Loewe are quite identical with those published by Kötschau and also that they tend to support the Arndt-Schulz rule. The difficulty with his presentation is that exclusive attention is directed toward the dose, whereas other factors also play important roles.

A situation not unlike that mentioned in reference to the vitamins will be recalled in connection with the iodine therapy of colloid goiter.

Here as well as elsewhere nature had given a clue in that relatively small amounts of iodine are necessary to maintain iodine balance or to secure an A curve in so-called iodine deficiency. But disregard of these ideas leads to iodized salt, in some places by legal enactment, with the result of more than occasional iodine hyperthyroidism. Thus the A curve is converted into a B, or C curve, which at times leads to marked thyroid syndromes. On the other hand, iodine in Lugol's solution remains the best pre-operative measure for so-called Graves disease and there are not a few who refuse to accept the entity of "toxic adenoma or adenoma with hyperfunction" and employ iodine in this hyperthyroidism.

Kroetz finds that the results in healthy adults after the administration of Vitamine D are opposite to those in ricketic children.

Hottinger reports "the antiricketic factor is able to produce a metabolic change in the healthy similar to the ricketic change."¹⁶⁷ These remarks are interesting in connection with the simile as a finding principle as well as in regard to substitution therapy. Likewise Knipping¹⁶⁸ has shown the reversible effect of iodine in goiter and that small doses may give a monophasic action in hypothyroidism and under certain conditions in hyperthyroidism. In this country the experimental work of Gray and Loeb has the same implication.¹⁶⁹ The same inferences are to be drawn in tetany due to parathyroidectomy where it has been noted that the serum calcium is much more readily changed than in the normal individual and where hypercalcemia may be caused by the oral administration of calcium. Countless other applications are available to the reader, for instance, the entire subject of allergy. Recently attention has been drawn to the use of opium in diabetes. Hirsch¹⁷⁰ has shown a deprivation treatment in diabetes lowers blood sugar when opium is used. Simenauer and Pulver cannot understand this when they note increase in blood sugar in rabbits from opium.¹⁷¹ Hirsch¹⁷⁰ reports a number of authors who have noted decrease in blood sugar in diabetics. All these contradictions are eliminated by the Kötschau rule.

The same ideas obtain in x-ray therapy. The well known C curves which occur in the lethal action of x-ray on cancer cells need no emphasis here. But it has been with considerable difficulty that medicine has been made to realize that there are "stimulative" doses of x-ray which may be valuable in the treatment of anemia, agranulocytic angina, etc. Even now the application of this phase of x-ray therapeutics is receiving but minor attention.

This opportunity should also be grasped to mention the relation of these thoughts to the le Chatelier theorem:

The principle of le Chatelier may be stated as follows: "when a factor determining the equilibrium of a system is altered, the system tends to change in such a way as to oppose and partially annul the alteration in the factor. The same idea is conveyed by saying that every system in equilibrium is conservative or tends to remain unchanged. That is, considering a physical or chemical system in equilibrium, the equilibrium being fixed by the nature of the system and conditions such as temperature and pressure, the principle states that if we alter one of these conditions or parameters, say the temperature, the system will change in such a direction as to annul this change in temperature."¹⁷² Pike¹⁷³ has shown that some of the phenomena of adaptation may be considered as a special case under the theorem of le Chatelier.

Many years ago the writer offered the following suggestion. The simile presupposes that the intrinsic tendency of the organism to maintain a functional norm can be supplemented by stimuli, usually administered in the form of drugs, only small amounts of which are necessary because of hypersensitivity in disease and whose action in these small doses will be directed opposite to that of large amounts because of altered receptivity in disease. The intervening years have brought the Kötschau rule of typical effects, the Wilder initial value rule, Danielopolu's rule of predominance, Loewe's formulation of the dose problem—all of which seem to fit without force into this conception, and have necessitated no change in this programmatic suggestion. Pharmacologic investigations mentioned but not discussed in detail have tended to confirm this impression.

One example may be cited in passing. While studying the effects of the venom of *lachesis trigonocephalus* on the cat, it was noted that the cardiac effects were indistinguishable from those produced by chloral hydrate. This similarity was evident not only in kymographic tracings but also in electrocardiographic studies. In this case a dose of lachesis, insufficient to produce any discernible change in the normal animal, was sufficient to restore normal cardiac rhythm at once in cats whose circulation had been altered by chloral. The implications of this experience will be readily grasped, and not all experiments along this line will be immediately successful. The writer recalls his failures up to the present time to protect animals injected with lethal amounts of tetanus toxin by means of strychnine which has a very similar action. The same may be said of the results obtained in experiments with lethal doses of diphtheria toxin and attempted protection with cyanide of mercury. In view of the fact that the writer failed in his experiments in which the "protective" doses were 1 mg., the following reports of Walbum may not be without interest.

Walbum's initial work dealt with the theoretic presumption that antitoxin forming processes were more or less of enzymatic character and as such they could be promoted or depressed through the action of certain catalytic agents. In short he attempted to stimulate the formation of antitoxin by means of metal salts.¹⁷⁴ He investigated the effect of metal salts on the formation of coligglutinins and diphtheria antitoxin,¹⁷⁵ on the formation of goat blood amboceptor,¹⁷⁶ on the bactericidal substances of the blood,¹⁷⁷ and the lipolytic enzymes of the blood plasma.¹⁷⁸

Early in this work it became apparent that the dose of the injected metal salt played a great role in the effect and that there was an optimal concentration with decreasing action in both directions.

For this reason Walbum soon became aware of the importance of the Arndt-Schulz rule. To show that these considerations had practical importance rabbits were injected with lethal doses of virulent streptococci and 4 of 10 were saved with manganese chloride. When staphylococci were injected all could be saved with manganese. Thus it had been demonstrated that it was possible to increase decidedly the ability of the organism to destroy bacterial toxins. In studying ratin infection, a paratyphoid-like disease to which rats are susceptible, it was noted that certain metals in definite concentrations prolonged life and with some metals (caesium and iridium) the animals were immune. Incidentally if 0.007 milligram of caesium was the optimal dose, a dose either three times as large or one third as great did not save the animal.

In another series of experiments, tuberculosis was produced in 400 animals. Most of the metals were without effect, some gave prolongation of life (gold salts), and some were very successful (aluminium and manganese).¹⁷⁹ The optimal concentration varied with each metal. If the dose was too large, there was a stimulation of bacterial growth and the animal soon died. The therapeutic optimum was found in small doses which do not stimulate bacterial growth. The curves that show the optima of antibody formation and therapeutic activity lie at the same point. Large doses stimulate the growth of the tubercle bacillus on the one hand and decrease the defense processes on the other hand.

Helms¹⁸⁰ tried the method experimentally in the treatment of human tuberculosis with improvement of 16 of 28 cases.

Walbum¹⁸¹ later reported on the ultimate results in the experimental tuberculosis of guinea pigs. Metals without effect or practically no effect were: Li, Rb, Cs, Be, Mg, Ca, Sr, Yt, Si, Ti, Zr, Th, Bi, Te, Cu, Ag, Au, Zn, Hg, In, Tl, Sn, Pb, Cr, U, Mn, Fe, Os, Co, Rh, Ir, Ni, Pd, Pr, Nd, Sm, V. Animals in this group died of typical tuberculosis.

In the second group are Tu, Pt, Er, the animals becoming tuberculous but are cured by continuous treatment.

In the third group the animals showed no signs of tuberculosis; Ba, Al, La, Ce, Se, Cd, Mo, Ru.

Thus 11 metals in certain concentrations show an effect in tuberculosis of guinea pigs. It may be mentioned that group one contains gold and copper which have been employed in human tuberculosis and beryllium and manganese have shown favorable results in tuberculosis of man.¹⁸²

Walbum also tried the effect of combined therapy with vaccine and metal salts.¹⁸¹ It was possible to save animals with both when each alone failed.

Vaccine	Vaccine and Manganese					Manganese				
	0.01	0.003	0.001	0.0003	0.0001	0.01	0.003	0.001	0.0003	0.0001
3.....	5	5	Rec.	6	5	5	4	5	6	5
5.....	6	5	Rec.	5	5	4	5	6	6	5
5.....	5	5	Rec.	4	5	5	7	6	6	6
7.....	5	5	Rec.	8	6	6	8	4	6	5

The animals all received an absolutely lethal dose of ratin bacilli. Treatment was started the second day after, and then repeated daily for four days. The numbers refer to the duration of life after injection. Experimental results of so-called non-specific substances such as caseosan, aolan and yatren-casein showed that none were successful; life could be prolonged with the addition of metal salts, but all died.

Experiments were also arranged to determine the possibility of metal salts in conjunction with serum therapy. Mice were injected with lethal amounts of tetanus toxin. After the symptoms of tetanus appeared anti-tetanic serum and manganese was administered intraperitoneally. Those receiving certain amounts of manganese plus serum recovered by the 10th day. Those receiving either serum alone or manganese alone were dead by the 6th day. Similar experiments were carried out on 80 mice with dysentery with the same general results, animals receiving both recovered, one alone died.

The results of Walbum may be summarized as follows: 1. The concentration of the metal salt used has the greatest significance. There is an optimal concentration with an optimal effect. This effect diminished as the dose increased or diminished. 2. Such doses act by increasing antibody formation. 3. Such small doses may increase the power of the body to decompose or destroy bacterial toxins since animals properly treated survive an otherwise fatal dose of toxin. 4. There is evidence of "specific" effect from non-specific substances. 5. Larger doses of the metal salts apparently activate the bacteria and cause more rapid death.

Another aspect of Walbum's work¹⁸³ is indicated in the table below:

0.0025 mol caesium	10% survived
0.002 " "	27% "
0.0015 " "	74% "
0.0012 " "	95% "
0.001 " "	87% "
0.0005 " "	22% "

In this experiment rabbits were injected with lethal amounts of ratin and treated with caesium. Optimal doses were also found in staphylococcus endotoxin toxemias treated with manganese. The more acute the illness, the greater the necessity of the optimal dose. Similar results were obtained with dysentery though the amount differed from that with other diseases. Similar results were also obtained with experimental diphtheria and tetanus toxin injections. Large amounts of manganese accelerated death. Small doses of manganese averted fatal tuberculin shock. Caesium was both prophylactic and curative in ratin infections.

The time factor is also important, but cannot be discussed here. Another fact may not be fully appreciated and must be emphasized. The reader fully appreciates the immunologic properties of typhoid vaccine in protection against typhoid fever, so-called specific therapy or specific prophylaxis. Naturally this is "isopathic" rather than the simile. But the experiments above show specific immunity from non-specific agents. These observations do not stand alone. Obermeier and Pick¹⁸⁴ have shown increased amounts of precipitins in immunized animals. Heektoen¹⁸⁵ injected serum of other animals into rabbits immunized with horse serum and demonstrated increase in specific antibodies, and Conradi¹⁸⁶ had confirmed this principle in general. Flechseder¹⁸⁷ observed an increase in agglutinins after the injection of albumose, Parlaveccio after nucleins,¹⁸⁸ and Lohr¹⁸⁹ has added the colloidal metals. Incidentally Walbum was also able to demonstrate specific actions of zirconium.¹⁹⁰

Roncali¹⁹¹ long ago showed that animals injected with non-lethal doses of tetanus spores died from acute tetanus when they were subsequently infected by other micro-organisms. This was confirmed by Tarozzi.¹⁹² Francis¹⁹³ and Reymann¹⁹⁴ showed the value of staphylococcus for producing the fatal tetanus. Using these experiments as a basis Walbum showed that manganese treated animals did not develop tetanus although living spores could be demonstrated in the viscera. Extensive experiments¹⁹⁵ were carried out on experimental bovine tuberculosis which cannot be included.

In conclusion a word should be added on the problem of dilution directed more at the question of whether or not doses which have been employed in connection with the simile are capable of producing objectively recordable actions. Here the experiments of Walbum on experimental tar cancer in white mice may be cited.

Experimental cancer in white mice, where the tumor is transplanted, has been treated successfully by a number of measures (trypan blue, adrenalin, choline, cerium), but such transplanted tumors cannot be considered identical with tumors arising in the animal itself.

In these experiments 3-4 month old mice had tar applied between the shoulder blades, 2-3 times a week for 4 months. The animals developing cancer were placed in a special group.

The metals were all tested and the most favorable results obtained with silver nitrate. 16.99 grams of pure silver nitrate was dissolved in 1000 ccm. of water making a 0.1 mol solution. The water was secured from quartz stills. 1 part of the above was added to 9 parts of the vehicle and thus 10^{-2} , 10^{-3} up to 10^{-21} were prepared. As a vehicle 0.9% sodium chloride was employed to make the solution isotonic. With the strongest solutions there was a precipitate of silver chloride, but with 10^{-5} precipitates were no longer obtained. No solution stronger than 10^{-5} was employed. The water of the salt solution was obtained from quartz stills.

The strength of the solutions is naturally only approximate. There is no certainty that the pure sodium chloride did not contain small amounts of silver; there might be adsorption of silver on the walls of the containers. Naturally detectable amounts of silver and other metals in the salt were not discovered. Incidentally it should be mentioned that tar cancer animals usually have a slightly sub-normal temperature.

Mice with proven cancer treated with one or a few injections of 0.1 cc. of 10^{-5} mol silver (that is 1/10,000 of a milligram) show a decrease in the temperature and the animal dies. "In spite of the apparent smallness of the dose, one may still consider it so large that it is able to destroy the defense of the animal, to stimulate the tumor cells and their toxins (perhaps through increased catalysis)." In normal animals a dose 1000 times as large does not produce increase in temperature. But in tumor mice even smaller doses increase the temperature.

"I therefore have endeavored in the treatment of cancer mice to adjust the dosage in such a manner that the temperature of the animal is gradually lifted to the normal level and to keep it there if possible. It has been proven to be of greater advantage to use too small doses than too large, because in the latter case the temperature is subjected to too great variations.

"The experiments have shown that the optimal acting dose of silver as a rule is found between 10^{-11} - 10^{-15} but in some cases it is necessary to go up to 10^{-21} . On the other hand in some cases we could go up to 10^{-7} . Ordinarily the use of the large dose cannot be recommended even if the animal is in the stage of progressive improvement. At any rate I have observed in some cases after injection of 10^{-8} or 10^{-9} into mice a reappearance of the growth, in cases where they had practically disappeared with 10^{-13} - 10^{-16} .

"Of the silver solutions in question, 0.1 cc. were injected at the

base of the tail at 2-5 day intervals subcutaneously. The duration of the treatment varied from 2-4 months. In no case did the tumor disappear in less than 1-1½ months."

Space forbids discussion of the result in detail. 225 cancer mice were used. 136 treated with the metal, 89 controls. In the last 178 mice every other animal was used as a control, although spontaneous cures are extremely rare in tar cancer. Typical carcinoma was proven by excision and microscopic examination. Controls were also established with salt treatment alone (that is saline solution). The cured mice were watched for the duration of life; at death were autopsied and found cured. 10.3% of the silver treated mice recovered. Of the remainder there was a general extension of life over that of the controls.

Walbum concludes: "the optimal effective dose of silver was usually between 10^{-15} - 10^{-11} mol solution. 0.1 ccm. subcutaneously. Large doses, for example, 10^{-5} mol solution, that is, 1/10,000 of a milligram seems to have a favorable effect upon the growth of the tumor and frequently leads to rapid death of the animal."¹⁹⁶

From all this it becomes apparent that the amounts of strychnine and cyanide of mercury employed by the writer were much too large, and experiments ought to be carried out with much smaller dilutions. It is interesting in this connection that small amounts of drugs often may give quite specific responses in the blood of animals. For example, Henshaw working in the writer's laboratory has noted a peculiar "flocculation" of the serum of animals poisoned with diphtheria toxin when the serum placed in contact with dilutions of cyanide of mercury, and this reaction occurs in a greater dilution than with other substances which have been studied, suggesting some relationship between diphtheria toxin and cyanide of mercury. When the rabbits have been infected with staphylococcus aureus in amounts sufficient to produce abscesses, their sera will flocculate with small amounts of sulphur; moreover this reaction is not observed prior to the appearance of suppuration. As this work remains in the preliminary stage it is mentioned merely as suggestive.

