HOMŒOPATHY
AND
CHEMOTHERAPY

by

Dr. O. LEESER

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FOREWORD

THESE lectures were given, in the summer of 1943, in response to a request from a number of German refugee doctors in this country.

Hence the standard of knowledge assumed is that of a non-homoeopathic general practitioner.

The publication has as its sole aim to get diverging schools of medical thought and method better acquainted with each other. With this end in view, a topical problem of contemporary Medicine is examined.

O.L.

High Wycombe, Bucks.

July 1945.

Chapter I

AN INTRODUCTION TO HOMOEOPATHY

In this introduction no attempt will be made to give anything beyond a rough sketch of the method known as Homoeopathy. Indeed, once you have realised that we have to deal with a wide field of applied scientific knowledge—a subject still omitted from the ordinary medical curriculum—you will not expect more than a bare outline.

I would suggest that as practitioners you can best approach homoeopathy by regarding it as a method, indeed, *the* method, of individualising the application of medicines to the sick person. In homoeopathy it is not merely a question of considering the patient as an individual, a particular disordered living entity, but the medicinal substance too is taken as an individual entity and selected according to its particular merits or effects on human beings as observed by previous tests or experience. The trend of academic medicine is to generalise, to diagnose and to treat *illnesses* and their causes as far as these are accessible to diagnosis and treatment. The trend of homoeopathy is to individualise, to view and to treat each patient as a *person* suffering under and from particular conditions.

It may be safe to argue that both these approaches to our problem of re-establishing the patient in good health have their merits. On the other hand, it is obviously unwise to neglect one

of them if it holds possibilities which are denied to the other. And it is only after close study of both methods and a practical acquaintance with each that a fair judgment can be formed as to their scope and limitations.

I do not propose to dwell to-day on the historic aspects relating to the divergency of methods in Medicine. Interesting as is the study of the growth of applied knowledge in the course of the past century, it would, I suggest, reveal shortcomings on both sides. Furthermore, the task that lies before us is to help you to understand a method which receives no attention in ordinary medical education. So I will assume no more than the common knowledge that homoeopathy is a method of applying the principle of *similia similibus curentur*, which has become a mere catch-phrase expressing the principle of similarity and its use in Medicine. Hence the name " Homoeopathy " derived from ὅμοιος=similar, and πάθος=suffering, disorder, illness.

There may be some who share in the common error of assuming that this method centres on posology, in particular on the minimum dose ; but these start at the wrong end and are therefore unable to grasp the basic idea. Then there are those who confuse a methodical principle, a practical plan, with a dogmatic axiom, and therefore dismiss it as unscientific. Indeed, through their misapprehension they are even barred from a channel of thought which would take them in a new direction.

The principle of similarity, of the existence of some likeness between the sick person and the

helpful agent, is as old as Medicine itself. Homoeopathy is the break-away from its instinctive and pre-experimental use to the establishment of a scientific method based entirely on experimental knowledge. Similarity of symptoms, of effects on the human being : this is the subject of comparative study. The effects of natural substances, such as are employed for medicinal purposes, are expressed in signs and symptoms. So are the effects of noxious causes and conditions, those disorders which we as doctors are called upon to remedy.

Thus, if we are to choose the medicine which has been proved to provoke symptoms similar to those that are observed in our individual patient, the crucial question which arises is, " What is the meaning and significance of symptoms in the disordered process of life ? " *Theoretically* it all hinges on this conception of symptoms. For *practical* purposes all depends on how the knowledge of symptoms is secured and applied.

Let us take the practical side first. Signs and symptoms of any disease are, of course, a matter of direct observation, either by the patient himself or by an onlooker, including the doctor. Exactly the same applies to disorders provoked by any given substance which we call poison whenever the effects exceed an undefined degree of abnormality. We recall the inflammation of the throat from Belladonna ; the nephritis from Arsenicum or Phosphorus ; the intestinal ulcers from some Mercury salts ; all of which may, by their appearance, be indistinguishable from the signs occurring under other conditions of diseases. It is always

the same kind of organism which reacts in similar ways to various causes. The lesions from poisonings, however, provide only a very crude and insufficient level for comparing drug effects, and signs and symptoms of disease. To gain an adequate knowledge of drug effects, as required by the homoeopathic method, planned experiments have to be made ; not on animals unable to describe their symptoms, but on human beings, the same species which we expect to respond to our medicines. From experiments on animals we can learn only the crude poisoning effects and some intermediary stages of the processes leading to them.

Comparison of similar symptoms, to be of use, must aim at the distinctive individual features, such as can be supplied only, or at least mainly, by the psychosomatic unity of the human organism. It is therefore a pre-requisite to test the substances intended as homoeopathic medicines on the healthy human organism. This was realised by *Samuel Hahnemann*, the founder of homoeopathy as a scientific method, the centenary of whose death on July 2nd, 1943, passed almost without notice in these eventful times.

A new *Materia Medica* had to be built up with all the human traits such as we encounter in our patients. The signs and symptoms known from cases of poisoning or from experiments on animals, when such have been noted, form no more than the foundations of such an elaborate edifice. For example, Arsenicum, as well as Veratrum album (misleadingly called White Hellebore) may both produce, amongst other effects, a severe enteritis, indistinguishable by the local symptoms. But such

features as have been revealed by these experiments on man—" provings," to use the technical term—make the distinction easy. The sufferer from Arsenicum has his worst hours just after midnight, 12-2 a.m., while with Veratrum album the worst condition is seen in the early morning hours, 4-5 a.m. The intense thirst for cold water of Arsenicum is quenched by frequent small draughts ; that of Veratrum album demands great quantities which, however, are ill tolerated and often immediately vomited. Fears and restlessness dominate Arsenicum ; a state of stupor, which may alternate with mania, is characteristic for Veratrum. In the case of gangrene one may have to distinguish Arsenicum from Secale cornutum, ergot, and then it is important to know that the arsenicum patient is worse from cold, the ergot patient relieved by cold applications ; though in both, the limbs or the whole body may feel icy cold. Such distinguishing features, *modalities* as they are aptly called, could only be obtained by the observations of the prover or patient himself, able to express his sensations, emotions and impulses.

These few examples, of course, give only a glimpse of the subject. To give an outline in some measure adequate to the accumulated knowledge and the requirements of an educated homoeopath is impossible in the time available. Even assuming that for each of the above, Arsenicum, Veratrum album and Secale cornutum, the main toxicological facts are already known, an hour for the discussion of each would barely suffice.

When we recall the hundred or more well-proven

drugs, not to mention several hundreds more or less fully proven, it will be readily seen that to deal with the homoeopathic *Materia Medica* would require many lectures. Your knowledge of pharmacology and toxicology, extensive though it may be, forms but a mere stepping stone to this wider and far more detailed study of pharmacodynamics. And though academic pharmacology and toxicology may have impressed you as being particularly boring subjects, you would still find these, as it were, living, humanized drug pictures most enlightening and interesting. Enlightening with regard to the sick patient as well as to the manifold substances of Nature in their interrelation to Man.

It is this teaching which you have missed in your academic education and which, I am sorry to say, is not yet adequately provided for. Homoeopaths have so far failed to impress the profession with the need for such a new and advanced school of *Materia Medica*. It is this very knowledge of pharmacodynamics which makes, and is the measure of, a homoeopathic doctor.