It is difficult to summarize briefly the suggestions advanced in these last sections. However a few points may be reiterated for the sake of emphasis. It should be clear that there are no "stimulating" and no "depressing" substances. Any substance may produce either stimulation or depression under certain conditions, among which may be mentioned dose, the tissue, the state of the tissue, the environment, the time. If a function is not irreparably damaged, there is a possibility of returning it to normal in the sense of an A curve. To accomplish this stimuli producing mono-

phasic effects may be employed. Apparently this is effected most easily by small doses of substances whose characteristic, chief, and commonly known action is such that in large doses they would have aggravated the existing situation. The simile states nothing about the effect; in fact there is reason for believing that there may be stimulation of depressed tissues and further stimulation of already excited tissues. In other words there may be a similar or contrarium effect, or both. Some evidence is advanced to suggest that the doses necessary to obtain these effects are smaller than usually employed in pharmacologic investigation, which might be anticipated from the comparative resistance of the organism in health and disease. Likewise some further evidence is advanced in support of the contention advanced earlier that "specific" reactions may be obtained by the employment of "non-specific" stimuli. In so far as a plea is made it represents a request for a study and utilization of all drug effects and not simply those of maximum tolerated doses. This is a request for observations of the conditions under which drugs act, in place of attempts to employ drugs in such amounts that the effect will be independent from the conditions, and the production of polyphasic effects. The alkali therapy of gastric ulcer is a case in point.

Katsch writes:¹⁹⁷ "Alkalies have first a neutralizing effect in the stomach which varies according to their ability to bind acid; second a secretion stimulating effect (Bennett, Lange, Katsch). After the Sippy treatment (about 32 grams of alkali daily) authorities found in 44% of the cases a higher acidity (10-20) than previously, although the patients were without symptoms (Friedenwald, Gault and Morrison, 1924). Vandorfy and Barath¹⁹⁸ report that soda solutions, according to American authors, irritate the gastric mucosa and lead to a "defensive" hyperproduction of gastric juice (Smithies). Small amounts of soda stimulate the secretions, large doses at first depress and then stimulate. Silberstein and Pick¹⁹⁹ found similar conditions which are also cited by Leube, Jaworski, De Mesnik, Geigel and Abend.²⁰⁰ According to Katsch, Pawlow, Cohnheim, and Marshand found that HCl decreased the secretion of gastric juice. Vandorfy²⁰¹ was able to stop HCl secretion in the stomach by acetic acid and Maclean and Griffiths²⁰² report that hydrochloric acid formation in the stomach is automatically controlled by the hydrogen ion concentration."

One should note again that the simile is a finding principle. In the effect, it may cause aggravation and increase of the symptomatology; but the simile may also produce its result by evoking an opposite effect. In the latter instance the opposite is the normal, and to accomplish this the dose must be sufficiently small not to

cause further phase variations. But since it operates through the same means as does the natural healing power of disease, which is increased by it, perhaps it deserves the name biologic healing.

Again the Kötschau rule unites the various therapeutic rules into a heraclitic harmony which not only makes simile and contrarium comprehensible, but places them under one rule, both equally justified and necessary therapeutic rules. It cannot be over-emphasized that Kötschau's formulation is only a rule and not a law and that it cannot be comprehended physico-chemically with the knowledge available.

There are no biologic laws known at present, but only rules which have a practical fruitful application. These rules are based upon experience and collected observation. Of the two therapeutic rules generally known, the simile and contrarium, only the first is discussed here. In one interpretation of the simile, there is an assumption of a natural tendency of the body which maintains a functional mean called health. Deviations of the function mean are considered diseases. Many of these variations are reversible and health can be regained if the disturbances can be removed. In given cases this can be accomplished by assisting the natural healing power, which is done by imitating the phenomena of reaction or healing, the transference of such reactive products to the patient as in passive immunity, and removing obstacles to recovery.

In applying this simile, the selection of a remedy is made by employing the totality of the phenomena of disease as a guide on the one hand and the totality of phenomena produced by the remedy on the other. Therefore one approaches a true causal therapy, and individually specific therapy. This simile includes etiologic considerations, anatomico-pathologic or organotropic considerations, symptomatologic or functional factors as well as prognostic indications.

It is further presumed that in general small doses are stimulating in the sense that under the conditions of disease small doses (the physiologically effective doses) assist in the return to normal without inducing further phase variations. What is small and what large is always an individual question. Furthermore large doses are depressing when applied to the totality of phenomena since they induce further phase variations in the sense of B curves.

The above does not state that all the phenomena of disease are purposeful nor that all are healing. Many of them are direct results of the damage; nor is a given symptom always to be conceived as healing. Fever, so valuable in infections, may be lethal in the hyperthermia of heat insolation. Leucocytosis, so valuable in infectious diseases, may be a preagonal phenomenon of diseases of the

blood forming organs; cough may be a life-saving device or a fruitless reflex starting somewhere in the distribution of the vagus. If nature is infinite it cannot be only wise. But there is the distinct and emphatic suggestion that nature does not err as frequently as the physician has imagined in past eras of medicine. Nor is the physician to become a mere spectator in the treatment of disease. His activity is not simply confined to the removal of damages, but to the stimulation of healing. The task in the treatment of gastric ulcer is not solely the neutralization of the gastric acid, but the initiation of healing in the ulcer. Normal gastric mucosa is not corroded by physiologic strengths of hydrochloric acid. Nor is a blood transfusion which results in a normal blood count a cure for pernicious anemia; nor insulin which restores a normal blood sugar a cure for diabetes. Under hippocratic orientation the indications for assistance are greatly widened, not lessened.

Nor should it be inferred that indications of the shortcoming of the contrarium rule make that rule less valuable. It has been said above that the simile school has nothing to approximate insulin in the treatment of diabetes. The intent is to imply that in all probability the cure of diabetes may be ultimately found in something that stimulates the formation of insulin by the pancreatic tissue or perhaps even the formation of new islands. Again the remarks directed against the large dose should not be misconstrued. If one desired to cause catharsis, castor oil in large amounts and only in large amounts will accomplish this purpose. If one wishes to stop a diarrhoea, large amounts of opium may be necessary. But therein one should not forget that other actions are also possible and that small doses of opium may be efficacious in constipation.

In conclusion then one may reformulate the conception of the "small" dose. With the Arndt-Schulz rule, in so far as that rule is one of dosage, it is the amount necessary to produce the "stimulating effect." More accurately stated it is the amount necessary to produce healing effects, which if exceeded produce damaging actions. With the Kötschau rule of typical effects, it is defined more clearly as the dose necessary to produce the "A" curve. To some extent it is the minimum effective dose in contradistinction to the maximum tolerated dose of the "C" curve.

The actual amount of the drug must necessarily vary with many conditions, among which are: the drug itself, the tissue on which it acts, the size of the dose, the form of preparation of the drug, the state of the tissue on which it acts, the environment in which it finds the tissue, the time, etc.

Finally it is obvious that this dose is one which is comprehensible scientifically, and demonstrable experimentally.

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THE INTERVAL IN THERAPY.—It is probably generally known that in the application of the simile principle, the interval between the doses of the remedy plays an important part in the result. Broadly speaking in the application of the simile relatively large doses repeated at frequent intervals are employed in what may be termed acute diseases and relatively small doses at longer intervals in chronic diseases. Until recent years these observations have remained quite neglected. Through the work of Bier,¹ Zimmer,² and Könniger³ they have been rediscovered for the profession at large.

The opinion of Bier can be summarized as follows: "Personally I realized the significance of the interval at the end of the last century when applying hyperemia. It took me ten years to work out the interval correctly, which at that time I would have subordinated to the Arndt-Schulz rule, but which is better considered separately due to its clearness and importance. Also in my book "Hyperemia as a Curative Remedy," published between 1903-1907, the interval of the application of hyperemia was changed as well as in the application of heat, the congestion bandage, likewise with the absorption apparatus, depending upon the remedy used, the disease and the patient. Finally definite rules were worked out for the time of application and for the interval in respect to the point enumerated.

"In regard to the sun treatment of tuberculosis which at that time was based upon the principle, the more sun the better, I thought, on the contrary, how lucky it was the sun did not shine all the time, and thus one could not yield to the temptation to expose his patients every day to its rays. 'It depends on the reaction which the sun produces as is the case with other allied effects. We know that in other similar phenomena (hot air, congestion, hyperemia, Priessnitz applications, etc.) an interval is necessary in order to allow the reaction to become complete and that a change in the agent is useful.'⁴ The stimulation treatment with injected remedies led every careful observer to the great importance of the interval, as formerly with the treatment with tuberculin. In the

beginning I used intravenous injections of animal blood for infectious diseases, severe boils, in nutritional disturbances, in most cases once a week. And that is too often. In cases of tuberculosis we have a rather certain measure for the frequency of injection. Before repeating one waits as long as the process of improvement continues, which as a rule can be excellently judged by the increase in body weight.

“In the treatment of Basedow’s disease, in applying intravenous injections, we chose an interval of a week between the first two doses and then gave a third injection to those in whom improvement is not obtained or stops.

“In the treatment of rheumatism by the injection of formic acid we wait two to six weeks and often as long as eight weeks until the effect of the first injection becomes evident. Krull⁵ the discoverer of this method stresses the value of not giving the second injection before 10-12 weeks.

“By reading Hahnemann’s work one reads with astonishment that all these things were known to him as a general rule although he made all these observations not with the injection of the so-called foreign bodies where they can be easily observed but with remedies given internally. I quote a few of his expressions in addition to those already quoted from the Organon: ‘to give similar remedies and not to give a second until the effect of the first had passed; this leads to the right path into inner holiness and art.’⁵ ‘Each actual progressive improvement in an acute or chronic case is a condition which, as long as it lasts, excludes any further application of the drug whatsoever. Each new administration of any drug would disturb the improvement.’⁶

“This also holds true for various drugs as well as for the drug last given. Only after the improvement following the administration of the drug ceases should another dose of the same remedy be given or the remedy changed to comply with the new simile.⁷

“Thereby Hahnemann does not insist upon the interval of administration in all diseases and in relation to all drugs. How one should proceed in individual cases must be based upon experience which taught him that in acute diseases more frequent administrations were required than in chronic conditions. In regard to the first, occasionally he went so far as to administer the dose of the same medicine every 1, 2, 4, or 6 hours.

“Hahnemann believed that frequently one single administration of drug is sufficient to cure disease: ‘The disease (frequently even through the first administration of the drug and while during the period of effect of the drug) is neutralized and eliminated without difficulty’⁸ and I thoroughly agree with him. As a splendid exam-

ple of this I refer to acute conditions as bronchitis and in chronic conditions to salvarsan poisoning. I have seen the first healed so quickly and thoroughly after an injection of ether that a second was unnecessary and Richter has described several cases of severe salvarsan poisoning in which a definite improvement and a final healing was obtained.

“While Hahnemann changed his opinion in almost all fields during his life, he remained on a fixed basis as far as the question of the interval is concerned. . . .” (Bier continues to show the importance of the interval in joint diseases, in surgical procedures, etc.)

In regard to Koniger much the same may be said although apparently he does not know the simile. He states:

“The *acute* infectious states usually require a *continuous* polytropic alteration. One can accomplish this most by *rapidly successive* and fairly powerful (increasing) doses of physical or chemical agents in order to obtain a persistent favorable influence over the organism.”⁹ In addition to this continual increase of resistance in acute infectious diseases and other states of hypersensitivity, he describes an intermittent increase of reaction in chronic infections and subacute local diseases. To carry this out one employs “*great intervals and fairly small doses.*”¹⁰

In his very interesting book (p. 96) the late A. Zimmer wrote the following remarks on dose and interval: “The posology plays a decisive role in every irritant therapy. The correct dose always depends upon the existing capacity for reaction of the patient and his focus of disease. Every attempt at schematization must lead to failure. The dosage must be particularly adapted to each patient and controlled by the reaction. This is one reason why all irritant therapy cannot be adopted by physicians who will not habituate themselves to this individualization and who will not devote the necessary time and care to each patient. Still the dosage question does not offer any insurmountable obstacle. As soon as one has accustomed himself to it, it is usually quite easy to ascertain the suitable dose after a short observation of the patient. It is more difficult to determine the approximately correct amount from the start. This requires prolonged experience since the various groups of diseases respond differently. Even the experienced worker will encounter unanticipated accidents. But the danger is not great with a single over-dose but much more in continuous over-dosage. Indeed there is an initially marked reaction which is usually favorable for the course of healing. But it is important to draw the patient’s attention to the expected reaction, since unanticipated increase of pain can easily frighten him with regard to further

treatment. In general we follow the rule to approach with moderate doses the limit at which the patient notices distinct focal reactions or feels tired and "done-up." Then we go below this dose so far that the reaction is scarcely noticeable. One must be particularly careful in arthritis deformans coxae where any distinct local reaction may aggravate the malady for a long time. On the contrary with other joints, for example, the knee, moderate focal reactions are desirable. . . .

"Before a new dose the old reaction should have faded away. If one selects too short an interval, then generally no distinct reaction occurs and with the continuation of treatment the pains gradually become worse. Then one must interrupt the treatment for a longer period and frequently after the decline of this aggravation there is a useful result if the treatment has not been carried out for too long a period. But it is well if one awaits the decline of each single reaction before giving another dose. In acute processes this passes off soon, in chronic cases the pauses must be greater."

Crowe's recent work¹¹ is written entirely around the subject of posology and interval so that it does not lend itself to summarization. A few remarks from it may be of interest in this connection.

"In order to succeed (in the vaccine treatment of the chronic rheumatic diseases)—and let it be understood that the treatment is by no means difficult—all preconceived ideas must be scrapped and totally fresh principles adopted. What happens when a therapeutic vaccine is injected remains entirely unknown and thus the sole basis of a successful method is experience. We have always been taught to follow the method which Koch originally applied in his treatment of tuberculosis with tuberculin, i.e., to increase the dose by considerable fractions (if not double the dose) each time as long as there was no reaction. The object of the treatment was to give as large a dose as the patient could tolerate. In fact, we all received the impression that the bigger the dose, the better the result. Now this method was based upon the fallacy that the blood immunity thus built up, killed off the microbes. Unfortunately however high the blood resistance may be forced, as shown by agglutination, opsonic or bacteriocidal tests, the patient may get steadily worse. The vaccine has probably produced a tolerance to itself and equally to the microbes which may therefore continue to grow unchecked! Whether this is the correct explanation or not, the fact remains that in the rheumatic diseases which in many respects resemble tuberculosis, it is quite possible, in fact easy in some cases, to force the dose above the reaction point, after which the patient gets steadily worse despite all efforts. The principle involved in 'the bigger

the dose, the better the result' is wrong and must be completely discarded . . ." (p. 3). "But never must the first principle be forgotten that the smaller the dose, provided that there is a sufficient response, the better the effect" (p. 33). "In my previous book the general idea was suggested that the size of the dose should be the governing factor in deciding the interval between the doses. This is definitely a wrong principle. An arbitrary interval is inadvisable. The interval must be regulated entirely by the length of time during which response, i.e. improvement, lasts. In other words 'relapse' is the deciding factor" (p. 34).

In this field also one finds medicine becoming interested in a most important therapeutic problem, long a feature of the simile method.

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THE EARLY TELEOLOGICAL CONCEPTION IN MEDICINE.—Although Ostwald and Traube¹ have shown that physical chemistry is not incompatible with simile thinking and the inferences drawn by this method of approach, it has been urged in the earlier part of this work that simile thinking does not thrive in an atmosphere of physico-chemical mechanism. Considerable stress has been placed upon the fact that the simile is most compatible with descriptive and observational methods, namely "what" investigations. Reference was also made to the fact that simile thinking is entirely in harmony with the teleological method of consideration.