The application of such knowledge follows almost automatically ; there is no place for dogma and sectarian faith. For how else could you possibly use these data but by comparing them with the data gained from observing your patient ? What else could guide you in selecting the individually fitting remedy but the similarity of symptoms ? Facts as symptoms *are* or *are not*, but they have no *contrarium*. Or what is the contrary of headache ? The non-existence of corresponding symptoms in the pharmacodynamics of a drug would

obviously be a valueless key for unlocking the patient's symptoms. Though there is no other way of utilising the noted symptoms but by comparing them as to similarity, why are we to assume that a medicine thus selected should be the most suitable to assist the particular patient? The pragmatic mind would answer, Assume nothing, but test and see. That is not within our province here, but a little thinking will convince us that at least we have a good chance of assisting the patient with the remedy able to elicit symptoms similar to those he presents and feels.

As I said, the problem hinges on the meaning of "symptoms." If symptoms were all there is in illness, if they were the only trouble, as the prejudiced patient may suppose, then surely provoking more and similar symptoms would be an absurd proposition. It would be uncivil to suppose this level of primitive thinking in any physician. To him the symptoms are outward signs of disordered life processes. These processes themselves are due to the interaction of noxious causes or conditions with the human organism. The signs are given by the organism, indicating its reactions to the noxious agents. The symptoms in themselves are neither good nor bad, neither friend nor foe, but they come from the side we intend to assist.

In giving the simile, or better *simillimum*, the medicine apt to provoke the most similar syndrome, our aim is not to intensify the symptoms but the reactive processes of the disordered organism. That is obviously a good plan in all those cases where the defensive activities of the

organism are insufficient to overcome the noxious influences within certain time limits, where the disorder tends to become chronic or is so already. Where the reactions of the organism are up against insurmountable obstacles, say a gallstone too big for passing the gall duct, it is clearly useless to give the stimulating remedy. However, the great majority of cases calling for our help are of the kind which may benefit from speeding up, broadening or intensifying the defence activities. Those acute cases which develop to a speedy and complete recovery by themselves we may leave alone altogether.

There is, however, little doubt that in some situations, stimulation in the proper direction by means fully under our control may be vital. Indeed, you are quite used to the principle when you prescribe ipecacuanha or ammonium salts or any so-called expectorant in bronchitis, or a purgative in certain diarrhoeas. The remedy, however, may be chosen somewhat indiscriminately, on a very low homoeopathic level, as it were. Clearly, if you had the better fitting tool, you would need less force. That is exactly the position, once you have learned to see the medicinal substances in full, as individuals, and to discriminate between them. The more you know of their pharmacodynamic properties, the better you will be able to choose the remedy which best fits your particular patient. Thus, homoeopathy is the knowledge, which may become a highly developed art, of finding the individually fitting

remedy, from the patient's symptoms on the one hand, and the elaborate, quasi-personified drug pictures, on the other.

As I said, we aim at the defensive reactions of the organism. But in giving a stimulant tuned in by means of signal symptoms, we may well intensify the patient's symptoms too. He might feel an aggravation, and in the case of a chronic disease, perhaps an acute outburst of the original trouble. There is, however, no danger involved. First, the medicinal substance does not add to the original causes and conditions of the disorder; we have given a simile upon symptoms, not an identical cause of disease. Active immunotherapy takes this latter course in infectious diseases, but then the specific germ product is dead and attenuated, and moreover, carefully controlled as to dosage. Equally, we have the simile under our control. It is given only when stimulation of the defensive activities is required and then, by diminishing the dosage, we are able to restrict the extent and intensity of reactions almost at will. With some skill the initial aggravation of symptoms can often be kept at a level unnoticed, or scarcely noticed, by the patient. But if he feels and reports it, and if it corresponds to our expectations within a certain time limit, we are so much the surer that the remedy acts according to plan, and that in speeding up or completing the recovery of the patient to normal health it has played its part.

In chronic diseases this reactivation may sometimes take even astounding forms; for instance, when in an asthma cure an almost forgotten

eczema-residue of many years standing becomes acute and spreads all over the body, then the asthma attacks cease and much later the skin eruptions come to an end. Such occurrences greatly modify our habitual all too simple conceptions of chronic diseases, and open possibilities of removing inveterate, deep-seated derangements by arousing the past condition of the patient, where it took the faulty turn,—*acheronta movebo*—as is done in psycho-analysis.

As already stated, one means of controlling the reactions to the individually fitting stimulant is to give and repeat the dose at the proper time; another and more intricate one is to choose the optimal quantity and form. As to the quantity, we face the famous homoeopathic minimum dose. That the dose has to be diminished to such a degree as to avoid unnecessary aggravation goes without saying. How far one has to scale down the dosage is obviously a matter of experience. But there are one or two dominating factors to be kept in mind. The more delicate the balance of the disordered processes, the more subtle the stimulative push required; hence, in general, constitutional and chronic disorders require and respond to subtler dosage than acute diseases. Further, the better the remedy fits the individual case, the less medicinal energy is needed. For these and other reasons, it oftens happens that the weight of the medicinal substance is no longer an adequate measure for the particular task. Just as with vaccines you soon leave behind mass and weight and resort to dilutions, 1 : 10, 1 : 100, 1 : 1,000,000, and beyond, so in homoeopathy a

scale of dilutions or "potencies," as they are called, is established. They are prepared by a special technique designed to liberate and enhance their potential energy. We shall come later to that point.

Every homoeopath is free to choose from this scale of preparations, from the ponderable mother substances to the highest, *i.e.* most highly attenuated, potencies, whatever he thinks optimal for the case before him. He may gain his own experience with or without regard to his teachers or fellow-homoeopaths. There is therefore no need to go into the antagonistic views and arguments on these points within the homoeopathic ranks. We may well leave that to investigation and experience on a broader scale, brought about by a future recognition of the homoeopathic method and its value for the advance of Medicine.

It is of importance to keep in mind that a medicine adapted to a particular situation is not a food, not even on the vitamin level ; in a chemical sense it is not part of a mass equation, but comparable to a catalyst-activator of processes. Thus, so long as there are molecules of the original substance, the scientific chemist has no difficulty whatsoever in attributing results to their interaction with an unbalanced equilibrium of life processes tuned in, as it were, to this particular catalyst.

Considerations from the point of view of the physicist are of even greater importance for the problem of the homoeopathic dosage. The energy of a medicinal dose depends not only upon the quantity but also on such structural factors as

solubility, surface, distribution in another medium as regards distance and regularity of particles. The homoeopathic preparation obtained by the procedure of so-called potentizing is not a simple attenuation on the decimal or centesimal scale. It achieves increasing degrees of sub-division and regular distribution of particles in a second medium. The progress of sub-division, of distancing and regular distribution in an indifferent medium, is in direct proportion to the potential energy of the medicinal particles. Experts in physics will readily substantiate these assertions by laws and formulae. Within the sphere of the lower, that is, the less attenuated, potencies, say up to the 6th decimal (or 3rd centesimal), being one part of medicinal substance to 1,000,000 of medium, these facts are conspicuous, because they lend themselves to investigation under the microscope or in the test tube. For those acquainted with the physico-chemistry of colloids it is unnecessary to comment further on this point. The ingenuous, simple, but subtle technique of homoeopathic preparation aims at and achieves exactly the structural qualities mentioned.