It may be well to recall in this connection that although "one may be able to explain the origin and constitution of world systems and heavenly bodies according to the law of mechanical causality he will not be able to explain the smallest organ, a straw, or a grape" (Ernst). Hüber has written in his well known text book: "In spite of all progress not a single one of the fundamental living processes is clearly understood. We are far away from a real

conception of the mechanism of muscular contraction; we have no idea as to what the principle of nerve organization is, etc.; wherever we look the word 'ignoramus' holds true. We see a cloud with its definite irregular shape. We are convinced that this form represents the result of numerous physical forces of certain intensities which act according to definite rules. But since this form is dependent upon temperature, air currents, light rays, electron content of the air, gravitation, and many other factors, it is impossible for us to explain the formation of the individual cloud, that is, to determine quantitatively all the factors concerned in its formation. Only if we subject the water vapor formed in the cloud to an experiment, that is, we keep all the other factors constant with the exception of one which we vary, then only we can speak of a 'law' regularity in the appearance. Just as each organism is a natural phenomenon, a product of numerous forces, it cannot be analyzed, even more, it cannot be approached by experimental investigation since life, in general, is dependent upon microforms, the cells, which are so delicate that we run the danger of destroying them."²

It is possible that the objection may be advanced that it is unscientific to engage in treatment for which there is no explanation. The remarks of Neuburger will be of interest in this connection: "The request to not administer any remedies in disease, when the chemical and mechanical action in the organism is unknown, would be analogous to the request which the scrupulous investigator could ask the physiologist, namely, to withhold foods until their physiologic action on the animal body could be followed in detail. Moreover even the most exact knowledge of the physiologic effect of a remedy could not bring any conclusion in regard to its applicability in disease. For the inner conditions still remain practically unknown to us and those who, with their therapy, wish to wait until these matters are cleared up, can quietly allow their patients to die until the perfection of medicine has arrived. . . . We should be clear about the fact that the modus operandi of not a single remedy in disease is exactly known to us and that all explanations relating to the value of the same finally end in ingenious hypotheses, the value of which cannot be denied for facilitating a comprehensive view and for making an impression on the memory of the student. There is nothing less difficult for the talented man to prove, where necessary, the requisite effectiveness of a medication on physiologic grounds and by the same right, if demanded, to deny it. Therefore if one desires, out of pure ambition to proceed in medicine according to the manner of natural science and not to offend the first rule, then experience must be given its due right and no premature attempt at explanation be made. Certainly

nothing would be more appropriate to the spirit of natural science than to attempt to decide on the usefulness or otherwise of a remedy on purely chemical grounds. . . . Observation at the bedside should be the only deciding factor; therapeutic investigation must be the guiding star of medical action."³

Just as no attempt was made in the discussion of mechanism to penetrate deeply into the philosophical implications, so the following remarks do not pretend to constitute a profound or exhaustive philosophical discussion of teleology. A brief of certain facts which tend to support the contention that the acts of the body are directed towards the realization of a purpose, that is, they are teleological, is all that is intended.

Since teleological considerations are often confused with vitalism, it may be well to mention briefly a few of the more obvious shortcomings of vitalism. At present a neo-vitalism is in the ascendancy, but reflection will reveal that in past decades, like mechanism, it has been too successful. Vitalists once asserted that the organic compounds would never be prepared synthetically, that optically active compounds would never be artificially produced, etc. Just as Loeb once "completely" explained regeneration physico-chemically, as the chemist explains protoplasm as a "sol," the chromosome as a "coagulate," so the vitalist has frequently closed the door to further investigation of problems by an explanation. Perhaps the vitalist has had a more successful explanatory hypothesis than the mechanist since he could immediately assign every unknown to the "vital activity." In short the range of adaptability of the explaining hypothesis was extraordinarily great. Paradoxically it was also very small, for when some vitalistic conceptions are examined more closely, they often shrivel under the microscope. For example Driesch's valuable discussions of the "entelechia" are difficult to grasp. His entelechia morphologica is neither substance, energy, nor constant; it is non-spatial but works in space; it cannot be conceived but is imaginable, etc. His entelechia psychoidea is a something, not a psyche, but can be discussed only by psychological analogies. Viewed from this angle, his system is a system of negations. Much the same holds for many other vitalistic conceptions. How has Reinke advanced the situation by his conception of "dominants" or how are things explained by the assumption of "diaphysical powers"? All these, as explanatory hypotheses, seem to be premature in the absence of more "what" information. The reader will be less liable to misconstrue the import of the following remarks, if he bears in mind that the teleology presented here remains on an observational basis.

Perhaps this may be the place to introduce a few citations

designed to make the heuristic value of the teleologic notion clearer.

"Every phase of activity in a living being must be not only a necessary sequence of some antecedent change in its environment, but must be so adapted to this change as to tend to its neutralization, and so to the survival of the organism. This is what is meant by "adaptation." Not only does it involve the teleological conception that every normal activity must be for the good of the organism but it must also apply to all relations of living things. It must therefore be the guiding principle, not only in physiology . . . but also in the other branches of biology."⁴ "The principle of adaptation is the only formula which will include all the phenomena of living beings and it is difficult to see how this principle can be expressed by means of the concepts of the physicist."⁵

"The purpose of a reflex seems as legitimate and urgent an object for natural inquiry as the purpose of the coloring of an insect or blossom. And the importance to physiology is, that the reflex cannot be really intelligible to the physiologist until he knows its aim."⁶ "We cannot but feel that we do not obtain due profit from the study of any particular type-reflex unless we can discuss its immediate purpose as an adapted act."⁷

"From a consideration of the general characteristics which distinguish a living organism from a machine I had become convinced that a living organism cannot be correctly studied piece by piece separately as the parts the machine can be studied, the working of the whole machine being deduced synthetically from a separate study of each of its parts. A living organism is constantly showing itself to be a self-maintaining whole, and each part must therefore always be behaving as a part of a self-maintaining whole. In the existing knowledge of the physiology of breathing this characteristic could not be clearly traced. The regulation of breathing did not, as represented in the existing theories, appear to be determined in accordance with the requirements of the body as a whole; and for this reason I doubted the correctness of these theories and suspected that errors had arisen through the mistake of not studying the breathing as one of the co-ordinated activities of the whole body. In so far as the investigations detailed in the succeeding chapters originated with me, they were mainly inspired by the considerations just mentioned; and, as will be seen in the sequel, the same considerations have led to a reinvestigation and reinterpretation of other physiological activities beside breathing."⁸

It was only after considerable deliberation these notes on the teleologic conception were included because it is extremely difficult to approach the simile without awareness of the teleologic method

of consideration. At the same time it is fully appreciated that the notes must remain sketchy in outline so that there is considerable danger in being misunderstood. By rigid exclusion of all that pertains to general philosophy, it seems possible to remain within the limits of the work—namely, securing a practical conception of the modern viewpoint of the simile. Naturally mere mention of the word teleology is repugnant to many scientists, and this is particularly true of those who forget that mechanistic causalism, materialism, etc., are likewise only philosophies. The viewpoint assumed here will not be that of teleology versus mechanistic causalism, because they are not mutually exclusive but actually both extremely fruitful methods of consideration. Here as with the simile in general, disagreement with mechanistic causalism holds only for the use of it as the exclusive method; the attitude assumed toward so-called contrarium is not that it is in error, but merely that it is not the only method of procedure.

When one encounters an eye for the first time he may proceed to consider it in various ways; but if he asks for what purpose the eye exists he has already entered the realm of teleology. In one school of philosophy man must see because he has eyes (in the other he has eyes in order to see). In the latter school effect follows cause, for example:

A bag containing a bottle filled with water is thrown over a precipice. The bottle is broken and the bag torn and the water runs out upon the ground. A man is thrown over the same precipice, the skin is torn, the arteries were ruptured and the blood runs out upon the ground. Bones are broken like the flask in the sac. The two events proceed in accordance with mechanistic causalism. But if the events are followed still further, the bag and flask remain in their present status and the water continues to run out as long as gravity continues to act. In the other instance: the circulation is readjusted to assure perfusion of the vital centers rather than to the entire body, the peripheral pressure is lowered, the blood clots, the hemorrhage ceases, the skin and bones undergo repair, fluids are re-distributed to maintain volume of blood, the hemopoietic organs restore the lost cellular constituents, etc. In one series of events blind mechanistic causality acts. In the other a series of purposeful phenomena which are called "defense" phenomena are initiated and teleologically speaking have the purpose of preserving the organism. Purpose is incompatible with mechanistic causalism: effects follow given causes.

Naturally the last presumption is based upon the proposition that equal causes have equal effects, a theory based upon the idea that the equal causes act on equals. For example:

Two mothers stand before a burning building in which their children are being consumed by the flames. The presumption would imply that the two mothers would react in the same way. However the first rushes into the flames at the risk of her own life. The second rushes up and down the street, screaming and finally faints. Not a single move is made to enter the building. This example chosen from the realm of "psychic causality" implies the vast difference in individuals, and that there is a strong reason for believing that equals act upon unequals in biology. To explain this event one might say teleologically: motive gave rise to action. In the first case the instinct of race preservation dominated the individual, while in the second the instinct of self preservation dominated. But these terms are not physico-chemically (mechanistically) comprehensible; teleologically the motive or purpose gave rise to the action which followed. In these two examples are found instances of physical and psychic causality which necessitates another mention of "cause."

Mechanistic causality believes that it can find a cause for biologic events. A paraphrase of an example from Bier may be suggestive in this respect:

A hunter shoots a deer. Modern medical science attempts to investigate the cause of the death of the deer. But it is actually unable to do this. To begin far along in the causal series one may proceed as follows: the hunter sees the deer and gradually approaches it. His advance must be in such a manner that the deer does not know of the approach; there must be no noise, the wind must be in the right direction. Finally the hunter gains a point of about 120 meters and further approach is impossible. To slay the deer at this distance requires a rifle of the latest perfection. This in turn requires a causal series which begins with the discovery of gun-powder and the evolution of guns up to the modern rifle. The gun must be properly aimed, the bullet must be perfectly made; the gun sights correct; the sun must not shine in the hunter's eyes; the deer must be struck in the proper place; there must be the proper co-ordination between the sensory and motor apparatus of the hunter so that the proper perception is followed by the correct motor response at the right moment so that the trigger is pulled. The bullet which modern science calls the cause of the death of the deer is fired. But just at that moment the wind was too strong and the bullet swerved. It is impossible to investigate a causal series completely. In pharmacology at present one attempts to make the bullet so large and the gun so powerful that the wind and other influences cannot successfully act. Whether this intrudes into the field of toxicology and departs from

the field of biology which is the mother science of pharmacology will not be discussed here. At least medicine believes itself able to find the cause of biologic events. (If one desired to approach the cause of the death of the deer in this instance, they might approach it from the standpoint of psychic causality; the will of the hunter was the cause in that it gave rise to the complicated actions resulting in the death of the deer.)

With these preliminary remarks one may turn to the teleologic conception in medicine.

The sole implication of the following remarks is if symptoms or phenomena of disease are purposeful (useful, defensive), then it may seem rational to imitate them; this is the simile in its teleological aspect.

a) The Hippocratic physis: As Hippocrates is credited with the elimination of the theosophic element in medicine, one may begin with his conception of the physis. Without attempting to characterize Hippocratism nor to analyze the various meanings of the word, one may say that the Hippocratic collection is permeated by the doctrine of natural healing. The organism does not only passively receive injuries but attempts to equalize them through self-regulation. Therefore the symptomatic picture is composed of signs of injury and signs of defense. Nature (physis) is the healer of disease.⁹ It is an expression of life and not a special power; it prevails over physiologic processes; it heals diseases; it is unconscious or instinct-like; it is frequently incomplete and must be assisted by the physician. It works purposefully but is based on elemental laws.

"Though nature is unschooled and uninstructed she does what is proper."¹⁰ "Nature finds pathways by herself, not in consequence of deliberation."

If these few expressions are read in connection with the remarks made early in this study on the subject of the physis, little more need be said on this particular problem. The Hippocratic physis is essentially that power which prevails and guides in the healthy organism and also constitutes the natural healing power in disease. However, the word is employed in conjunction with certain related ideas which may be mentioned in passing.

Subordinate to the conception of the physis is the theory of the correct mixture (eucrasia) constituting health, the false mixture (dyscrasia) constituting disease. In the Hippocratic writings innumerable substances contribute to this mixture.¹¹ Of these modern medicine knows the hormones, vitamins, minerals, acid-base, etc. Health then becomes the constantly disturbed and rhythmically established equilibrium and disease the arrhythmic sharply

disturbed equilibrium, both of which tend to be controlled by the physis. The trend of modern investigation in regard to the hormones would seem to support this suggestion.¹² In regard to the previously mentioned "modalities" it is not without interest to note that the correct mixture is supposed to be seasonably affected in the Corpus.¹³ Modern investigations would also tend to confirm this suggestion:¹⁴ "Investigations, carried out with great care, in which the relations between the entire body and heart, liver, kidneys, gastro-intestinal tract, brain, thyroid, hypophysis, spleen, thymus were determined, in all animals revealed certain variations of the relations, that is, the glands were not a constant fraction of the body weight but a variable fraction at various times. Even from this it follows that their activity varies at different times for internal reasons as yet unknown to us. But the most remarkable results appear in the distinct and clear seasonal rhythms of single parts. . . . To cite an example, the group heart, liver, kidneys, brain obtained a maximum in June and October, a minimum in November."¹⁵ It is probable that every living event in the body displays a similar rhythmic activity although medicine as yet knows but a few of the more prominent like menstruation, etc.

All these and many others are subject to the physis for "nothing is without the physis." Among them may be mentioned the constitution, attraction, etc. Each part has its physis, a thought not without interest in connection with the peculiarities of manifestations and course of various diseases, the tendency of tuberculosis to involve only certain bones, the marked variations in the susceptibility of different joints to ankylosis, the peculiar liability of the elbow joint to metaplastic bone formation, the relative rarity of thrombosis in other than the femoral vessels, the tendency of myositis ossificans to involve certain muscles, the rarity of carcinomatous involvement of the spleen, the immunity of skeletal muscle to streptococcus and staphylococcus infection and its susceptibility to gas bacillus infection. The age constitution may be considered in the rarity of embolism in children, and countless other examples. However, sufficient has been said perhaps to indicate the similarity of this conception with the etiologic, anatomic pathologic, functional and prognostic indications employed in conjunction with the simile. It seems, to the writer at least, that a detailed study of the physis conception in the Hippocratic writings would be an extremely fruitful task for a competent physician with adequate philological training. An excellent start has been made in this direction by Bier.

Hippocrates regarded many events of the body as "defensive,"

for example, fever,¹⁶ particularly quartan fever,¹⁷ skin eruptions,¹⁸ etc. Aesclepiades,¹⁹ on the other hand, jeered at the vainly laboring physis. Celsus, like Hippocrates, held that fever serves as a healing agent²⁰ and attempted to produce fever for curative purposes.²¹ The viewpoints of Aretaeus²¹ and Rufus²² are the same.

Galen likewise taught that the physis not only conditioned and regulated the building of the body, nutrition, and growth, but was also the chief factor in the re-establishment of health.²³ The physician may bring the ends of the broken bone together but the physis must effect the healing.²⁴ Alexandros of Tralles regarded diarrhea as a favorable symptom, for the purpose of eliminating spoiled humours, and made no effort to check it unless exhaustion was produced,²⁵ and Palladios went much farther in his high regard for the physis as protecting the body.²⁶ Aetios,²⁷ Judeaus²⁸ and the Arabian School, particularly Rhases and Maimonides²⁹ adopted the natural healing power of nature as a guide in their practices.

Only a few writers in the centuries which followed held these views, at least until the time of Paracelsus. Gilbertus Anglicus³⁰ wished to follow the Hippocratic method, but dared not brave the ridicule of his contemporaries. Arnald de Villanova³¹ thought the physician was the servant of nature, and Petrus Turisanus³² offered the important suggestion, still neglected by many, that drugs do not act directly but indirectly through stimulation of the natural healing power. A few surgeons, for example, Theoderich³³ and Henri de Mondeville, Bruno, etc., were guided by the natural healing power but they represent exceptions.

b) The Paracelsian archeus: Although Galenism was supposed to be founded on the Hippocratic physis, actually it was far removed from supporting *vis medicatrix natura*, and as time passed, it became increasingly remote from the Hippocratic method.

With Paracelsus matters changed once more. The organism was no longer a fixed entity but was characterized by continuous creation and destruction. The parts were independent to some extent, but as a totality it was governed by purposefulness. The alchemist, conditioning the process, was the archeus or internal physician. Disease was regarded as a parasite engrafted on life, a phenomenon which was combated by the archeus or that reaction of the body which makes healing possible. The task of the physician is to support nature through arcanum (drug) therapy or physiatry-hygienic-dietetic). One can produce conditions favorable to healing or may evoke similar processes by drugs.