All insoluble substances, as well as many soluble ones, are subjected to the process of trituration. One grain (0.06 gramme) of the medicinal substance is triturated in a mortar for one hour with 99 grains of sugar of milk. The product is the first (1) centesimal potency. You will note that no human effort is spared, and on a very small quantity at that, to do the job thoroughly. One grain of the first centesimal potency together with 99 parts of fresh sugar of milk is triturated in exactly the

same way for another hour and gives the 2nd centesimal potency ; and in a third hour 100 grains of the 3rd centesimal potency are made from 1 grain of the 2nd to 99 grains of sugar of milk. At that stage the sub-division of particles is sufficiently advanced to proceed by solution and succussion in diluted alcohol. The latter procedure is applied from the onset to alcoholic extracts of plants and animals. These mother tinctures, wherever possible, are made from the fresh plants or animals. Alterations through drying, which often render the products ineffective, or less effective, are thus avoided. That is one reason why so many herbs of old reputation, but now obsolete and even unknown in official Medicine, are widely and successfully used in homoeopathy ; to mention only Pulsatilla, Bryonia, Aconite, Rhus toxicodendron, Chamomilla, Chelidonium, Dulcamara, Euphrasia, Hypericum, Ruta, Symphytum, Thuja, not to mention many more.

Equally, the discovery of the technique of trituration has largely enriched the homoeopathic armamentarium. Insoluble and otherwise indifferent substances like calcium, magnesium and barium salts, light and heavy metals, also Lycopodium spores, are transformed by subdivision into a state which enables direct interaction with the living system from the mucous membranes. Similar but more lasting and more easily controllable effects say, of calcium, magnesium, silver or gold may then be achieved to those produced by injecting their soluble salts into the blood-stream.

However far reaching such augmentation of our

tools may be—and of improved, refined tools at that—it is overshadowed by the prospects the principal method holds for the future of Medicine: the new conception and shape of pharmacodynamics with all its practical consequences. The actual achievements of modern Medicine, like the knowledge and use of endocrine, vitamin, and chemotherapeutic agents will not be encroached upon, but will be substantially enhanced and complemented by this infusion of new thought. To that end homoeopathy has to come out of its seclusion, incurred by shortcomings from within and inflicted upon it by short-sightedness from without. The common ground can and must be found in science and its methods, to the benefit of both "schools." It is the privilege of the homoeopath who, after all, has passed through the academic school as well, to give and to lead, being always, of course, conscious of his own shortcomings.

Chapter II

Malaria—Quinine

Homoeopathy and Chemotherapy are both methods of applying medicines in diseases. At first sight they appear totally independent of each other. The objective of chemotherapy is to achieve direct internal disinfection. It aims at destroying, or at least weakening, the germs by chemical action of the drug itself. Homoeopathy's plan, however, is to stimulate the defence of the suffering organism against noxious causes and conditions, whether germs or not. There is thus no reason, why both methods should not exist amicably together in any enlightened physician's mind and practice.

Such separation of the two methods for their different plan and purpose would, however, not take account of the ill-defined borderlines, when it comes to the factual processes, which are not necessarily in accordance with the preconceived theory. You are aware that throughout chemotherapy discussion is still going on—and nowhere the exact modes of action have been ascertained sufficiently—to decide the question, whether any particular drug acts directly, without involving the body-defence, as an internal germicide, or whether stimulation of the defence plays a dominant part in overcoming the aggressors. If the latter should be the case, chemotherapy would obviously enter the sphere of homoeopathy ;

not that it intended to do so and not on merits of homoeopathic research, but because the facts do not lend themselves to an interpretation on the line of the original plan, but point rather to a conception of drug action concurrent with that of the homoeopathic method.

The views in modern chemotherapy are still in a state of flux, dependent upon the relevant facts revealed so far. We therefore cannot do justice to the problem by discussing the present position in respect of one example, say the sulphanilamides, only. In order to obtain a detached opinion, let us follow the historical development of chemotherapy in its main stages : Cinchona bark and its alkaloid quinine in malaria, mercury and the organic arsen-compounds in syphilis and the sulphanilamides in the various cocci-infections. Each stage would have to be confronted with the corresponding chapter of homoeopathy, i.e., with the drug pictures of cinchona (or china as the old name is) and its main alkaloid ; of mercury and arsenic ; and of sulphur and sulphides.

To see the whole in its proper setting, one might further consider the many more remedies of old reputation for wounds and infections. Some other heavy metals have come lately into the orbit of chemotherapy ; penicillin has opened a great field of research promising new insight into anti-bacterial actions, and, with a fuller knowledge of their active principles, the use of plants as *vulneraria* may well have a scientific revival in a not too distant future. The time has not yet come for undertaking a comprehensive synthesis, while so many essential facts are undiscovered or

not yet seen in their proper connection. All the same, an interim survey under a comparative aspect as proposed may prove helpful for better appraising both methods.

It was the success of local antisepsis which induced the attempt of internal *sterilisatio magna.* Antisepsis and chemotherapy, though both scientifically bound up with the discovery of pathogenic micro-organisms, have their ancient empirical era. When King Mithridates and the Macedonians of old used to cover wounds with silver lamellas, they anticipated the antibacterial use of silver. Neither they nor the Persians, who by law had to keep drinking water in bright copper vessels, had a theory of the oligodynamic action of these metals, but they experienced the effect of it. The Homeric Greeks fumigated with sulphur, *Hippocrates* used antiseptic alcohol when dressing wounds with wine. The biblical Jews had numerous preventive measures against contagion, they purified the houses of the sick, had balsamic ointments for the lepers. The ancient Egyptians, experts in embalming, must have known the preserving virtues of many ætheric oils, gums and resins. Indeed, local and internal use of plants, containing such balsamica against infection from wounds, is recorded through all the centuries of human history ; the old herbals abound in such remedies for fresh and foul wounds.

For a long time the use of cinchona bark in malaria was also on a purely empirical basis, and we are going to investigate, whether or how far it can be called " scientific " i.e., whether and how far the " reasons why " are known. in our days. By one of those remarkable whims of history this

first example of alleged chemotherapy had been, a hundred years before chemotherapy was thought of, the experimental starting point also of the homoeopathic method. The idea of chemotherapeutic action could, of course, not be entertained, before *Laveran* in 1880 had discovered the plasmodium malariae. *Hahnemann* experimented with the bark ninety years before that time, in order to find a scientific basis for its long and well-established use. It is not certain, but probable that the Red Indians of South America knew this medicinal virtue of the *kina-kina*, i.e., the good bark ; for who else should have taught the one who cured the malaria of a Spanish official in Ecuador in 1630 with that bark ? Eight years later this official suggested the same cure for the malaria of Countess Anna de Chinchon, wife of the viceroy of Peru. From that cure the name of the tree Cinchona is said to originate and the treatment spread all over the world. Attempts at explaining the curative action, when made at all, were bound to be arbitrary. It was against just such vague and unwarranted speculations that *Hahnemann* stood up and invoked the decision of the experimental method. When, in 1790, he translated *Cullen's Materia Medica*, he found the author attributing the specific antifebrile action of the bark to its stomachico-tonic virtue. Then why, *Hahnemann* asked, do not much more potent bitter stomach-tonics have any specific action in intermittent fever ? And he proceeded to his first experiment on the healthy human subject, on himself, with the purpose of elucidating a known effect on the sick. This plan distinguishes his

undertaking from any previous drug experiments which may have been made on man.