The following are typical examples of the Paracelsian archeus: "by nature man has drugs against each disease; . . . as he has

the destructor so he has the conservatorem sanitatis."³⁴ If it was not for the internal physician and its natural drugs, "life could not exist in spite of the external physician."³⁴ "Man is his own physician."³⁵ If a disease is in the body so must all healthy parts fight against it."³⁶ Every surgeon should know that it is not he that heals but the balsam in the body that heals."³⁶

Likewise Fernel supported these ideas stating: "The laws of medicine should accord with the laws of nature,"³⁷ but he limits this rule practically to mild diseases.

Fernel's work was important in modifying Galenism and all the more so, since Paracelsus was not understood by his contemporaries. The works of Baïllou³⁸ and Lange³⁹ are based upon support of natural healing. Vallerioli,⁴⁰ who markedly influenced Stahl, regarded nature as the true healer of disease, a viewpoint supported by Trineavella,⁴¹ Caesalpinus,⁴² Mercurialis,⁴³ and Valesius.⁴⁴ For example, the last desired to anticipate the fever produced by nature by artificially evoking it. Naturally among the Paracelsians there were minor disagreements on the definition of nature, but Croll⁴⁵ represents the general viewpoint that only "nature's remedies are the healers of disease."

With the 17th century came endeavors to determine the limits of natural healing and early writers as Smet⁴⁶ and Hoffmann⁴⁷ concluded that some diseases are healed by nature alone, others by the physician alone, and finally a group requiring both, although Hoffmann goes a little farther in stating that medical assistance is of value in so far as it supports nature.

The great Sennert stood close to Galenism by combining extensive drug treatment with a theoretical recognition of nature as a healer.⁴⁸ Santoro⁴⁹ called attention to the fact that in epidemics the untreated recover, while the treated die in large numbers; Primrose⁵⁰ adopted a similar viewpoint.

The literature of this period is also replete with case reports of cure either by nature alone or with assistance by fever,⁵¹ skin eruptions⁵² and other symptoms.

With Helmont new conceptions arrived. The archeus influus is the supreme regulator of events in the organism and it operates in the single parts through the archei insiti. Disease is a composite: not exogenous factors acting upon the body, but morbid ideas of the archeus conditioned by exogenous factors. To defend against these injuries, the archeus becomes "infuriated."⁵³

According to Helmont fever is an instinctive activity of the vital principle against the damage, a view supported by Campanella.⁵⁴ At times the archeus alone is sufficient for healing; at times it requires help. The archeus of Helmont is much more

limited than the physis,⁵⁵ since most diseases are healed through the aid of the physician to nature or by the physician alone. The period is also characterized by several new names for the *archeus*.⁵⁶ Of the more or less forgotten writers Tulpius⁵⁷ contributed much to Hippocratism of that period.

However, the return to the Hippocratic method was largely due to the efforts of Sydenham who regarded nature as the sum of organic reactions proceeding purposefully and automatically.⁵⁸ The healing power is most evident in acute diseases, the necessity of activity of the physician greatest in chronic diseases,⁵⁹ and the efforts of nature are not entirely free from reproach.⁶⁰ Since the latter is true, Sydenham perceives the future of medicine in finding specifics which will eliminate the prolonged and possibly dangerous natural efforts. For him specifics remove the cause of the disease and are exemplified by cinchona in malaria, sarsaparilla, venesection. Fever was the most valuable aid to the natural healing power; therefore cinchona should be given after the febrile attack. In general, "disease is nothing else than an effort of nature, who, with all her power, is producing an extermination of the morbid matter for the patient's welfare."⁶¹ Schneider agreed with the Sydenham viewpoint.⁶²

Willis attributed cures in part to "fermentation" but Sylvius who founded the iatrochemical school denied natural healing power completely.⁶³ His views profoundly influenced medicine since they tended to discard the teleologic viewpoint entirely. Following him to some extent is Bontekoe⁶⁴ who eliminated purposefulness from nature, but conceded some useful manifestations do occur, a concession at which Muys jeered.⁶⁵ Intermediate literature between the Sylvian and Hippocratic viewpoints will be found in writers like Wedel.⁶⁶

Thus the century had witnessed the re-opening of the problem and modification of the basic ideas. The writings of Galileo, Bacon, Cartesius overthrew the Aristotelian world conception, and pure mechanical explanations for biologic events increased. With the discovery of the circulation, the teleologic method seemed finally overthrown. At this time Boyle appeared on the scene and his influence still remains on medicine: he admitted a cosmic purposefulness, but regarded the bodily processes as forced, bound through causal connections and proceeding according to mechanical laws. Thus the term "mechanism" was introduced.⁶⁷

The close of the century is characterized by Schelhammar's support of natural healing⁶⁸ and Sturm's argument favoring Boyle. Bohn⁶⁹ assumed an excellent intermediating role, namely, that medical assistance lies in the support or stimulation of nature

when necessary but also the curbing where advisable. Baglivi⁷⁰ emphasized that if a physician does not obey nature he cannot command her. The century closed with stress upon three trends: the Hippocratic, exemplified by Sydenham, the spiritualistic of Helmont, and the mechanistic.

In the 18th century Boerhaave joined the Hippocratic group and regarded the chief task of the physician as the removal of obstacles which thwarted nature,⁷¹ and fever as the best cause of recovery.⁷² On the other hand, Friedrich Hoffmann viewed the body as a machine,⁷³ and although admitting the natural healing power to some extent⁷⁴ he believed the healing influence of some symptoms was accidental.⁷⁵

G. E. Stahl held that the organism differed fundamentally from a mechanism⁷⁶ and contained a principle which harmonized all the living processes to unity, whereas the body itself constantly tended to disintegrate.⁷⁷ The aim endeavoring management of the body is due to an immaterial principle; fever and inflammation are healing,⁷⁸ as well as hemorrhages, spasms and convulsions.⁷⁹ The endeavors may need correction.⁷⁶ These views found considerable support in Germany⁸⁰ and were opposed by Hoffmann⁸¹ and Leibniz⁸² and others.⁸³ The school of Boerhaave refused to notice the doctrine and von Haller actively fought it.⁸⁴

Gaub,⁸⁵ who wrote the first textbook of pathology, attempted to unite all these trends without becoming a mere eclectic. He offered the opinion that disease was represented by two series of phenomena, one of damage, one of reaction to the damage; in short, he rejected absolute purposefulness.

De Haën was Hippocratic⁸⁶ and opposed the Chirac school of venesection.⁸⁷ Stoll conditionally recognized the healing effect of fever.⁸⁸ Storeck⁸⁹ admitted natural healing and the evil effect of much medication, a view in which Borsicri concurred.⁹⁰

Cullen⁹¹ was tepid in his support of natural healing but was compelled to accept it for his theory of fever, a contradiction for which he was severely criticized.⁹² A new viewpoint arose in Brown's theory⁹³ in which life lacked spontaneity but was forced through stimuli. The ideas of Stahl found accord in France. Sauvages⁹⁴ included some mechanism but Bordeu⁹⁵ renounced this entirely. Barthez⁹⁶ went so far as to introduce another immaterial principle, the vital principle. Pinel⁹⁷ fought in defense of vitalism as did Raymond.⁹⁸ The writings of Gilibert, Vitet, Baldinger,⁹⁹ Hecker,¹⁰⁰ Gall¹⁰¹ are in the same vein.

Another advance came with the work of John Hunter¹⁰² who concluded that inflammation was a work of restoration and thus a reform began in surgery which had been initiated earlier.¹⁰³ By

the end of the century the viewpoints are summarized by Frank,¹⁰⁴ Reil¹⁰⁵ and Hufeland,¹⁰⁶ all of whom adopted the natural healing power.

With the 19th century came the work of Virey in favor of natural healing¹⁰⁷ and Broussais¹⁰⁸ often called the "vampire" because of his propensity for bleeding. The healing influence of skin diseases was much studied.¹⁰⁹ However, the chief advance came from the French school who under Laennec¹¹⁰ taught that the healing of tuberculosis is not beyond nature. Similar views are found in the works of Chomel¹¹¹ and Alison.¹¹² Moreover the studies of Corrigan¹¹³ emphasized that cardiac hypertrophy was a protective mechanism. The major English school followed with similar works on spontaneous arrest of hemorrhage, development of collateral circulation,¹¹⁴ and this opinion found confirmation in the German school.¹¹⁵ On this basis developed the Vienna School in which natural healing was not a special potency¹¹⁶ and did not develop first on the occasion of disease.¹¹⁷ Disease again became a battle between the parasite and the self regulation of the body.¹¹⁸

On the other hand Henle¹¹⁹ turned all his efforts against teleology. Lotze¹²⁰ expressed views which are still quoted.

"When nature builds a system of mass and power, the living body, so homogeneously that it is in a position to maintain its integrity against a certain measure of external disturbances, it does not need, outside of the individual power of the natural field, the instillation of an impossible power for the selection and employment of opposing agents." Rokitansky¹²¹ added enormous pathologic material on the spontaneous arrest of tuberculosis and Skoda's therapeutic nihilism is actually a proclamation for the natural healing power. Dietl said:¹²² "Only nature can heal." Wunderlich considered the task of medicine to be unriddling the "mechanism" of the natural healing process.¹²³

The mere recitation of names in the preceding merely serves to show that the problem of natural healing has been regarded the most important of all therapeutics. Every physician must consciously or unconsciously take a stand on the question. Some have perceived the natural healing principle as dependent upon mechanical functioning of the body, others of power relationships proceeding out of it. Those admitting a single power termed it the *vis medicatrix natura*, others have employed numerous powers. Some believed the principle acted consciously, others unconsciously, some as synonymous with all the manifestations of disease, others as single manifestations, etc.

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PFLÜGER TELEOLOGIC MECHANICS.—The chief work of Pflüger¹ on this subject begins with a statement that the totality of processes in living nature is never in dynamic equilibrium; there appears to be only one working law or viewpoint, which, even if it does not prevail absolutely, it still prevails, and that is: only such combinations of causes appear in reality which are favorable to the welfare of the individual.

He calls attention to the remarkable regeneration of the cystic duct, the regeneration of nerve fibers. He asks what is more remarkable than that the most variable poisons of organic and inorganic origin which bring about alterations in the organism, upon injection into the body bring about those phenomena which are directed at their removal or proceed towards tolerance to the poison?

The next section of the work, deals with the psyche and the instincts. He begins with a discussion of the Aristotelian psyche which guides the development and nutrition of all organs as the ultimate entelechia² or working power. Pflüger does not accept a soul which depends upon special substrates. Then the instincts are considered.

He notes the care with which a bird builds its nest, the bee its honeycomb. How the butterfly emerging from its pupa, lifts himself into the air, an artist in flying which it has never done before and whose art it has never learned; it flies to a flower which it has never seen and rests there; it finds and extracts honey whose existence is unknown. None of these acts need be conscious. He relates an experiment with a turkey hen which had never been

mated but who had laid 16 eggs. As the eggs were unfertilized, the act was useless, although the eggs were perfectly formed. The hen then dug a shallow hole in a secluded spot and placed the eggs there as if they needed care. Day after day she brooded, leaving the nest seldom for food. As the days elapsed the hen sat more constantly and became quite emaciated. If she was taken to other parts of the garden she would immediately return to the nest. The same phenomenon was observed in other hens.

Pflüger calls attention to the variation in human appetites for certain foods in different seasons, now for proteins, now for starches. The purpose of the individual is the removal of the hunger; the purpose of nature is the maintenance of life and the promotion of health. Then attention is directed to the migration of birds in relation to temperature changes. The bird purposes to avoid the cold, nature to ensure warmth because life is warmth. He cites the methods used by animals to ensure reproduction and improvement of the species.

After citing many examples he derives what is now termed the teleologic causal law: the cause of every need of a living organism is the cause of the satisfaction of the need.

A few of his examples may be noted in passing: food and drink return the starved and thirsty organism to health. The need for reproduction has the normal result in the sexual impulse. The second law which he derives states in general: if the need involves only one organ, this occasions this organ alone to its satisfaction. If the need occurs in many organs, that it may still require only one organ to satisfy the need. In respect to the first he cites the pupillary reactions which result in contraction in bright light and dilatation in the dark, both in the interest of clarity of vision. The need here is correct stimulation of the retina and the satisfaction of the need, the correct adjustment of the pupil. To the same group belong the effects of a foreign body in the eye which causes a flow of tears or as he states "the damage is the cause of removal of the damage." Moreover, the secretion of gastric juice when food is taken into the mouth; the flow of saliva which accompanies a dry diet; the stimuli which are set up when the bladder or rectum is filled; the question of whether the existence of mature spermatozoa is the occasion of their discharge. To these also belong the "defense" acts of sneezing, coughing, vomiting. To it belongs hypertrophy of the left ventricle with high intraortic pressure; the enlargement of the remaining kidney when the other is removed.

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BIER'S CONCEPTION OF THE PHYSIS.—To develop all of Bier's conception of hippocratism, for that matter even of the physis, alone would occupy more space than is available. However, since his interpretation of the physis presents the subject broadly it seems advisable to present briefly some aspects of the problem here.

Detailed study of the meaning of the word throughout the hippocratic writings permits a fairly definite conception to be derived, particularly since the various writers are essentially agreed upon the meaning.

In general one understands by physis, "the creating and healing power of nature." Some understand that which is commonly interpreted as constitution. Most frequently physis can be interpreted as the norm in the widest sense of the word. Both Coic and Cnidic works imply this same idea. "It is the tendency of old Greek medicine to restore normal conditions when some abnormal anatomical relation exists which is found in the Hellenistic taste for form and beauty."

But in addition to the rough anatomical form, the finer inner relations must be correct. In antique medicine this obtains when the humours are properly mixed. The normal formation of the body through the correct mixing of the humours is taken care of by the physis. If incorrect coction has occurred and disease has developed, then the physis sees that correct coction proceeds and disease cured in this way. Therefore the physician must support the physis.

In this manner arose the conception of the physis as the creating and ruling power of the organism, the so-called natural healing power. This conception was widespread in Greek philosophy and is noted in Heraclitus:¹

"Like a spider sitting in the middle of a web is aware as soon as a fly has destroyed some thread of the web and therefore speeds to this area, as if it was concerned with the repair of the web, thus similarly the human soul, upon injury of any part of the body quickly rushes to that area as if it had to be at the site of injury with which it is firmly connected and according to a definite relation."

The most famous citation in the hippocratic writings is in "Epidemics."² "The physes are the physicians of diseases." The author continues—"the physis itself finds ways and means not with conscious intent as the winking of the eye and as the tongue also renders service and similar things. Because without being educated, without being taught, the physis takes care of what is necessary. Tears, moistness of the nose, sneezing, ear wax, saliva, expectoration, inspiration and expiration, yawning, coughing all in all, yet not in the same manner. Urination, discharge of flatus,

regurgitation, utilization of nutrition and respiration, and in women what belongs to them and the entire body, namely sweat, itching and whatever else there may be." Here physis is the natural healing power. In the work on nutrition one finds "the physes are without teachers in everything,"³ "the physis is sufficient in everything for everything."⁴ Similar points are made in the work on anatomy,⁵ diet,⁶ although the physis is not able to accomplish everything.⁷ The physician is to guide⁸ by imitating the useful and preventing the damaging.⁹ Coughing may be useful or damaging,¹⁰ eruptions may be healing, or may be the disease itself.¹¹

Thus as is mentioned elsewhere: 1. The physis rules the physiologic processes and guides them in correct ways. 2. It heals diseases. 3. Both are unconscious, instinct-like. 4. It is not able to accomplish everything and is frequently incomplete.

The physis conception underwent widening in two directions: 1. Through the conception of a life power. 2. Through the *entelechia* of Aristotle, "that has the aim in itself." To follow Bier: "all seeds have characteristics in common: for instance they require heat and moisture for development, they are made up of cells, they develop roots and leaf buds. Besides this general physis, there is a special. The seeds of various types have definite morphologic signs, some spread this way, some that. Only a beech tree can develop from a beech, only an oak from an oak. One calls this the general physis of the type. Within this is the individual physis. The seeds are different in regard to color, size; sprouting proceeds with varying rapidity, seeds as well as young plants have a different power of resistance against diseases and if they grow to become trees, then no two look alike."

This gradation of the physis is found throughout the hippocratic writings. All individuals have certain common characteristics. This Bier calls the general physis. As a supraordinated conception it stands above constitutions which are understandable only through it. This general physis is the norm without which the organism cannot exist.

This gradation of the physis is found throughout the hippocratic writings in the property of the nature of organisms to vary. Those varying within the limits of the general physis have the ability to live. Humans vary toward useful and harmful sides. Thus in Bier's interpretation the general physis becomes the normal, its variations the constitutions. The organism is subject to influences of the external world, but extrinsic factors alone are insufficient to account for variations. Organisms, including the human, would probably differ under exactly the same external conditions. This variation is

accepted as a matter of course in the Hippocratic writings, and is applied in judgment and treatment of diseases. Though there is an absence of the thought of higher development of some types, the entire conception of origin and healing of disease, depending upon the constitution, remains its guiding thought. Like Lamarckism and Darwinism, not only types vary but special types also develop, leading to races, which by inheritance, environment and change are stamped into the mixture. The temperaments, asthenic and sthenic types are thereby found in outline in Hippocratism.

To describe the general physis and its variations: "many physes there are and yet merely one."¹² The *one* general physis is opposed by variations within the limits of the normal. Thus the physes (plural) are the physicians of disease. Subordinate to the one physis is the general human physis. Between it and the superior is the physis common to all animals, for example, respiration is common to all animals.¹³ Yet this differs for man and animals: "because not all species of living animals have and have not the same. If now air is not purified from the miasms which are the enemies of the human then the body becomes sick. But if the air becomes unsuitable for another species of living beings, then they will not become ill."¹⁴ "At the height of the shoulder the physis of the human body is different than that of all other living beings."¹⁵ "It is according to our physis to grow during the day and to sleep during the night."¹⁶ "From the age of 14-42 the (human) physis is the carrier of every disease."¹⁷ "All human beings possess the physis of joint fluid."¹⁸ In respect to diet, the finer organization of the human differs from animals and from this medicine arose: "Medicine invents in regard to the human physis."¹⁹ "They mix everything with regard for the human physis."²⁰ "They believe the strong of everything and that which is stronger than the physis of the human body is damaging." But also the individual physis is stressed: "The physes of human beings differ."²¹ "If the factor had been bad for the human physis in regard to its health then it would have damaged all human beings."²² Other remarks are in the same direction,²³ which differentiate a general physis common to all humans as well as a special for the individual.²⁴ "In the diagnosis of disease we must direct ourselves according to the individual in every one."²⁵ "Because treatment differs considerably from treatment and the physes of the body from the physes in regard to welfare."²⁵ The necessity for arranging the diet according to the constitution is stressed.²⁷ The same holds for the prescription of exertion and exercise.²⁸ Moreover certain diseases occur with certain constitutions.²⁹ The healing procedure should be of such strength as to be within the

constitutional power of the patient.³⁰ The various physes in the sense of constitution are mentioned.³¹ The constitutions may change into one another.³² The significance of the physis in relation to inherited and acquired characteristics is mentioned many times³³ and epilepsy is attributed to the former.³⁴ In regard to acquired characteristics the shape of the skull³⁵ and malformations³⁶ are noted. Likewise it states that the male and female germ cells find their origin in the entire body,³⁷ a 2000 year predecessor of Darwin's pangenesis.³⁸ In regard to acquired constitutions the place in which the person lives, the time of year³⁹ alters the physis of shape.⁴⁰ Racial differences depend on such factors.⁴¹ Bier has also reported the influence of weather on races and species. The role of nutrition is given less importance⁴² than today.⁴³

Different ages of life have different constitutions.⁴⁴ Particularly important to medicine is that the same remedy may have different effects in different constitutions,⁴⁵ a subject on which Bier has made observations.⁴⁶

The sexes have their general physis, particularly the female.⁴⁷ Within the general physis of the woman is also the individual constitution.⁴⁸ The male receives less consideration.⁴⁹ Incidentally other words are also used to imply constitution in the Hippocratic writings, but no attention need be paid to this point here.⁵⁰ Moreover disposition to disease is frequently mentioned under diathesis, and likewise "hexus" implies much the same as the latin, habitus. Great attention was paid to the external appearance (eidos). The passages referring to tuberculosis are known to every medical student.⁵¹ Further details concerning the physis of women may be found by those interested.⁵²

Physis, also means, in addition to the bodily, the spiritual disposition as is well known from the Hippocratic Law, "where the physis works against it, all is in vain."⁵³

By considering the physis as the norm, everything has its place under it, not only the organism, but all its individual parts. The physes of these individual parts unite to the form physis of the individual, which is subordinated to them. Thus change in a part may result in a change in the entirety.

In spite of repeated warnings⁵⁴ this constitution theory has been discarded and early writers⁵⁵ of our era prepared for the present conception which now threatens to overwhelm medicine.⁵⁶ Now constitution is considered inherited by one, by another acquired. Now changeable, now unchangeable, now anatomic, now functional, now cellular, now humoral, now both, etc. As Lubarsch⁵⁷ has said: "lately it has become the fashion not to put much value upon sharp conception determination and more to 'feel' than to recog-

nize the content of conceptions. This has the advantage that it is easy to write thick books and in order to turn the facts around. But for understanding and scientific explanation it is of no use and as a rule the scientific reward stands in reversed relation to the thickness of books and the number of learned sounding words. "This holds in a high measure for the modern constitution theory."

Bier summarizes constitution briefly for students with Reuter's parable: "Everything is like leather. Sheep leather tears, calf leather holds (type constitution). The leather of red mountain races is more suitable for shoes than the spotted lowland types (race constitution). Calf leather is again different from heifer or cow leather (sex constitution). If the leather is good it stands much, if it is poor, little (individual constitution). The best leather may contain some flaws (*locus minoris resistentiae*). This property of leather is largely inherited (inherited constitution). All leather must be cared for. The leather of poorly nourished and poorly cared for animals is no good (acquired constitutions)." But all this is subordinate to the supra-ordinated expression "leather" with its definite signs (general physis). In this connection the early writings of Bier may be consulted.⁵⁸ Bier believes that Virchow⁵⁹ was not responsible for the disappearance of the constitutional theory through his attacks on the "sedes morborum," although this tended to re-shape constitutional conceptions. Virchow over-emphasized local disease.

When the hippocratic physis was discarded a fight over the physis in the sense of natural healing power began. Medicine now realizes its mistake in some instances; here general pathology has led the way, particularly those investigators who have considered inflammation as useful.⁶⁰ Medicine is beginning to appreciate this better at present since chemotherapeutic agents are now beginning to be understood as not directly killing micro-organisms but acting through the biologic detour (physis). With the re-introduction of ancient ideas of alteration under the name of "umstimmung," internal medicine changes, and pharmacology must follow. Incidentally alteration (which concerns the physis) is rarely mentioned in hippocratic writings.⁶¹

Since Hippocrates left much to the physis he has been scolded for his therapeutic nihilism⁶² and called seminihilist.⁶³ Such an idea is easily refuted.⁶⁴

With this basis one may turn to Bier's explanation of the general physis. He states that medicine is returning to the teleologic conception, and unfortunately many are adopting it who do not understand it.⁶⁵ His views may be summarized as follows:

1. Since Descartes, many philosophers have assumed the *only*

sign of the soul was consciousness. Now many agree that there are unconscious soul processes.

2. For the latter all definitions of soul are unsatisfactory.

3. In order to consider medicine scientifically it is necessary to introduce new signs for the conception of soul.

4. The soul is the living ruling power of the organism.

5. It has two characteristic aspects: aim-endeavoring management, irritability.

6. All living things have a soul (Aristotle).

7. The soul is not dependent upon a single organ or even upon brain.

8. The brain is merely the chief instrument on which the soul plays. Conscious acts are connected with it.

9. The soul (physis) does the necessary. That is, the hippocratic physis is a soul power subordinated to psychologic and not natural scientific investigation.

10. Aim-endeavoring is directed through the will. Will processes do not proceed according to cause and effect, but according to motive and action.

11. The two greatest motives are the instincts of self preservation and the preservation of the species.

12. Satisfaction of these instincts awakens pleasure; dissatisfaction feelings of displeasure.

13. The physis acts instinctively and unconsciously.

14. Physical causality (cause and effect) and psychic causality (motive and action) work hand in hand although (or because) they are contrasts, forming a heraclitic harmony.⁶⁶

15. It is impossible to find biological causes mechanistically, but they may be found psychologically.

16. Consciousness or subconsciousness may participate in complicated acts, the motive giving rise to the action.

17. Motivation for respiration, internal tissue respiration, thirst of roots (so-called taxis), reaction of trees to wind with development of "immunity" to storms⁶⁷ illustrate unconscious motivations.

18. The relation of "unconscious cell" memory to bacteriologic immunity might be included here.

19. No matter what the origin or nature of inflammation, it occurs with each damage and the relation of motive to action becomes clear. The same holds for wound healing. These points concern aim endeavoring.

The signs of irritability are mentioned elsewhere in this work and need not be repeated. Incidentally Bier's unconscious "mind" has nothing to do with Freud's meaning of the word⁶⁸ but resembles Schopenhauer's meaning.⁶⁹

Finally it is very important to note that Bier is *not* a vitalist. He combines the mechanistic and the vitalistic to a heraclitic harmony.

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BIER AND TELEOLOGY.—Originally the writer included at this point two long sections which constituted about one third of the study. The first dealt with the problem of inflammation, which it seemed advisable to discuss at length because it represents one of

the most important problems of pathology. An examination of the history of various doctrines is very illuminating in several respects. In the first place few subjects show equally well the change in conceptions during different eras of medicine and the relative nature of the apparently final pronouncements on the subject during various epochs. It is extremely instructive to note how theory prevailed over practice, rather than arose from practice; moreover it is interesting to note how successful therapeutic procedures were abandoned when they did not merge with theoretical conceptions. It also seemed significant to note that greatest progress was made, therapeutically speaking, when teleologically oriented thinkers (Hippocrates, Hunter, Bier) turned their attention to this problem. Whereas contrarium thinking has always referred to the antiphlogistic treatment of inflammation as the chief proof of its validity, examination of the various measures (rubefacients, vesicants, pustulants, moxa, seton, injections, etc.), all employed for centuries, reveals that they have the common and rather obvious property of producing inflammation and in reality constitute one of the best proofs of the wide applicability of the simile. The situation is similar with the modern method of induction of hyperemia whether induced by diathermy, hot air, or other means.

The second section considered the second bulwark of mechanistic thinking, namely hemodynamics. Perhaps no other obstacle of equal importance opposes the dissemination of simile or biologic thinking, because the pump and tube conception of circulation prevails quite exclusively in medicine and teleological ideas are not allowed a place in this important field. Whereas the first section required considerable space by virtue of its antiquity and importance, the second was equally voluminous because of the wealth of experimental material available. Furthermore the evidence tends to show that the tissues do regulate their own blood supply, that they are capable of attracting blood, that the field of capillary circulation, the site of real metabolic change, does not proceed according to the laws of mechanics.

Since neither of these topics lend themselves to brief summary and since Bier has recently published exhaustive studies on "Inflammation" and "Circulation," and finally since the writer has taken occasion to make these works available (their appearance will be almost simultaneous with this study), it was thought unnecessary to include material on these points in this particular work. This procedure seemed particularly advisable when the author (Bier) has worked so fruitfully in the field as to accomplish almost a revolution of conceptions, at least in the field of hyperemia, and

when he possesses unrivalled wealth of experience in this phase of therapeutics.

The chief purpose of citing the work of Bier has been to select a worker who has admittedly employed the teleologic conception and to indicate that it may be very fruitful; more than this cannot be demanded from any conception.

His first major study dealt with the development of collateral circulation¹ and led directly to his revolutionizing application of hyperemia to the treatment of disease.

At that time medicine accepted the "collateral wave" theory² as the cause of development of collateral circulation. However it was well known from experience with transfusion and other studies³ that extreme variations in pressure were soon equalized. Moreover such a rise would be non-purposeful in that it would not insure better supply of blood to a given area and would be an excessive device. Appreciating the importance of the heart muscle as a propulsive force, Bier doubted that a "pump and tube" system could account for many complex events; in short, he accepted the cardiac factor only for the forward propulsion of blood, but regarded the distribution as due to other factors. For phenomena not mechanically comprehensible he employed the term "vital influences." Latschenberger had shown⁴ that anemia of a part raises the local blood pressure as long as the nerves are intact, whereas shunting of blood lowers the pressure. Steffani⁵ likewise stressed the importance of integrity of the nervous system on the development of collateral circulation. Though these facts imperiled the mechanical explanation, Bier proved the development of circulation in an extremity deprived of nerve supply.

Ancient physiology had taught the theory of attraction, that is, that distribution of blood was regulated in part by attraction of the tissues in need of blood. John Hunter tersely said: "blood goes where it is necessary." Stark attempted to prove the influence of carbon dioxide accumulation on blood supply.⁶ Much of the work of this period can be omitted since experiments were conducted largely on excised tissues.⁷ After exhaustive experiments with intact animals Bier concluded that organs regulate their own blood supply, increasing it when increased amounts are necessary and postulated a sense of "blood feeling" of organs.

One should recall that at this period in medicine every physician believed it a duty and obligation to attack hyperemia by every available agent. The obvious result of Bier's studies was the conception that hyperemia was the reaction to the damage, that it was a useful phenomenon. The innovation, so obvious at present, was revolutionizing to surgery.

Naturally the teleology implied in hippocratic medicine has nothing to do with anthropocentric teleology in which man is placed in the center of the universe, but in a Darwinian sense, man becomes one of the innumerable phenomena of nature. Likewise Bier's teleology recognizes purposefulness in nature merely as a fact and is not an explanation of phenomena.

Space prohibits exhaustive consideration of theologic teleology, the excessive teleology of some of Darwin's followers,⁸ and similar topics. Bier⁹ has considered the teleologic problem in various writings so that attention need be directed at only a few points. It is clear that the body adopts rational procedures for the removal of obvious noxious influences; the cough which dislodges foreign bodies in the larynx, the vomiting which ejects gastric irritants, effusions of tears and spasm of the lids in ocular foreign body, etc. The sad fate of so much work spent upon antipyretics, emphasizes the reluctance with which medicine begins to appreciate the usefulness of fever, a fact known to Hippocrates and emphasized by Hunter¹⁰ or as Sachs had stated a century ago: "It (fever) represents a reaction of the organism for the restoration and assertion of its integrity with increased expenditure of force in all systems."¹¹ In more recent times inflammation has become added to the defensive reactions of the body through the work of Leber,¹² Neumann,¹³ Marchand,¹⁴ Buchner,¹⁵ and Metschnikoff¹⁶ though as Marchand stated that a majority of pathologists "have not yet freed themselves from the conception that inflammation is a deleterious phenomena *per se*."¹⁷

Although non-specific protein therapy has received brief attention in an earlier note, it may be well to approach this same subject from another angle, namely, the healing power of inflammation and fever. In the popularization of foreign protein therapy under the name of Schmidt's parenteral protein body therapy and the explanation by Weichardt that the results are due to "protoplasmic activation," the pioneer work of Bier¹⁷ is often overlooked.

By his early attempt to employ animal blood transfusion he was the first to employ consciously protein therapy.¹⁸ Apparently it resulted in cures, for he has never abandoned the method. Earlier writers¹⁹ had employed blood on the basis of transplanting blood, that is, they attempted to "parenterally nourish." In view of this largely erroneous presumption, coupled with the ancient idea that "much helps much," they did not secure results, Hasse²⁰ became branded as a swindler, and the subject (which has a great tendency to rebirth) was buried by v. Bergmann.²¹

As Bier concluded that inflammation and fever were curative measures he then sought physical measures which would increase

them. Inflammation found a partial answer in physical measures and the production of fever by animal blood.²² Therein he proceeded on the basis: the blood introduced, is destroyed and its destruction acts as a stimulus on all cells of the body (healing fever), but especially on the inflammatory focus and since nearly all foci of disease are found in a state of inflammation, it acts there more than upon normal tissue (healing inflammation). His attempt was identical to that of Hahnemann, that is, to make chronic processes acute. He attempted to produce an "artificial infectious disease." Thus he approached the subject not unlike Matthes²³ who obtained tuberculin like reactions with deutero-albumoses.

Injection of blood causes fever followed by improvement, lessening of pain and exhaustion, improvement of appetite and digestion, of blood formation, stimulation of smooth and striated muscles, improvement of sleep. Tuberculous patients with cough and expectoration are marked aggravated and then improved.