As this experiment is not merely one among thousands of others, but is to be understood as a turning point of methods in Medicine, it may be as well to have it stated in *Hahnemann's* own words : " Ich nahm *des Versuches halber* etliche Tage zweimal täglich jedesmal 4 Quentchen gute China ein ; die Füsse, die Fingerspitzen usw. wurden mir erst kalt, ich ward matt und schläfrig, dann fing mir das Herz an zu klopfen, mein Puls ward hart und geschwind ; eine unleidliche Aengstlichkeit (aber ohne Schauder), eine Abgeschlagenheit durch alle Glieder ; dann Klopfen im Kopfe, Röte der Wangen, Durst, kurz alle mir sonst beim Wechselfieber gewöhnlichen Symptome erschienen nacheinander, doch ohne eigentlichen Fieberschauder. Mit kurzem : auch die mir bei Wechselfiebern gewöhnlichen besonders charakterischen Symptome, die Stumpfheit der Sinne, die Art von Steifigkeit in allen Gelenken, besonders aber die taube widrige Empfindung, welche in dem Periosteum über allen Knochen des ganzen Körpers ihren Sitz zu haben scheint—*alle erschienen.* Dieser Paroxysm dauerte 2-3 Stunden jedesmal und erneuerte sich, wenn ich diese Gabe wiederholte, sonst nicht. Ich hörte auf und ich war gesund."

" (*As a matter of experiment,* I took for some days, twice daily, a 4 drachm dose of good Cinchona bark ; my feet, finger tips, etc., first became cold ; I began to feel languid and sleepy, then my heart started throbbing, my pulse became hard and accelerated ; an intolerable anxiety

(but without rigor), a weariness through all limbs ; then throbbing in the head, flushes of the cheeks, thirst, in short, all the symptoms known to me from intermittent fever, appeared one after another, but without distinct feverish rigor. Briefly: also the particularly characteristic symptoms, experienced in intermittent fever, the dullness of the senses, that kind of stiffness in all the joints, and more particularly that numb disagreeable sensation which seems to be located in the periosteum over all the bones of the whole body—*all made their appearance.* This paroxysm lasted for 2-3 hours each time and was renewed, when I repeated this dose, but not otherwise. I left off and I felt well.) "

There has been much argumentation, whether the observations of *Hahnemann* were correct ; for some time past the power of the bark to provoke fever has been hotly disputed. Nowadays it is generally acknowledged, that amongst other symptoms, fever may be part of cinchonism, be it either from poisoning by large doses or from hypersensitiveness to small and sometimes single doses ; in the latter case termed idiosyncrasy. Thus *Hahnemann* had his facts correct ; but that does not say that his conclusions too were right. However, he did not jump to conclusions. First, it was not the single symptom " fever " which set him thinking, but the full syndrome resembling an attack of intermittent fever. Then, when struck by the similarity of the symptoms provoked and cured by the bark, he did not generalize his conception without more tests, but went on testing other drugs on this hypothesis for several years.

Lastly, when in 1796 he announced his conclusions, he did so not in the manner of an axiomatic assertion, not of a law of nature, but as a scientific method of selecting the remedy most promising for a given case of illness. He never said, *Similia similibus curantur*, but *curentur*. He was a good classical scholar. In short, his is the model of scientific procedure, despite all that has been said by minor epigones until this very day. It is for the sake of his paving a new road full of promise that we have to recognize *Hahnemann* as one of the few great masters in Medicine.

From the historical sequel of events, to which the china experiment acted as a spark, we turn back to our limited subject, the relation of china to malaria. The gist of *Hahnemann's* observations was apparently that the favourable action of the bark in malaria is part of its actions on the human organism ; it can be understood from its stimulating the reactivity of the organism in response to just such noxious agents as those of malaria. Though the specific cause was not known at *Hahnemann's* time, and though the actual mechanism of defeating the aggressor plasmodium with the help of china or its alkaloids is not yet ascertained to this very day, we have to-day some more evidence that the homoeopathic conception as outlined is in accordance with the facts.

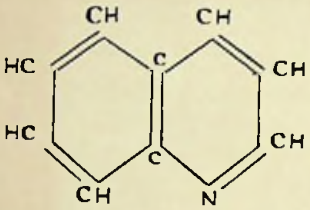
Before dealing with this evidence, however, let us take up the case of chemotherapy. The issue must not be confused by the fact that meanwhile, in 1820 by *Pelletier* and *Caventou*, the alkaloids quinine and cinchonine were isolated and that by now some twenty such alkaloids have been found

in the bark. Principally the actions of the full drug and the main alkaloids are the same, though there are good reasons rather to stick to the entire natural product in most cases. The chemotherapeutic problem is and remains : Does cinchona or its alkaloids destroy or at least weaken the living plasmodium *in corpore humano* by direct chemical action ? The answer given by the experiments available is decidedly negative. Even for arresting the motility of plasmodia in vitro, a concentration of quinine at least ten times that safely attainable in the bloodstream is required (appr. 1 : 10,000 against 1 : 100,000). Even the doubled concentration of quinine-salts (1 : 5,000) did not render, within 24 hours, malaria blood non-infectious to man ; neither did it kill plasmodium sporozoites of mosquitoes introduced into blood serum ; the serum remained infectious. (In neither case are the gametes concerned, these sexual forms are resistant to quinine anyhow, so that quinine leaves the malaria patient a "carrier".) Yet to the schizonts thriving on erythrocytes in man, life is made unwholesome by concentrations of quinine 1 : 150,000 in the blood ; the schizonts disappear from the bloodstream, some, maybe, to the spleen, or they are forced to develop into the sexual forms of gametes which are incapable of producing attacks of malaria. As matters stand at present, the case for chemotherapy regarding quinine in malaria is not only not supported by experiment, but is refuted. Several new hypotheses have been put forward in its place ; one assumes that quinine actually kills some plasmodia and, by that, sets free antigen

which would stimulate anti-body formation against the remaining parasites (*Yorke* and *Macfie*, *Lancet*, 1924, I, 1017); another assumes simply that quinine stimulates the production of immune bodies; a third, that quinine, by its surface activity, would concentrate on the surface of the erythrocytes and render them impermeable to the merozoites (sporozoites) or somehow else would interfere with the development of schizonts. All these hypotheses are so far not supported by facts, but they have all abandoned the chemotherapeutic case in favour of the stimulation theory.

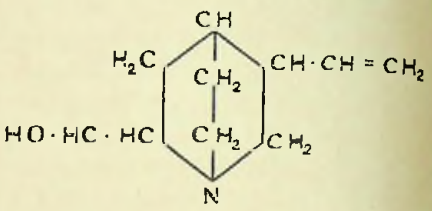
The study of the alkaloid molecule as to groups and bonds essential to the anti-malarial action (cf. table p. 28) can, of course, not alter the position as long as it is unknown with what group, be it of schizonts or erythrocytes, the alkaloid interacts. Anyhow, the preponderant action of the laevo-rotatory isomerides, (for these as for most other alkaloids,) shows that the stereo-structure of the alkaloid is important for fitting or fixing its correspondent cell molecule.