Older writers were acquainted with the stimulant effect on all organs but Bier attempted to secure an elective action on diseased areas.

Virchow²⁴ had said: "This activity (action) of life never proceeds, at least as far as we can judge, through a cause entirely inclusive in itself and approaching any single part from the start but we see everywhere that a certain excitation is necessary for it. Every living activity presumes an excitation, a stimulation if you will. This consists of a *passive* alteration (*passio*, *pathos*) which the living elements experience through an external force, but which is not so great that the essential functions of the elements are destroyed by it. From this passive alteration (*irritamentum*) follows an *active process*, a *positive* performance of the elements themselves, from which one concludes that it follows from the living properties of the elements as an independent event. Hence the excitability of a single part seems to us the criterion by which one decides whether it lives or not. . . . But there are various activities which can be provoked by external influences and essentially three types. . . ." It would lead too far here to discuss the functional, nutritive and formative stimuli of Virchow. Sufficient has been said to indicate that the recognition of two series of events, one of which is reactive, has been long known to medicine. In fact it might be easily shown that if Weichardt intended to imply a prolonged effect in the term protoplasmic activation in contradistinction to the brief action suggested by the word stimulus,²⁵ then he merely accepts the very ancient conception, alteration. To be sure there are still some²⁶ who hold the conception of the cura-

tive nature of fever as unproven, but in general the view that both fever and inflammation have curative properties is now in vogue.²⁷

One must clearly separate the effects of damage from those effects constituting the reaction to the damage. Only the latter are curative. In other words the passive phenomena must be separated from the active, the reaction to the damage.

Otherwise ridiculous conclusions are drawn; for example, death is the reaction to the damage. Bier regards pain purely as the result of the damage. He also regards *functio laesa* as foreign to the inflammatory reaction and he was able to remove this symptom by increasing the inflammation. Naturally full appreciation is given to the fundamental significance of rest in the therapy in inflammation. Ribbert's view that a "sick organ accomplishes less, never more than usual" is obviously erroneous, as anyone knows who has ever had a "cold." Here the discharge of mucus in health and disease may be compared.

Like Virchow and H. Schulz, Bier agrees that the inflammatory site shows increased irritability, and Schulz has repeatedly emphasized that the sick organ reacts to a stimulus which it would not if healthy. Schulz, writing in earlier times, was compelled to make observations like the photophobia in ocular inflammation in which the ordinary light of day could not be tolerated, while Bier could employ examples like the hypersensitivity of the tuberculous to tuberculin. He was led to make observations of this type by noting that the inflammatory focus resembles a lymph gland in the removal, collection and separation of foreign materials lying in it. Others have observed that salicylic acid and iodine²⁸ given by mouth are retained at the site of disease.

Thus Bier's conception may be summarized as follows: inflammation is a healing phenomenon and one can act particularly on the diseased foci because of hypersensitivity, and should act in a manner so as to increase the inflammation.

This naturally raises the question of dosage which is discussed elsewhere. Bier accepts the Arndt-Schulz generalization in that small doses of protein bodies act opposite to large, the first stimulating and the latter depressing. They also work differently individually on the sick and healthy organ. Thus the correct dose becomes all important.²⁹ Whereas Schulz originally spoke of drug effects in his early works, in the later publications the conception was extended to all stimuli. The relationship of this rule to the problem of hyperemia is admirably discussed in Bier's work on hyperemia.³⁰

Attention must here be again directed to the question of specificity and non-specificity. Bier has always held that non-specific

stimuli are valuable in a wide variety of disease.³⁰ Even early his publications deal with the innumerable rubefacient agents applied in the neighborhood of inflammatory foci (so-called *derivantia*) as well as those applied at a distance (so-called *revulsiva*). All reactions excited by cauterly, seton, hot packs, cataplasms, hot air, bougies in the treatment of strictures, water, light, stasis producing bandages, foreign and homologous blood, protein bodies, now widely used in medicine, the so-called internal antiseptics, all these act in the same sense of increasing inflammation and fever. To the same group belong all agents which destroy body proteins when injected into the blood or which can destroy proteins by other means: liquids from water to milk, acids, alkali, turpentine, salts, drugs, oils, etc. Thus it makes little difference whether one injects a protein which is destroyed or causes body proteins to be destroyed, the general effect is the same, with, of course, the differences due to the peculiarities of each agent.

A word may be added here that most pathologists are not teleologically oriented although they accept Wiegart's definition of inflammation as "a reaction to injury," a conception which is neither new nor comprehensible except teleologically. Others state that the teleologic conception of inflammation is a partial definition which emphasizes but one phase of the problem. Undoubtedly the latter statement is true, but this phase is the most important one from the standpoint of practical medicine, namely, therapeutics. A few observations may be added to indicate the value of the conception.

Probably no surgical procedure is now more universally recognized than the appreciation of the inflammatory barrier set up by an inflammation, and all surgeons are fully aware of the necessity of keeping their operative intervention within this inflammatory barrier in order to avoid extension of disease. Billroth³¹ found the application of infected dressings to granulating wounds did not cause infection of the wound, but if the dressing was fastened by a suture, infection occurred at the point of suturing and not in the wound itself. Afanassieff³² made similar observations with anthrax organisms. Durham added the fact that previous excitation of an "aseptic peritonitis" increased the resistance of the peritoneum to subsequent peritonitis.³³ Issacff³⁴ was able to increase resistance against subcutaneous inoculations of cholera by injecting the same site previously with a number of agents capable of provoking inflammation. Besredka³⁵ was able to protect animals against anthrax locally by previously injecting a filtrate of the culture into that part of the skin. He later found that the same obtained for staphylococci³⁶ and his co-worker found it held for streptococci³⁷

and these observations have been confirmed.³⁸ Citron and Picard³⁹ used polyvalent vaccines for a number of diseases on the basis of a specific effect but this was shown to be due to the excitation of local inflammation. Arloing and Langeron⁴⁰ were able to secure local protection against *B. Pyocyaneus* by injecting bouillon into the site. Similar results have been obtained by Rivalier,⁴¹ Gratia,⁴² Mallory and Marble,⁴³ Miller⁴⁴ with other organisms and variations of the method.

Still other workers while admitting the importance of non-specific factors were able to obtain a still higher immunity with specific serum. Gay and Morrison have shown the importance of macrophages in immunity and have protected animals against streptococci by injecting meat infusion, dilute egg white, broth, into the area⁴⁵ and similar results have been obtained by Nakahara⁴⁶ with olive oil.

Thus one can obtain local immunity by creating local inflammation. Naturally the problem is not simple. The right kind of inflammation (macrophagic) must be created, the proper degree of inflammation attained. For example, Hanger⁴⁷ has shown in a study of rabbits infected with *B. Lepisepticum* that animals injected with bacterial filtrates 24 hours before infection have a non-specific immunity in that area. If the tissues are severely injured by chemicals or there is an excessive antibody-antigen reaction, there is a loss of resistance even in immune animals. Mild injuries with the same causes produce increased resistance. Miller has also noted that if the inflammation (damage) was too great there was no local defense against infection.

In older medical literature these points were generally appreciated. The cautery was used freely, a method which Bier has attempted to revive. Setons, moxa, fontanelles of ancient medicine, tartar emetic ointment of Jenner, the ancient treatment of paralysis with measures designed to produce suppuration on the head may be contrasted with the modern procedure of introducing malaria in the paretic.

Elsewhere attention has been directed to the favorable influence of some infectious diseases on paresis, as well as other late syphilitic processes. Such infections are erysipelas, malaria, certain forms of sepsis. All of these have in common high temperature and relatively short course. The work of Hoff⁴⁸ is particularly interesting in this respect. He divides the febrile process into two phases, the first phase of fever increase and maintenance of height, the second phase or convalescence with decline of temperature and subsequent events.

In the first phase there is a distinct alteration in the blood picture

with leucocytosis followed by young forms of white cells, so-called myeloid shifting, and decrease of eosinophiles. In the second phase young cells lessen and relative lymphocytosis occurs. Schilling calls the first phase the fighting phase,⁴⁹ and the other phase the monocytic conquering phase. Hoff has detailed these blood pictures.⁵⁰

Equally well known is the acidosis of fever which has been studied by Akiya⁵¹ so that the reduction of alkali reserve is now generally appreciated. With the decline of fever the acidosis disappears and normal alkalosis or over-compensation occurs. Müller⁵² has shown the presence of acidosis in the usual meaning of the word in recent times. It is the short lasting fevers which are characterized by acidosis; in the chronic, it may be absent or alkalosis may exist. At any rate brief infections are characterized by an acidotic orientation of the metabolism during the first phase⁵³ which may be reflected in the increased uric acid excretion.⁵⁴ Jahn and Stum have shown that increase of metabolism is associated with the acidotic phase, decrease of metabolism with the alkalotic phase. The increase in blood sugar in the first phase⁵⁵ as well as lowering of blood cholesterol⁵⁶ is well known. Changes in the blood proteins have also been reported. Thus the changes may be summarized (Hoff):

SHORT LASTING FEVERS

<i>1st Phase</i>	<i>2nd Phase</i>
Increased fever, febrile height	Decrease of fever
Leucocytic increase with myeloid tendency	Leucocytic decrease with lymphocytic tendency
Decrease of alkaline reserve	Increase of alkaline reserve
Increased metabolic changes	Decreased total metabolism
Increased blood sugar	Decreased blood sugar
Decreased cholesterin	Increased cholesterin
Preponderance of sympathetic	Preponderance of parasympathetic

It seems hardly necessary to add that the febrile period is characterized by sympatheticotonia in the sense of Meyer Gottlieb⁵⁷ and Toeniessen⁵⁸ or that acidosis is an accompaniment of preponderance of the sympathetic⁵⁹ or that the leucocytosis with myeloid phase is in keeping with a sympatheticotonia.⁶⁰

If now one turns to the question of what happens in the organism when malaria⁶¹ sodoku⁶² or pyrifer is employed in so-called fever therapy the following is obtained. Hoff⁶³ has shown the same blood shifting in malarial therapy of paresis as well as shifting in the acid base equilibrium. Gothein and Schilling⁶⁴ likewise have shown the same picture in malaria. The increase in metabolism as well as destruction of protein has been proven by Burger.⁶⁵ The same holds true for rat bite fever⁶⁶ and for pyrifer.⁶⁷ Thus it may be

assumed that artificially produced fevers have the same phenomena as the natural disease.

At risk of reduplication attention is once more called to the basic work of Bier on "healing fever." Wagner-Jauregg⁶⁸ attributes his remarkable results obtained in the treatment of paresis to fever and designates the method as febrile therapy. Schittenhelm,⁶⁹ speaking of protein body therapy, mentions the production of fever as necessary for the healing effect. Mendel and Walinski showed the value of fever in late syphilitic manifestations⁷⁰ and Kahler and Knollmeyer⁷¹ have confirmed it. Welchbrodt⁷² showed the value of overheating in experimental rabbit syphilis, a practice which is reflected in the present attempts at "radiothermy." On the other side Freund and Grafe⁷³ have unsuccessfully attempted to minimize the importance of fever. It is hardly necessary to relate the work of Metschnikoff in regard to phagocytosis and its role in immunity, but allusion should be made to the importance of the blood forming organs as sites of formation of immune substances. Hoff has shown the relation between blood pictures and recovery a viewpoint supported by Kaufmann.⁷⁴ Here too the work of Hirschfeld and Hittmair on experimental peritonitis deserves mention.⁷⁵ On the other hand the absence of defense in agranulocytosis is generally appreciated. Even if one approaches the subject from the standpoint of acidosis, one encounters evidence of increased resistance from this viewpoint.⁷⁶

Hoff concludes the discussion of some of these points with the following remarks: "In conclusion we may say: we consider as acute infectious diseases diseases in which the above presented double phasic changes in the vegetative regulatory processes take a spontaneous course to a high degree. We have reason to assume that in these processes we are concerned with natural defense measures of the organism which can be seen especially in fever, in leucocytosis, and acidosis. The spontaneous course of these defense measures which are effective is the factor which stands in close relation to the nature of the acute disease and its short course which is usually favorable. If erysipelas, sepsis, cannot be conquered by the body, but lead to death, a breaking down of these defense mechanisms always can be observed, and it is best seen in the definite unfavorable alterations in the white blood cells, and often from a terminal cessation of heat regulation. The so-called chronic diseases are characterized by the fact that the body is not able to produce by its own power the defense measures which we find in acute infectious diseases with a rapid conquering of the morbid condition. Especially in late syphilitic diseases of the central nervous system, these defense measures are lacking almost entirely.

Here experience teaches us that the artificial production of these defense powers produced by febrile therapy, increases the absent defense measures and thus brings about a favorable change in the picture of the disease. The so-called alterative treatment here consists in repeatedly releasing the course of natural defense events artificially."

With this brief presentation of only a small fraction of the evidence on one aspect of the teleologic problem, one may turn to other problems. It must be appreciated that the teleologic conception is merely a method of consideration and as such does not exclude other methods of approach. As Bier⁷⁷ points out the essential importance of any theory does not lie in its absolute correctness, for what theory has endured throughout the ages. A theory to be a good theory should either contain a nucleus of truth or foreshadow the truth in a tangible manner. In other words few workers now accept the Ehrlich side chain hypothesis, but none deny that this theory was fruitful.

Prevailing in medicine for the last twenty years has been the mechanistic method of consideration. It presumes to be able to comprehend the living organism in physico-chemical terms and to be able to explain its activities according to physico-chemical laws. Its supporters stress that they accept the causal law and that this is not a theory but a natural law. Naturally this is unprovable or false. But, and this is the important feature, many supporters of the causal method presume that this one method supplants all other methods of consideration. In short it is assumed that our present knowledge is sufficient for gaining a view into the essential features of life. Indeed this same opinion was also held by the iatrochemists and iatrophysicists 250 years ago.

Naturally none of the above is to be construed against the high merit of the mechanistic method of consideration if one views it in the above-mentioned light, that is, it is a theory, the first requirement, and that it is fruitful, the second requirement.

With the exception of Bichat and O. Rosenbach, the mechanists have stressed that Harvey founded the physics of life with his studies on circulation and presume that circulation can be explained in its details causal-mechanistically. Actually Harvey's teleologic interest in the purpose of the valves of the veins led to his discovery of the circulation. It was Bier's great sin in the eyes of such workers to have shown "vital influences"⁷⁸ or as the modern physicians state, integrative forces. To make it full measure, Bier⁷⁹ showed in his studies on regeneration that so-called mechanical causes played very subordinate roles in the formation of pseudoarthroses, a viewpoint in which Martin⁸⁰ concurs. Bier like all

modern teleologists does not present a cosmic teleology nor an anthropocentric teleology. He limits himself to a teleology in living nature which, though fragile and easily destructible, maintains and increases by virtue of purposeful structure and purposeful activity.⁸¹

Older teleologists had conceived an unknown something which had nothing to do with physical and chemical powers. Later vitalists were compelled to take cognizance of the physico-chemical powers and mechanism began to play a role in vitalism. Those who followed the rigid dogma of a vital power naturally were carried to the acceptance of supernatural powers. The neovitalists like Rindfleisch, Bunge, Reinke, Driesch and others admitted the physico-chemical nature of events of life but denied that life can be mechanically explained. Bier adopted a more practical position which was that he considered the purposefulness of living nature a fact of experience and not requiring explanation. Furthermore he believes that the teleologic method alone is insufficient, but that an attempt should always be made to comprehend subjects physico-chemically. Thus he does not object to Pflüger's attempt to explain purposefulness mechanically. His viewpoint approaches that of Kulpe-Messer.⁸² In short, he adopts the viewpoint that man has eyes to see, ears to hear and the brain to think rather than that a man must see because he has eyes, etc.

That many things in man are recognized as purposeful is clear: but many things are said to be dysteleologic. But here one recalls that many of the "rudimentary organs" of Haeckel⁸³ have been shown to be endocrine organs whose existence is absolutely necessary to life.

Every mechanist should read Thöle's⁸⁴ attack on Bier because it proves, though it intends just the opposite, how difficult it would be to actually proceed mechanistically. A fragment from the writer's translation of Kötschau may be cited: "In a similar manner Thöle rejects a large number of conceptions without which medicine could hardly progress. Darwinism does not belong to the exact natural sciences because it does not attempt a scientific causal explanation. Terms such as organism, active cell activity, stimulus, regulation, precipitin, agglutinin, and other 'ines,' the assumption of a hypothetical heat center, according to him are all teleologic in conception. He calls Ehrlich's side chain theory, gymnastic play of the brain, an application of Pflüger's teleologic causal law and Weigert's law of regeneration. All these terms should be eliminated from the exact natural sciences which seek merely causal explanations and be placed in the field of biology which he considered as a kind of natural philosophy."⁸⁵ In short, it is wrong for

an anatomist who sees a new and unknown organ to ask himself what is its function? It is surprising that Thöle denies teleologic thinking and immediately reverts to Rickert's essentially teleologic hypothesis.⁸⁶

More recently several workers have deserted the mechanistic cause, and for the one cause of many vital phenomena, several conditions have been substituted by Verworn⁸⁷ and v. Hansemann,⁸⁸ but these ideas already find opposition in scientific circles.

In place of Bier other prominent scientific workers could have been selected. For example, Otfreid Muller:⁸⁹ "The confusion of our present day is found in the fact that one has tried to use knowledge in order to create a belief, for we are actually dealing in a materialistically directed biology, which means metaphysics and not based on experience." Krehl had experimental speculation in mind when he wrote:⁹⁰ "The experiment which we should use in questioning nature under clear conditions, serves many observers in their investigations under still less clear conditions than simple observation offers us, because it simplifies nature speculatively, not inductively." Some experienced workers go so far as to distrust the causal method entirely. Lehmann⁹¹ states that a complete science is completely lacking in biology, namely, the teaching of the natural healing process. In another place Krehl adds:⁹² "Naunyn knew the complication of processes at the bedside and strictly refused considerations of disease from a simplified physiology . . . and when he came to the conclusion that in reality the physiologic method of consideration ran parallel to old medicine and was not uniformly melted into it, a crisis appeared. Also words as a pretext of causal explanation again started to play a considerable role. . . . Not only the understanding of symptoms in the healthy and sick patient but general understanding of nature requires the physician to go beyond pure causal methods of consideration. . . . Rokitansky in one of his discussions mentioned the purely mechanistic viewpoint in very plain words and Virchow testified in the same direction. I hereby gratefully refer to the constant work of Bier and Krause. Also pathologic anatomy points in the same direction. . . . With the investigation of psychiatry, not even a start has been made. And yet, as mentioned before we physicians live therapeutically mainly on psychiatric thought. . . . Goldscheider too has the same viewpoint in that he conceives the natural therapy which attempts to follow the course of self-healing as typically hippocratic: *quo natura vergit, so tendere oportet*. He replies to the statement that thereby a dogma is set up by stating that the regulatory activity of the organism is so well founded as a process that we can place it in the center of therapy."

Goldscheider whose opinions are highly regarded has also spoken on this topic. He states that a former period of medicine considered the entire complex of symptoms of a disease as an enemy against which one had to fight. He adds:⁹³ "The *contraria contrariis* is frequently based upon a scientifically false deduction, for example, the treatment of nephritic oliguria with diuretics, of external inflammation with ice, of increase in blood pressure simply with rest, and because exercise physiologically increases the blood pressure of compensated heart disease one forbids movement, of thinness by a fattening cure, etc. It is also a false deduction to treat acceleration of the pulse with digitalis, because the acceleration of an insufficient heart is decreased through digitalis. In this it is overlooked that this behavior is not in accord to the general law but occurs only under special conditions."

Since the discussion has wandered somewhat from Bier's conception of teleology it seems advisable to summarize in closing the opinions directly attributable to him. Reference should be made to the remarks on his conception of the physis for further elaboration.

As the technical sciences are purposeful sciences, their fundamentals must be fruitful for practical results.

1. If one studies an eye and asks the cause of it, its parts, he could never come to an answer. If he asks what is *the purpose of the eye*, what is *the purpose of its parts*, then he works with fruitful questions. In medicine the question of the cause is frequently asked, the question of purpose rarely. As long as the cause of reactive hyperemia was studied it had no fruitful results, but these were immediately evident on asking what is the purpose. Bier asked what is the motive of the physis: in the answer appeared reactive hyperemia as physiologic inflammation,⁹⁴ from whence it is a short step to considering inflammation as defensive and deserving imitation.

2. The motive is able to make causes ineffective, because the will sets all instruments in motion. Physicians cannot prevent a wound from healing, nor suppress fever with antipyretics or inflammation with antiphlogistics. The same holds for joint pathology.⁹⁵

3. The causal chain can often be checked as to its past, rarely as to the future, but the will has only one aim, the maintenance of the individual and his type. Therefore the teleologic conception points to the future.

4. Medicine almost universally makes a mistake: it believes there is *a* cause for *a* life process. The physis sets in motion one or more mechanisms when the organism is confronted by danger.

5. Destruction induces regeneration. In addition for reconstruc-

tion specific hormones are necessary.⁹⁶ In the healing of bone fractures many conditions are present: a) presence of specific hormones, b) the blood clot, c) correct mixture of endocrine hormones, d) correct nutrition (vitamine), and others.⁹⁷

6. Even where the physis does not seem to stand in the foreground it is active. Whereas immobilization is said to cause ankylosis (that is, *one* cause), it does not occur unless a toxic stimulus is added.⁹⁸ The alleged cause of pseudoarthrosis, namely movement, does not exist.⁹⁹ While stones in the various ducts of the body are alleged to be caused by faulty nutrition, but can be induced in animals by foreign bodies.

7. The destruction is the stimulus for effecting compensatory hypertrophy; thus destruction is the stimulus to the physis to remove the disturbance.

8. Causal thinking is unfruitful in medicine whereas final or teleologic thinking is fruitful.¹⁰⁰ Bier does not consider self regulation as teleologic mechanics in the sense of Pflüger¹⁰¹ but as the unconscious aim-endavoring of the individual. The decomposition products arising in life physiologically are the stimuli for removal and displacement of decomposed substances. Thus there is an ison for physiology as there is pathology.¹⁰²

9. Aim-endavoring does not occur in the absence of perception. The bone fracture is not the site of development of tuberculosis but a trivial injury. The absence of perception in carcinoma remains the block to proper therapy.

10. Stimuli can be given to the physis to increase its perception of stimuli and reactive activity. Old medicine knew this as alteration.

11. Thus stimuli of opposite natures may lead to success in the same condition. Both an ice bag and hot compress increase hyperemia and tend to be curative.¹⁰³

12. If one calls the diseased parts of the body hypersensitive, then one admits the irritability of the psychic factor.

13. Stimuli entering the body may stimulate organs in distant parts.

14. The vitalistic school held "the vital power" ruler over the mechanistic causal processes ("force hypermechanique"). This is rejected. The physis directs the aim striving individual and guides physico-chemical powers and thus deserves primary consideration. Sutures do not cut normal tissue but infected tissues. Bougies cure strictures by exciting inflammation.¹⁰⁴

15. The physis contains the entire mechanism of metabolic and energy changes and the inner relationship of the decomposing and passive organism which is continuously disturbed and again rebuilt.

If the external gains the upper hand, the body is subjected to putrefaction.

16. The physis requires the support of the physician.

17. There are parts which are regarded as dysteleologic and incomplete. The aim-endeavoring of the individual and species is a rule and not a law.

18. Many of the events and mechanisms which are considered dysteleologic are not correctly understood.

19. The physiologic and pathologic processes serve for the totality of the individual and the species.

20. Overemphasis on the cause and the neglect of the meaning of the organism is the outstanding neglect of biology, and has led to detail investigation.

21. Detail investigation has had a destructive effect: an example is the effect of detail investigation on the conception of inflammation.¹⁰⁵

22. In inflammation the entire energy of the organism is concentrated to one aim, the defense against the danger.

23. The highest fundamental of healing is hippocratism: the correct mixture of all the uncountable substances and powers in the organism in the heraclitic meaning of harmony through contrasts. (The general physis with the constitution, alteration and attraction which are subordinated to it.)

24. The true meaning of progress must include the past experience of physicians and peoples, a new science, the applied history of therapeutics. It must be created from the sources and not from opinions.

In these 24 heads Bier has summarized the nature and basis of medicine as he perceives it. What here may seem like dogmatic assertion will become more comprehensible for the reader having leisure to study the original and collaterals.

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A NOTE ON SOME MODERN TELEOLOGIC CONCEPTIONS.—As occasion has been taken elsewhere to present the ancient teleologic conceptions at some length,¹ ending with Virchow,² some notes on more modern views may be presented. These suggestions arise largely from Bier,³ who considers the subject from the so-called signs of life, some of which may be mentioned.

a) SELF PRESERVATION.—a) In injury the stimulus of the wound stimulates the damaged tissue, connective tissue and epithelia to replace the gap for the purpose of excluding the external world. b) Bacterial poisons stimulate the body to the formation of opposing substances, antitoxins, bacteriocidal substances, etc. c) Physical and mental stimuli permit man to escape dangers or to meet them with enormous powers.⁴

b) SELF REGULATION.—Similar to above. For example, self regulation of respiration, Bier's blood feeling.⁵ If it was not for the stimulus of hunger and thirst, mental desire for food, one would not eat or take suitable food. The decomposition products arising from metabolism stimulate the tissue to take up nourishment.⁶ Here enter the problems of hormones, ferments, etc.

c) REGENERATION.—The detailed and noteworthy studies of Bier have shown that scar formation can be avoided by the development of and use of local hormones.⁷

d) REPRODUCTION.—Probably the most powerful teleologic urge next to hunger.⁸

e) VOLUNTARY MOTION, so-called intentional movements.

f) ADAPTATION of species unable to adapt themselves.

g) SENSITIVITY AND FEELING.

In all these phenomena one may perceive the underlying thought so admirably expressed by Fredericq: "The living being is an agency of such a sort that each disturbing influence induces by itself, the calling forth of compensatory activity to neutralize or repair disturbances. The higher the scale of living beings, the more complicated and perfect do these regulatory agencies become. They tend to free the organism completely from unfavorable influences and changes occurring in the environment."⁹ Much later Richet¹⁰ added: "the living being is stable. . . . It must be so, in order not to be destroyed, dissolved or disintegrated by the colossal forces, often adverse, which surround it. By an apparent contradiction it maintains its stability only if it is excitable and capable of modifying itself according to external stimuli and adjusting its response to stimulation. In a sense it is stable because it is modifiable . . . the slight instability is the necessary condition for the true stability of the organism." In this respect one might cite the matter of heat regulation and adaptation to high and low altitudes. Claude Bernard has said: "all the vital mechanisms, however varied they may be, have only one object, that of preserving constant the conditions of life in the internal environment,"¹¹ to which Haldane¹² comments "no more pregnant sentence was ever framed by a physiologist."

These expressions of "object," "purpose" are teleologic and

the use of the word *mechanism* is not unwarranted, but not in the customary sense of causalistic philosophy. To the above generalizations a few specific examples may be added.

CLOTTING OF BLOOD.—This phenomenon is obviously teleologically comprehensible. Hewson¹³ noted that as hemorrhage progressed clotting occurred more rapidly. Cohnheim¹⁴ noted that the last fragments clotted almost immediately. These results have been confirmed by Gray and Lunt.¹⁵ Tournade and Chabrol¹⁶ have shown that when hemorrhage occurs and the blood pressure is falling, the adrenals are stimulated and the secretion causes a shortening of bleeding time. Likewise the lowering of metabolism in hemorrhage is useful in the absence of sufficient oxygen. To be added here is the adaptation of the caliber of the vascular system in the presence of deficient amounts of blood, the contraction of the spleen, a blood reservoir, when hemorrhage has occurred, the adaptations which ensure cerebral circulation, the vaso-constriction of the peripheral circulation which not only tends to increase blood pressure in the vital centers, but also to narrow bleeding vessels, the conception of a carotid sinus¹⁷ to insure adequate cerebral circulation: all these are fundamentally teleologic conceptions. The removal of fluid from the tissues, the thirst of the patient with hemorrhage, are likewise comprehensible teleologically. And if all these phenomena are brought about through the agency of the sympathetic nervous system, this so-called regulation is conceivable only teleologically.

HUNGER AND THIRST.—As water and food are constantly lost from the body, supplies can only be maintained by intake provoked through hunger, thirst and variations in supply depots. Mayer has shown that there is no appreciable change in the blood in dogs deprived of water for 3 days,¹⁸ which suggests a strong regulatory mechanism. Data on hunger are more abundant. Cannon¹⁹ noted the frequent and rhythmic contractions in the stomach during so-called "hunger pains" and showed that the sensation of hunger was the "cause" of the contractions. Carlson²⁰ extended these observations. Among the factors which may provoke these contractions the following may be mentioned: sugar is one of the most easily available sources of energy. Bulato and Carlson²¹ found that when the blood sugar was reduced by insulin, the contractions became more intense. Quigley and Carlson²² have also shown that insulin induces gastric and duodenal motility corresponding to hunger sensations. Thus the individual becomes aware of his necessity for food by hunger contractions, whenever the blood sugar level reaches a definite point.

As indicated above, the water content of the blood is surprisingly

constant in spite of constant losses and irregular intake of fluid. Wettendorf²³ found a change in blood water only on the fourth day of deprivation in dogs, yet Haldane and Priestley²⁴ have shown the constancy of blood in spite of ingestion of large amounts of fluids. Again if sodium chloride reaches the blood, water may be retained in large amounts;²⁵ again when water is lost by hemorrhage, large amounts flow out from the tissues. Attempts have been made to explain the deviation of water by shifting of sodium,²⁶ shifting of reactions,²⁷ and while interesting, these embrace but an infinitely small part of the totality.

The story is quite the same in regard to salt content of the blood. The effects of salt deprivation have been carefully studied²⁸ and the well known "salt fever" from excess amounts of salt. Salt storage²⁹ in the lungs, kidneys, and skin³⁰ is well known; if insufficient salt is available, it is zealously retained by the blood.³¹

The ease with which blood sugar estimations can be made and their importance in metabolism and diabetes have led to investigation in this field with similar results. On the one hand, is the discharge of excessive amounts when blood sugar exceeds the "threshold" of the kidney. On the other hand, there are the hypoglycemic reactions from too little sugar.³² When carbohydrates are ingested the blood sugar rises to just below the "leak-point."³³ Insulin formation is largely controlled by the amount of blood sugar³⁴ and there is also a nervous control.³⁵ The complications of this regulatory system are revealed even further by the relationship to the adrenals³⁶ and the so-called balance of adrenals and pancreas. Evidence could be introduced for storage and regulation of blood proteins, and the regulation of salt and water contents of the blood.

To conserve space it may be said that the same answer is given by investigations on blood fat, blood calcium, the ensurement of oxygen supply, so-called neutrality regulation of the blood. In other fields there is similar evidence: heat regulation, so-called reflexes of sneezing, coughing, salivation, winking, lachrymation, callous formation on used parts, so-called repair, inflammatory barriers, etc.

To present adequately the teleologic conception would require a review of dominant trends in philosophy, a consideration of the so-called soul problem, psycho-physical parallelism, the hippocratic physis, Heraclitean philosophy in medicine, each of which would demand a volume.

The entire situation may be summarized as follows: *if there are purposeful reactions in the body, it would seem rational to imitate them. This is the simile in its fundamental form. The simile prin-*

ciple is a principle by whose application the defensive reactions are to be stimulated.

The simile conception, hippocratically viewed, implies that one series of phenomena in disease, the injury, the passive effect upon the body, the phenomena of damage are peculiarly susceptible to the contrarium, but in the symptoms of reaction are useful active reactions which deserve imitation. It is obvious of course, since nature is infinite it is not simply and purely a matter of arbitrary decision as to whether or not a symptom is useful. For example, a patient presents cough as a symptom. The patient under consideration is suffering from lobar pneumonia and the cough is occasioned by exudate in the large bronchi. Morphine or codeine in sufficient doses might suppress the cough, but could hardly aid in the removal of exudate. In another patient the cough may be precipitated by cerumen in the ear stimulating the vagus. In this instance it would be ridiculous in the light present knowledge to regard the phenomena as protective, and to treat the isolated symptom by the simile.

In still another case of pneumonia the disease may be in an initial phase and the patient harassed by a dry irritative cough which is fruitless, exhausting, disturbing to the night rest and preventing sleep. Even if the cough were due to exudate, there might be greater damage from loss of sleep than any possible harm from suppression of exudate. Assuming that the simile was ineffective, it is obvious that abolition of this symptom by morphine or codeine might do more good than harm.