A modern textbook of pharmacology (*Goodman* and *Gilman*, 1941) summarizes the present position significantly thus: "Although quinine has been employed for three centuries in the treatment of malaria, the basis for its use is as empirical to-day as it was when the Countess of Chinchon was given a decoction of cinchona bark." That is the verdict of modern pharmacology 150 years after *Hahnemann's* experiment which it has not deemed worth while to note or to consider. True, the symptomatic likeness of china and malaria offers no explanation in an analytical sense, it does not

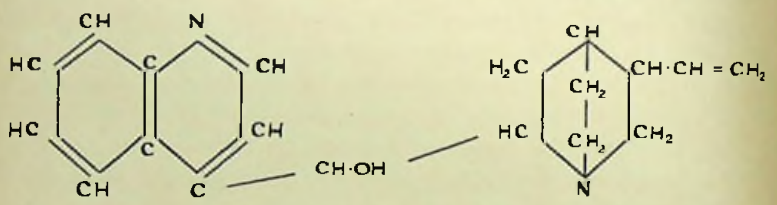


QUINOLINE

$C_9 H_7 N$



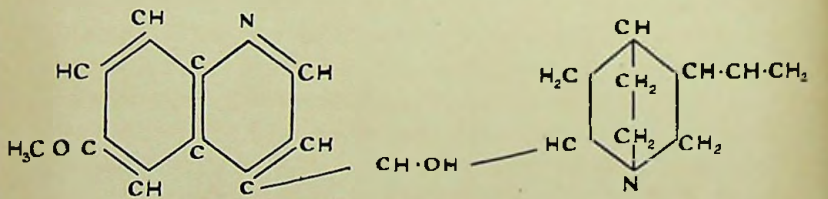
"SECOND HALF"



ISOMERIDES, $C_{19} H_{22} O N_2$

l- ROTATORY: CINCHONIDINE

d- ROTATORY: CINCHONINE



ISOMERIDES, $C_{20} H_{24} O_2 N_2$ (*p*-METHOXY-CINCHONINE OR CINCHONIDINE)

l- ROTATORY: QUININE

d- ROTATORY: QUINIDINE

reveal the actual mechanisms by which similar symptoms in either case are produced, nor the chain of intermediary processes. The china syndrome might even as well counterfeit a very acute feverish cold, beginning with a chill, followed by a sudden rush of blood to the head and palpitation and then perspiration. That is, perhaps, why a rough shot, homoeopathically rough, is sometimes made at such colds with quinine. The observations on the symptomatic plane could and should, however, have served to start thinking in the right direction about the quinine-malaria problem. Just see how well a number of known, but so far strange, facts would have fitted into this line of research and interpretation.

When there is diagnostic doubt about a latent malaria, one way of provoking an acute attack is by smallest doses of quinine. Other measures are cold douches, etc., capable of causing sudden changes in blood circulation in the manner of an acute cold. The point is that smallest doses of quinine can, in latent malaria, provoke similar changes in blood distribution and, by that, make the case acute. The subdued but unconquered schizonts may have lingered in the spleen and perhaps liver ; by the gentle quinine stimulus they are brought into the bloodstream again, the open struggle between the schizonts and the protoplasm of the red corpuscles is renewed, schizonts break up erythrocytes and cause the rigor phase followed by fever due to the unloading and spreading of toxic protoplasm. Though initiated for purely diagnostic purposes, this occurrence is an example of how by a fitting drug in smallest dose a latent,

chronic disease can be transformed into an acute one. One might well assume that also in the case of malaria this is all to the good, because one would not feel happy about a chronic struggle of the schizonts within the depth of the spleen, with the possible end in kachexia with severe anaemia, spleen and liver tumor, ascites and the rest, but that is another story. Suffice it to say that the fact in itself confirms the similar trends of quinine and plasmodium-malariæ-effects or, better, of the reaction of the organism against both of them; this is just what *Hahnemann's* experiment on the non-infected person could have revealed.

And what about the masked malaria attacks which may occur many years after the infectious process has ceased, when no more plasmodia are to be found or even suspected? These pseudo-attacks of general malaise, headache or neuralgias with the typical accompaniment of chilliness, heat and sweat, still counterfeit the china syndrome. Maybe, non-living residue toxins are still released from their cell fixations at intervals. The similarity which is not one of causes but of sequels expressed in symptoms, and the beneficial use we can make of it in such a situation, remain all the same.

Then think of the rôle of quinine and malaria in black-water fever. No doubt this haemoglobinuric crisis is part of certain malaria cases. The causes of this predisposition to haemoglobinuria are still obscure; one condition may be a low level of cholesterol which protects the erythrocytes against haemolysis. There is, however, no doubt either that this malignant haemoglobinuric fever is provoked or precipitated in

most cases by quinine, according to *Nocht*, in 99 out of 100 cases. Further it is significant that this mostly happens right at the beginning of the first quinine treatment. Yet concentrations of quinine corresponding to medicinal doses are certainly unable to bring about haemolysis *in vitro* (that needs approx. 1 : 500); on the other hand there is the fact that in some cases of oversensitiveness as well as of poisoning, haemoglobinuria from quinine has been observed. It may be that similar predisposing conditions, e.g. low cholesterol level, are also responsible here. The point is that again the plasmodium and the quinine affinity to the red blood corpuscles appear similar in producing, under certain conditions, the same sequels and that, therefore, we can probably expect a similar mechanism in their interaction with the red blood cells.

To the schizonts, the asexual, schizogenetic, phase of the life-cycle of plasmodia, erythrocytes are the indispensable medium on which they prey and thrive. It is with their recurrent partition in the red blood cells that the quinine interferes; how exactly, we do not know; but it is an important fact that only those quinine derivatives which can penetrate red blood corpuscles have shown this effect on the life of the schizonts (*Hegner, Shaw* and *Manwell, Am. J. Hyg.*, 1928, VIII, 564). The development of the sexual gametes in erythrocytes is not hampered but may even be favoured by quinine, but then they can no longer provoke malaria attacks, but need the alimentary duct of Anopheles to complete the sexual phase of their life-cycle.

All the facts suggest that quinine, by its own affinity to erythrocytes, is able to deteriorate the living and propagating conditions of the schizonts in the red cell protoplasm. Not a chemical affinity of quinine to schizont, but the competitive affinity of both towards erythrocytes is at the bottom, and as both show similar effects, the unknown mechanisms too are likely to prove similar. Whether quinine spoils the protoplasma food or releases lysins or any other anti-bodies from the red blood, it means stimulating the defence. That is the interpretation already forced upon us by the apparent similarity of syndromes expressing the respective responses of the human organism as a whole.

It would follow that china or its alkaloid is a suitable homoeopathic medicine in malaria. So it is, but not for all cases the most suitable. Great personal differences as to sensitiveness to quinine are seen ; the particularly sensitive cases would appear the most promising ; they would respond to very small doses ; while those for which quinine is only a rough shot, obviously require massive doses of it, not always avoiding the Scylla of cinchonism or the Charybdis of repulsion of the malaria into the spleen, thus making it latent and chronic. These patients may, however, yield better to another more fitting remedy, say, arsenic. Though the main features of the three malaria types are fairly constant, personal variations of the accompanying symptoms may point to another of the many drugs able to provoke fever of the intermittent type.

On the other hand, the malaria-likeness is only

a very limited cut-out of the homoeopathic drug picture of cinchona. Indeed, the total picture presents so many likenesses to various common disorders that china is frequently called for in homoeopathic practice. These indications can, however, not be enumerated by so many diagnoses; such abstracted typifications remain too far removed from the particular china case. Even less applicable are generalizations of the drug action, such as *roburans*; they are merely empty frames. The picture itself must be drawn from true observations, and to be recognisable, it needs to distinguish the characteristic traits.

For a brief sketch we may well start from that part on which some light has already been thrown from its malaria likeness, the affinity to circulation and blood cells. The sudden changes of blood afflux, of chills, heat and sweating, indicate a peculiar rhythm of action, what our medical ancestors used to call "erethism." Animal experiments showing short contraction of smooth muscles followed by prolonged dilatation do not tell us more but less than what we can learn from *Hahnemann's* vivid description of his sensations. A step further in this process of action on the blood vessels, we encounter the tendency to bleeding from various organs or into the skin or mucous membranes. Uterine haemorrhages are particularly marked from china; too early and too profuse menses. To this effect the influence of quinine on the tonus of the uterus may well contribute. It is known from its use as abortivum, the miscarriages of women workers in quinine

factories and also from its now rare use for intensifying too weak labor intra partum.

The tendency to bleeding in china must not be confused with the much rarer haemoglobinaemia from cinchonism. The trend towards disintegration of red blood cells however is also present and it appears connected with a distinct affinity of china to spleen and liver, the transformer stations of the blood. Icterus is not seldom seen in cinchona poisoning, not necessarily of the haemolytic kind, but also from interference with the functions of liver cells. In distinguishing china from another remedy showing similar "erethism," ferrum, one does well to remember the destructive faculty of china. The chlorotic type of ferrum, marked by deficiency in the anabolic phase of red blood cell life, has a white and rosy complexion, while that of china is an earthy or yellowish paleness, if not distinctly icteric.

The action of quinine on the white blood cells was the subject of early studies by *Binz*. He saw that small doses stimulate and large doses inhibit phagocytosis, and that then the amoeboid movements of leucocytes are impeded ; finally, the cells disintegrate. Under medicinal doses in vivo leucocytosis is first marked by increase in the number of lymphocytes, later lymphopenia with polynuclear leucocytosis occur. It has been suggested that the leucocytosis may be caused by contraction of the smooth muscularis of the spleen, but then this is followed by a prolonged relaxation. Thus an influence exerted on the formation and metabolism of the leucocytes seems far more likely. Benefit, though transitory, from china in

enlarged spleen even of leukaemic origin may be connected with this action.

A similar biphasic action of quinine was seen by *Binz* on enzymes and ferments. Very dilute solutions increase the action of the autolytic enzyme of the liver, and of pepsin and of rennet. That has an apparent bearing on another detail of the china picture as revealed by the experiments on healthy persons' "provings." Amongst the many digestive symptoms of china the most characteristic are : undigested stools immediately after eating. This "lientery" as the old physicians called the syndrome, is not at all rare, the condition persists often over many years, but china gives very satisfactroy results, as I have frequently seen. The nearest diagnosis would, of course, be achylia gastrica, though no complete degeneration of the rennet and pepsin glands is to be assumed in curable cases. When you read of achylia gastrica as one of the sequels of chronic malaria, you may well ask whether that was not due to cinchonism, just as it will often remain debatable, how much of a so-called malaria-kachexia is actually quinine-kachexia. The mixed effects of disease and drug are bound to confuse judgment on both ; the pure observations established beforehand on the healthy, on the other hand, allow a proper assessment of the rôle of the drug ; and that not in the fragmentary manner of test-tube reactions but straight at that formative and functional living organization with which we have to deal. It would be an almost hopeless task to arrive from the glass-tube tests at the regulating action of china in such a peculiar syndrome as

has been briefly outlined. Reversely, the test-tube findings may *afterwards* assist our understanding of the complex and specific process of interaction.

More and useful china symptoms in the digestive sphere would have to come into a fuller picture, e.g., the kind of flatulence, of hungry feeling without appetite, aggravation from fruit and from beer, milk being badly tolerated, and so on.

In the sexual sphere we should encounter a first phase of stimulation and then a prolonged depression of functions with great weakness.

Profound debility generally is the background of the picture, involving also the skeletal muscles. Here we remember that substantial doses of quinine aggravate myasthenia gravis or make doubtful cases manifest ; that on the other hand they, temporarily, relieve myotonia congenita, *Thomsen's* disease. Whether the early stages of myasthenia gravis are benefited by small stimulative doses has not been tried to my knowledge. The large-dose effects illustrate clearly the depressing phase of action on striated muscle ; the first, less spectacular, phase is commonly employed in muscular weakness.

A similar course is followed by quinine in the nervous system. Disturbances of hearing and vision are early events in cinchonism. When you give quinine sulphate in *Menière's* syndrome or similar conditions of vertigo, bad hearing and ear noises, you act unwittingly as homoeopaths, for this syndrome is common in cinchonism. The final effects of atrophy of auditory and optic nerves can be left out of the discussion. But the initial stages of increased sensitiveness of these

senses supply some valuable symptoms for china. Equally, with the peripheric sensory nerves, you will find the ending in numbness and anaesthesia ; quinine is known as a local anaesthetic, though long superseded by cocaine. The preceding phase of hypersensitiveness, especially to touch and draught, gives the more useful hints. Such peculiarities, trifling as they may seem, like a sensitive scalp, so that the hair is painful to touch and combing, may well sometimes give you the clue to a successful use of china.

Nervous and circulatory excitation combine in the china action to disturb the sleep by crowding ideas or fearful dreams, leaving confusion and exhaustion in its wake. You may then see the gentle stimulus of a minute dose restore normal sleep and the patient being spared the short-sighted palliation by a narcotic.

We might continue filling in many more details into our sketch and even add colour to it. Over and above the signs and symptoms from the cell and organ affinities, one would have to recognize china by its peculiar functional rhythm ; that erethism of blood and circulation and that hyper-sensitiveness coming on in periodic waves and grafted on to a state of extreme debility, a state of affairs which is often brought about by over-exertion of vital functions or secretions, losses of blood or exhausting diseases.

I am afraid we have wandered some distance from the chemotherapy-malaria problem, but then we have been confronted with the broader issue of china and homoeopathy.

Chapter III

Syphilis—Arsenicalia, Mercury, Bismuth, Iodide.

In syphilis the chemotherapeutic method has been deliberately developed, at least for the organic arsenicalia. With these, therefore, we shall concern ourselves mainly to-day. The other anti-syphilitica, mercury, bismuth and iodides can be discussed only cursorily. The homoeopathic relationship of arsen-compounds to syphilis will have to be examined more closely.

For the organic arsenicalia we shall take salvarsan as representative throughout, but we had better accept the newer name arsphenamine for it, because that recalls the chemical constitution of the compound to our minds. To begin with a practical aspect : Organic arsenicalia have proved the most effective means of rendering syphilis rapidly non-infectious. The prevention of the spread of infection is obligatory upon the physician over and above even his duty to cure the individual. In all those cases where the danger of contagion cannot be excluded, one is obliged to have recourse to arsphenamine. (In my textbook you will find this standpoint the subject of special reference.*)

Now, as to whether arsphenamine offers the best prospects for restoring the individual to complete health, that is quite a different question.

* O. Leeser, Lehrbuch der Homoeopathie, A. Die Mineralischen Armeimittel, Stuttgart, 1933.

As to the actual realization of the purpose of chemotherapy, to kill right out the spirochaetae *in vivo*, that again is another question which, for a reply, requires a critical review of the relevant facts accumulated in the extensive literature on the subject.

Let us consider first arsphenamine with regard to the biological, or at least clinical, healing of the syphilitic patient. Any conclusions must emanate from evidence as to whether syphilis in the early stage can be cured, and in what percentage, without recourse to medicinal treatment. We are here concerned only with primary and secondary syphilis. Reliable statistical matter on this subject is, quite naturally, not abundant. Still, we have access to a little. In 1929 *Brunsgaard* pursued enquiries into the cases of 309 living and 104 deceased persons infected with syphilis. These cases, in which the infection dated back up to 40 years, were all upon which there was a reliable check, out of 2,000 cases deliberately left without treatment by *Boeck* (Syphilis Clinic of Oslo). It was found that approximately 30 per cent. of these cases healed spontaneously, that a further 30 per cent. remained without manifesting serious disorders, that only 10 per cent. showed advanced syphilis in the nervous system and 10 per cent. in the cardio-vascular system. There was nothing new in the observation that syphilis can heal solely by the organism's defence activities, but that in 30 per cent. of untreated cases there should have been complete restoration and in another 30 per cent. practically satisfactory recovery, whereas only 20 per cent. suffered from

serious syphilitic manifestations, was a surprise to many.