From the above it will be seen that these rules do not supersede the necessity for sober judgment which can be given only by the adequately trained physician. It requires considerable experience and judgment to differentiate the signs of damage from the signs of useful reaction, particularly since the latter have received but little attention in general medicine until recent years. There is nothing in the application of the simile which implies that the obstacles to recovery should not be removed, if they can be determined and are removable. Even Helmholtz, who stressed the imperfections of nature,³⁷ indicated the extraordinary and remarkable results achieved by it.³⁸

In the original draft of this work a section, equal in length to the remarks on teleology, was included to discuss so-called organismal biology. After considerable deliberation this project was dropped since in the interim excellent reviews of the subject have appeared. Among them the frequently cited works of Woodger and Bertalanffy may be mentioned, the second containing an excellent bibliography up to 1932. Although organismal biology sur-

mounts the mechanistic-vitalistic difficulty by assigning many problems to psychology, the residuum is perfectly compatible with the thoughts expressed above. The fundamental of life is the organization and order of processes which are so arranged that disturbances conditioned by extrinsic or intrinsic factors tend to be eliminated and the original situation restored in that events are set in motion for the production of original systems. Likewise it has been possible to omit the "Gestalt" theory and related ideas since, in general, the fundamentals are included in the remarks on teleology and elsewhere throughout the text.

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FINAL SUMMARY.—The primary object of this study has been to provide a source of information about certain aspects of the simile problem. If successful, the various tenets can be examined by medicine as a whole, the valid features incorporated into medical science, the errors discarded and a united medicine can step forward. To accomplish this end two possible methods were available: the work might be historically and philosophically oriented or it could be largely experimental. In more capable hands both might have been skillfully welded together. After considerable deliberation the first approach was adopted and the following conviction was responsible for the decision: it is the domination of the mechanistic conception and not the presence of facts which has occasioned medicine to slight the simile. Several former and contemporary colleagues who kindly read the manuscript complained that they missed the "scientific" by which they meant the microscope, the kymograph, etc. Their criticism is perfectly valid. On the other hand if past judgments have been formed chiefly from opinion and hearsay, it seems worthwhile to attempt to initiate interest by an appeal to convictions. Perhaps now that a partial guide has mapped out a course through a maze of relatively inaccessible literature it will be easier at a future date to omit the historical aspects, to enlarge the philosophic phase which has been superficially treated and to introduce modern clinical and experimental evidence.

The current dominance of the natural sciences at present is reflected in the almost universal tendency to explain all nature physico-chemically. But it is clear that at present science is not able to do this. A search is being made for building stones; but the organism is a totality which cannot be comprehended from its building stones. Until a living organism can be built from physico-chemical structural elements, it is doubtful whether one can legiti-

mately speak of a truly *exact* natural scientific analytic explanation of the *living*. Since the living organism cannot be explained exactly then it would seem doubtful whether this method ought to serve as the *exclusive* basis of investigation for synthetic biological science and thinking.

The success with which industry operates in the inanimate world may be legitimately ascribed to ability to work with constant conditions and few variables. The relation between cause and effect is simple and often susceptible to exact mathematical treatment. But in the living, what is constant when "everything flows"? What is the cause when everything is variable? A considerable part of the text proceeds from the observation that there is never a single cause for a living event. A simple example reported elsewhere may illustrate this: Hornbeams are planted on arid poor soil in which they will not thrive. In time some vanish, some are misshapen, mutilated dwarfs reaching a few centimeters in height. On the other hand, a few are covered with pine twigs which are renewed from time to time. These grow to the height of six feet. What is the cause? Among the known are the following: wild animals which bite hornbeam will not approach the pine covered plants because the sprigs crackle. They will not mutilate the plant because of the discomfort endured by contact of the head with pine needles. The pine sprigs hold water. They protect the foot of the plant from the reflection of the sun. The falling pine needles provide fertilizer. The pine sprigs prevent destruction of the foliage by winds. The sprigs furnish protection and domicile for beetles, wood lice, worms which work the soil. They furnish bacteria the opportunity to develop and affect the soil. These constitute the known factors; presumably an infinite number of factors remain unknown. Moreover there is a reciprocal action of the factors. If water was not retained by the shaded soil the insects and bacteria could not thrive in the numbers and diversity necessary (Bier).

The same complex situation exists in regard to "causal therapy." There is no doubt that acid and base neutralize each other "outside" of the organism. But if corrosive acid A is swallowed it unites with all the "a" factors of the esophagus and stomach and in a few moments is no longer demonstrable. A corroded mass supplants the normal esophageal tissue. The administration of alkali Z permits neutralization of acid A, but is certainly not causal therapy. It cannot reverse the Aa reaction, moreover, it may produce further corrosion by alkali Z reacting with components z. There is no reason for assuming that components a and z are identical or that Aa and Zz are reversible. The fact that

alkali Z neutralizes acid A in a test tube has little bearing upon the biologic situation, among other reasons since the endogenous complex, Aa, is no longer a pure physico-chemical question but a biological problem.

The situation may be followed one step farther: Acid A is neutralized by alkali Z in a test tube. The transference of this idea to the body finds basis in the allegation of "causal" therapy of certain gastric disorders in which hyperacidity is presumed to be the cause. Overlooking entirely that hyperacidity is an event far along in the causal series, that fact remains that the administration of alkali Z will neutralize acid A, but in addition to this heteronomic event, and in opposition to all known physico-chemical laws, an autonomous secretion of acid occurs. As v. Noorden recently pointed out "alkalies are the strongest agents for the release of gastric acid." One notes here the combination of a pure mechanistic event with a biological one.

The same general ideas are carried out in research investigations. A given event of the organism may be associated with a number of conditions in which factors A participate in 15%, B in 13%, C in 10%, etc. In research according to physico-chemical laws factor X has particular interest for the investigator concerned; in order to demonstrate its "causal" nature it is emphasized so that, in artificial intensity, it participates in 90% of the event. Another investigator stresses factor M similarly and finds it to be the "cause." Whether or not such fixation of conditions and emphasis of single factors represent biological investigation must be left to the reader. But the extreme danger of mixing exact natural scientific data with biologic observations which are not comprehensible according to physico-chemical laws ought to be obvious.

Heisenberg, the recipient of the Nobel prize, recently pointed out that the conceptions of classical physics cannot be transferred even to atom physics; moreover classical physics is a strictly closed system which is not designed to comprehend entire reality. If classical physics forms a closed, non-transferable field to the apparently closely related atom physics, one ought to consider the justification of applying it to an obviously remote subject such as the biology of the living organism. It seems hardly necessary to state that the above is not intended to suggest that biological thinking is not causal thinking, for acausality is synonymous with chaos. On the other hand there is the distinct implication that in addition to mechanistic causality, a biological causality exists.

Considerable attention has been paid in the text to the fact that phenomena and processes in free nature do not proceed according to the laws of physics and chemistry (with the possible exception of

the movements of planets). If laws almost never appear pure and free in nature, the opposite situation prevails regarding rules, whose characteristic is frequent free appearance. The law involves fixed and known conditions and knows no exceptions; but the organism does not know fixed conditions as long as it is alive. In fact the organism acts as if it opposed fixation of conditions, if the example of acid-alkali is valid. If the organism merely follows physico-chemical laws, if the injection of acid into the blood proceeds merely mechanically, the terms regulation, isotonia, isionia, isothermia, etc. are meaningless because they imply that the organism attempts to oppose every physico-chemical assault.

The essential rule advocated in the text may be stated as follows: The body maintains itself and heals diseases itself. In other words the acts of the body are purposeful to the end that the organism and its kind may be maintained. Whether the purposefulness of actions is accidental or not need not be discussed here. If the rule advanced above is valid, the body does not behave simply passively but also actively. As a corollary to this view, a division of the phenomena of disease into two series was advocated: 1. passive (suffering) symptoms induced by the injury; 2. active (reaction) which serve as defense against the damage. The first must be attacked; the latter supported if the suggestions advocated in the text are adopted.

An attempt has been made to indicate clearly that no single therapeutic tenet is sufficiently broad to embrace the infinitely variable, indeed, composite phenomena of disease and the acceptance of simile thinking does not and cannot involve the acceptance of an exclusively valid rule of procedure. The nature of disease and the "if-then" nature of rules require the consideration of the simile only under certain conditions. Moreover it ought to be clearly emphasized that since medical technic often accomplishes much more than nature, the simile does not involve therapeutic resignation. Again attention has been directed to the relative nature of conceptions such as "useful" and "injurious" and the complexity of "active" and "passive" symptoms.

Since none of the problems with which therapeutics is occupied at present may be regarded as solved, the domain of applicability of any particular therapeutic rule will continually vary as advances are made in medicine. This seems especially true since there is ample evidence to suggest that medical technic can often accomplish more than unassisted nature. For this reason the true and ultimate significance of the simile cannot be evaluated at present.

If it is conceded that responses of the body, such as fever, anti-toxin formation represent active useful events, it would seem that

medicine ought to consider enlarging its armamentarium beyond removal of obstacles to recovery by actively enhancing those phenomena which represent useful restorative defensive events. At least recognition of the protective nature of responses ought to minimize thoughtless and dangerous intervention designed to depress or suppress prominent symptoms which may represent extremely useful reactions.

The search for discovery of measures augmenting defensive responses can proceed along various lines. A beginning may be made by observing what phenomena are associated with cure of disease; then a search may be made to ascertain what stimuli are capable of inducing similar phenomena in the healthy body. This is essentially the simile as a finding principle. As an observational rule, an "if-then" event which occurs with sufficient frequency to permit it to be regularly observed, it cannot be explained.

As a finding principle there is the presumption that the field of possible therapeutic application of the stimulus can be determined only by experimentation. This experimentation involves the administration of single stimuli in various forms and amounts, by different routes, and for periods of varying length to the healthy subject, including the human test object. The exclusion of the human test object and restriction to isolated events or organs of lower animals require the interpolation of "as-ifs" which are misleading, unnecessary and unjustifiable if a strictly "scientific" attitude is to prevail. The limitation to healthy subjects is naturally a temporary boundary which may be set aside as soon as results in the normal permit interpretation of findings in the abnormal. On the other hand restriction to healthy humans and the exclusion of animal experimentation tend to lead to mere symptomatic comparison and the primitive application of a superficial simile. If investigators would employ experimental studies in animals partly for the purpose of making observations comprehensible in place of exclusively looking for new facts, the supplementary nature of both procedures would become obvious.

In order to test this contention, it would be necessary to review the history of therapeutics to determine whether or not substances have been found by this method. Peculiarly enough no writer has written an "applied" history of therapeutics. Many believe that the highly treasured medicinal substances, which have been handed down from antiquity, were discovered by accident. Perhaps this is true. On the other hand, medicine would have a rather gloomy outlook if advances in therapy are to depend upon fortunate circumstances rather than a guiding rule. Recently medicine has employed another finding principle in the deficiency diseases, to

employ the term in a broad sense, with splendid results. The outlook in this direction appears to be very bright. But the discovery of one route ought not to close other avenues. How the ancients discovered valuable remedies is a matter for speculation; but it is difficult to discover any "chemotherapeutic specific" remedies whose discovery and modus operandi is incompatible with simile thinking. If one turns to the modern era with the remarkable achievements of specific immunotherapy, vaccine therapy, desensitization methods, the compatibility is even more striking. Moreover if the viewpoint of an outstanding worker, v. Behring for example, can be accepted, there is strong reason for believing that he was consciously guided by simile thinking. But even if these are matters of speculation, accredited workers who are still living assert that remedies have been and can be found in this manner. Reference may be made to the studies of A. Bier on ether and sulphur. If digitalis causes and cures auricular fibrillation, if arsenic causes and cures various disorders of the skin, to mention merely a few examples, it would seem that medicine might scrutinize the equipment available in curative pharmacotherapy in order to determine how far the simile is applicable as a finding principle. Does ergot cause and cure any forms of gangrene? Does thallium cause and cure any forms of alopecia? Do snake venoms cause and cure hemorrhagic syndromes? It is hardly an exaggeration to state that the question opens an enormous field because almost the entire knowledge of toxicology could be invoked in this direction.

Inspection of medical literature reveals considerable agreement in so far as the employment as the "etiologic" simile is concerned. It has been suggested, in connection with the studies of Richter and Landsteiner, that this idea may be applicable more extensively than many believe.

It is clear that this principle will be more extensively useful in prophylaxis than the treatment of some diseases. The nature of disease suggests that the possibility of a "causal" therapy in an etiologic sense must often fail. In the second line the simile involves anatomico-pathologic considerations. In view of the time element in biology, it seems reasonable to assume that elimination of the provocative element, while fundamental, should go hand in hand with the excitation of reparative processes in the involved organs. The problem of organotherapy finds consideration here, at times primarily, at times in conjunction with the etiologic factor. The third line is formed by the disturbances of function as revealed by objective and subjective phenomena. In the past the latter has received much emphasis, not merely because of the ease with which

they can be elicited, but also because they are more susceptible to therapy.

The final evaluating feature is represented by the prognosis. There is every reason to believe that the decision furnished by the prognostic considerations will determine whether or not the simile thinking can be applied successfully to the particular case concerned.

It will be perceived that the evaluation of the pertinent evidence requires expert training and that unskilled application may not merely fail but may be disastrous in single instances.

It is also evident that the application of this idea involves, in fact, demands more extensive individualization of patients than is usually in vogue. A knowledge of the totality of a symptom as well as the totality of symptoms is required.

Related to the application of the simile principle, but not limited to it, is the field of applicability of the minimum effective dose, if this term may be employed for comparison with maximum tolerated doses. If the effects of a drug differ not merely quantitatively but also qualitatively, according to the dose, here is a practically untilled field in therapeutics. The available evidence indicates the simile operates through monophasic effects. It is highly probable that other methods of thinking might also utilize this domain more extensively and effectually.

It may be anticipated, however, that operation in this field which involves intensities of a "biologic strength, will demand consideration of all the conditions under which the stimulus works. The dose is important but the other factors reviewed should not be neglected.

The most reasonable explanation of the simile available at present involves the presumption that the body tends to maintain a functional norm. Reversible deviations from this norm tend to set into operation certain phenomena whose chief characteristic is the re-establishment of the norm. The simile presupposes that this intrinsic tendency can be supplemented and actively assisted by the employment of suitable stimuli. Because of a non-specific increase in irritability and the desirability of the production of monophasic effects, relatively small amounts of "drugs" seem desirable. Teleologically expressed, the phenomena of disease consist of injury and reaction to the injury. The reactive phenomena are useful, defensive devices tending to maintain the organism. As such they may be rationally imitated. The phenomena of direct injury are not susceptible to management by the simile. In this case it would be thoroughly unimportant whether or not the current method of applying the simile is correct or not. The important feature would

be an appreciation of the "protective" nature of such phenomena and an active participation on the part of the physician. For those who do not accept the teleological method of consideration, the newer organismal biology will be found equally compatible with simile thinking. If one prefers to remain upon purely pharmacologic grounds, it is suggested that the Köttschau rule of typical effects furnishes the most acceptable pharmacological observations in the field of the simile. Until "stimulation," "depression," "irritability," "excitability," "action," "effect," "influence" are better understood, explanations may serve as useful excitants to investigation. But here, as in all fields of biology, it is premature to say "how" or "for what purpose" when the "what" is practically unknown.

In conclusion it is hoped that some of the objectives set forth in the Preface have been attained, at least, in part. Many subjects of interest in this connection have been omitted since the recital might easily prove tedious to the reader. Undoubtedly some over- and understatements will be found and the writer will be the first to appreciate correction of these or other defects which may have unintentionally entered the study.

With a keen awareness of many defects in the presentation, many of which have been created by condensation of material, and the probable existence of many equally glaring difficulties which the writer has overlooked it seems particularly fitting to recall the remark which Ockley made in the Introduction to his "History of the Saracens": "If any one should pertly ask me, 'Why then do you trouble the world with things that you are not able to bring to perfection?' let them take this answer of one of our famous Arabian authors: 'What cannot totally be known, ought not to be totally neglected; for a knowledge of a part is better than ignorance of the whole.'"

It is in this spirit that this work is submitted in the interest of a united medicine.