Medicinal therapy must show an improvement on these statistical figures, if it claims to be efficacious in the cure of the syphilitic patient. Reliable homoeopathic statistics useful for comparative purposes do not, as far as I am aware, exist. In their place we might avail ourselves of statistics, say, concerning cases treated with mercury ; for, as we shall try to explain, mercury can, at least in principle, be taken as frequently indicated on homoeopathic lines in early syphilis. But again, as far as I know, no such statistics exist which would satisfy modern requirements, including those of sero-diagnosis. Present-day statistics concerning the treatment of early syphilis refer mainly to combined therapy, i.e., arsphenamine with bismuth, or with mercury and potassium iodide, this being considered as the best method nowadays. For this prolonged treatment, beginning either in the primary or secondary stage of syphilis, the average of cures is asserted to be 90 per cent., while the average for all variations of treatment accepted by the official school at present is stated to be 60 per cent. It appears, therefore, that only what is held to be the best method can claim appreciably better results than those from unaided self-defence of the body.

If we follow American statements which are based on the most comprehensive statistics, the best routine treatment extends over a period of 70 weeks, during which weekly injections are given according to a definite schedule : first, a series of arsphenamine, then bismuth injections in

between, or instead of the latter mercury with potassium iodide ; arsphenamine being continued in increasing intervals throughout the treatment.

It is acknowledged that arsphenamine, or any similar organic arsenicale, does not, if used alone, suffice, if the best results are to be achieved. That means that expectations based on the original direct parasiticidal effect of arsphenamine had to be reduced considerably, though, of course, this does not mean to say that arsphenamine could not counteract the spirochaetae on chemo-therapeutic lines.

Now let us consider the therapeutic efficiency of arsphenamine used alone. Experiments on animals may easily lead to error and actually did so originally. Syphilis in rabbits can be eradicated rapidly by arsphenamine ; syphilis in the human being, however, requires, in the generally accepted opinion, many months of uninterrupted treatment, if the disease is to be cured. There may be some individual cases of sero-negative primary syphilis in which something like the original aim of *sterilisatio magna* is successfully achieved by the first injections of arsphenamine ; but only a very few practitioners dare to cut short the treatment, because there is no guarantee against a subsequent serious outbreak, such as affecting the meninges. In the case of rabbits, none of the pronounced toxic opticus, liver or skin (dermatitis exfoliativa) lesions are observed such as are seen in human beings. Thus no conclusions from animal to man can be made in respect of the therapeutic and toxic index. Hence one is bound to draw one's inferences

from the observation of the clinical course of the disease in human patients.

It is agreed that full doses of arsphenamine, in the primary stage, generally drive the spirochaetae from the surface within a fairly brief period. That is an important achievement as regards preventing contagion, something which could not be counted upon before *Ehrlich*. One can attribute it to the fact that, generally speaking, arsenicalia act more rapidly than mercurialia. That being so, it would be irresponsible on grounds of social hygiene, not to have recourse to the organic arsenicalia, when the risk of contagion cannot be reasonably excluded.

These demands being satisfied, may-be sometimes in preference to strict consideration of the individual case, it must be left to a fully informed physician's discretion, whether to follow a routine plan of 70 injections or a more individualizing course. His decision will largely depend on the opinion he has formed on the prospects of using arsenicalia, mercurialia, bismuth, iodides or any other preparations, and on the means of making sure of the results. It is therefore relevant to know what each agent can contribute to eliminating the parasites with the least possible danger, and how it is done. The question, how far the reactions of the host system to any such medicinal agent are indifferent, auxiliary or essential for the curative effect, is not purely academic; it has an important bearing on a proper assessment of events which may occur in the course of treatment.

So far as clinical cure is concerned, disappearance of the eruption on skin and mucous membranes

after two to three weeks of arsphenamine treatment is of no significance. Neither does a negative Wassermann-reaction, which for our purpose may represent all similar sero-diagnostic reactions, admit of a final verdict ; it is seen in 75 per cent. of the cases after eight weeks of injections. Since one has learnt to fear serious internal relapses in spite of that finding, it is no longer considered a sufficient reason to discontinue the treatment. Modern syphilis therapy insists on uninterrupted treatment for one year after the Wa-reaction in blood and liquor has become negative ; the sero-diagnostic control is to be continued in the subsequent years. When a pause of a month between injections was introduced during the first year, the sero-negative cases were seen to be reduced from 68 per cent. to 40 per cent. We are here concerned only with modern statistics and views. The significance of rendering the serum reactions negative, and whether that is always desirable, may be debatable ; but it should be noted that a negative Wa-reaction does not indicate disappearance of the spirochaetae from the system, but only cessation of certain interactions of spirochaetae and body-cell products in which serum complement (globuline) is used up. Thus negative Wa-reaction with latent spirochaetae may well prove worse than the manifest struggle indicated by a positive reaction. Meanwhile sero-diagnosis has to be employed, with due reservation, *faute de mieux*.

Inhibition or destruction of spirochaetae by arsphenamine *in vivo* has been found, in common experience, to be incomplete ; hence the combined

treatment. Bearing in mind the possibility of an abortive cure of sero-negative primary cases, forced cures have recently been tried under hospital supervision, by increasing the doses five- or six-fold over a few days. The percentage of serious arsenic poisoning, such as peripheral neuritis, fever, haemorrhagic encephalitis, toxic dermatitis of the exfoliative type, was, however, high. The method has not reached beyond the experimental stage and no opinion can be formed yet, whether the spirochaetae can be wholly eradicated that way.

One reason for invoking the aid of mercury or bismuth has been the observation that spirochaetae under continued arsphenamine influence appear to become arsen-proof. It is suggestive to compare this acquired arsen-tolerance of the microbes to that of the human system, as known from the " arsenic-eaters " of Styria. The phenomenon has been explored experimentally, mainly on mice infected with trypanosoma; this protozoon develops arsen-fastness more regularly than spirochaetae do. At first nothing else but interaction of microbe and arsenicale seemed to be involved. The trypanosomes disappeared, after a first atoxyl-injection, completely from the blood of infected mice for several days or weeks; then a few trypanosomes reappeared, multiplied rapidly, but disappeared again upon a second injection, only to show themselves once more in the blood after a shorter interval; the trypanosoma-free period became shorter and shorter with each succeeding injection, until finally atoxyl was no longer capable of clearing the blood from trypanosomes, even if the highest doses, not fatal to the

mouse, were used. If the blood containing such atoxyl-fast trypanosomes was transferred to a second mouse, atoxyl remained without effect against the trypanosomes. The acquired property of atoxyl-fastness is not lost or diminished in the following generations of such trypanosomes. So far there was nothing to suggest any interference of the host animal in the process. But it was discovered that arsen-fast trypanosomes did not remain so when used for infecting rats. Thus something peculiar to the host-species must play a part. If the selective protection of microbes cannot be explained without assuming some assistance of the host system, it stands to reason that the body-activities which are anyhow at work against the parasites, take a hand also in their selective destruction. We shall have to examine further, for the spirochaetae, whether there is evidence that these body-defence activities are even stimulated by arsenicalia.

Before doing so, let us briefly consider the position of mercury and bismuth regarding direct or indirect mode of action against the spirochaetae. For mercury salts, like hydrargyrum sublimatum, $HgCl_2$, the concentrations necessary for destroying spirochaetae *in vitro* are well within the range of those tolerated by the system. So the simplest theory of direct parasiticidal action was long accepted. Since the antiparasitic action is known to be reduced by the presence of organic matter, however, the direct mode of action is much less certain. In order to uphold that theory, it had to be assumed that the spirochaetae are more susceptible to mercury than body cells; in the

absence of supporting facts, such assumptions *ad hoc* serve to obscure rather than to clarify the issue. If mercury, like other heavy metals, works via the SH-group of cell constituents, there is nothing to suggest why it should prefer those of the spirochaetae. A number of modern authors have abandoned the chemotherapeutic hypothesis for mercury altogether and even assert that mercury alone can never cure syphilis but only assist other remedies. This extreme view can hardly be upheld in face of the experience of centuries, at least so far as clinical cures are concerned. It obviously overrates direct parasiticidal action which, after all, is only one possible alternative. Of course, mercury does not cure, and probably not even benefits, every case of syphilis. While its exact mode of action is still unknown, most authors take a middle course and admit that the body defences play a part in the action of mercury.

In homoeopathy mercury has always been considered as a prominent simile to secondary syphilis. The lymphocytic inflammation, localized on skin, mucous membranes and in lymphatic glands as seen in sub-acute mercury poisoning, can, indeed, imitate that stage of syphilis to such a degree that it has not seldom been difficult to discern whether the symptoms were due to syphilis or to mercurialism. Whatever details of mercury- and cell-interaction may be found by future physico-chemical analysis, this similarity in body reactions strongly supports a conception of the curative process as a whole that mercury co-operates with or stimulates the body defences

against spirochaetae. What is more, the method of comparing the syndromes of disease and of a certain substance as to their similarity permits us to distinguish the cases and stages where that substance is best indicated. For mercury in syphilis, then, the best chance offers itself, when the infection is mainly confined to skin, mucous membranes and lymphatic glands. Rapid invasion of the spirochaetae into the capillary system and bloodstream is not the course which mercurialism is seen to emulate. These more rapid and malignant cases correspond better to the syndrome produced by arsenicalia.

Bismuth therapy of syphilis is only some twenty years old. Its exact mode of action is not known. The small amounts of bismuth which come into the circulation from intra-muscular injections and reach the tissues are unable to destroy the spirochaetae outright. Thus participation of the body defences in its anti-syphilitic action is almost certain. Again, one has to look to poisonings to learn more about the processes peculiar to bismuth. However, extremely little of the metal passes into the circulation, when the ordinary preparations are given *per os*. Therefore toxic effects on a scale comparable to the sub-acute course of syphilitic infections are rare. Those known occurred mainly when bismuth preparations were applied to wounds. Granulating surfaces absorb bismuth more readily. The poisoning is very similar to that of mercury, especially on the mucous membranes of mouth, throat and rectum ; nephrosis has also been seen. These syndromes were confirmed by bismuth injections in animals. If anything, transition from

inflammation to gangrene occurs more quickly under bismuth than from mercury. That points to a more rapid pace of action on the mucous membranes and would place bismuth in between the arsenicalia and the mercurialia as regards its usefulness in syphilis. Homoeopathic provings have so far not contributed to making the bismuth indications more precise.

For the iodides parasiticidal action is neither supported nor assumed. Their beneficial rôle in tertiary syphilis is well established. The proliferative alterations, involving chiefly the connective tissue, of this late stage are resolved. It has been suggested that iodides antagonize substances which normally prevent autolysis of tissues. Whatever the actual intermediary processes may be, taking the affected syndromes as a whole, one cannot but admit their resemblance to such, admittedly rare, manifestations of chronic iodism as mesaortitis and iododerma tuberosum. Again, both end-results of tissue reaction to iodides, proliferation and dissolution, have to be accounted for, if we are to understand the detailed processes by which the iodides assist the body defence in tertiary syphilis. To some extent iodism can simulate also the skin-, mucous membrane- and lymphatic gland-manifestations of secondary syphilis. Certain well chosen cases of this stage, too, are benefited by iodides.

Coming back to the arsenicalia, we are searching now for further evidence for or against direct or indirect action. Firstly, some clinical occurrences under arsphenamine treatment require attention. There is the *Jarisch-Herxheimer* reaction. It is

seen in a number of cases, and then almost invariably after the first arsphenamine injection. In early syphilis the eruptions on skin and mucous membranes are provoked, if they have not yet appeared—or, if already present, they are intensified—the signs of inflammation, redness and intumescence become more pronounced. At the same time a general systemic reaction shows itself with chilliness, fever, uneasiness and pains in muscles and joints. There can be no doubt that this is a first reaction or initial aggravation, as so frequently encountered in any stimulative therapy. It is also seen, if not so frequently, after the first bismuth or mercury medication, and even after less specific milk injections. In the case of arsphenamine it might be argued that the focal and generalized first reactions are directed against fragments of destroyed spirochaetae and not against the arsenicale. But the close analogy of the phenomenon with that produced by other agents which are not parasiticidal at least lends no support to such a view. Moreover, microscopic findings (*Bergel*) on the focal tissue-alteration point decidedly towards reaction stimulated by the arsenicale ; local lymphocytic inflammation around the nests of spirochaetae was seen to be intensified. Accepting the *Jarisch-Herxheimer* reaction as an initial aggravation, we should infer that in the particular cases where it appears, the arsenicale was the appropriate stimulant. It is not surprising that the reaction should be somewhat excessive considering the dosage which was not chosen so as to stimulate defensive processes already at work. Fortunately, in the early stages of syphilis, such

excess has no serious consequences. In the tertiary stage, however, particularly with cardio-vascular lesions, such a focal flare-up has not seldom proved fatal.

The fact that arsphenamine acts in some cases of syphilis as a stimulant to the body defence, i.e., on homoeopathic lines, does not exclude the possibility that it kills or inhibits the spirochaetae also by direct action. That would be its chance of curing in those cases where arsenicalia do not fit in the defensive processes. So far clinical evidence of such strictly chemotherapeutic cures is, however, meagre indeed.

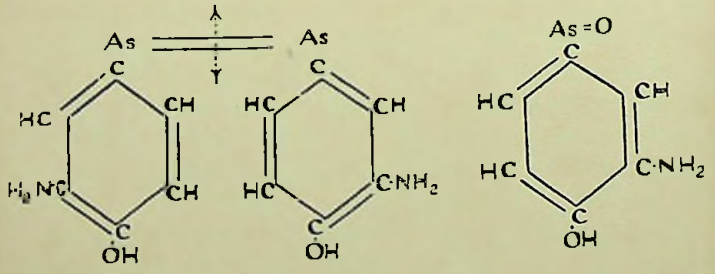
Another occurrence under arsphenamine treatment is of very different import. Meningitis and meningo-neuritis in the early stages of syphilis have become at least more frequent and violent since the introduction of arsphenamine. These serious events happen, when arsphenamine alone has been given, mostly about eight weeks after a course of injections has been stopped. Though occurring only in 2 per cent. of cases so treated, this danger has been the main reason for extending the treatment more and more, for combining it with bismuth or mercury and for warning against interruption of the course of injections. Under the circumstances mentioned in which this early neuro-syphilis manifests itself, there can be no question of ascribing it to initial aggravation through excess of stimulation. Certainly, too, the spirochaetae cannot have been thoroughly destroyed. The occurrence indicates that sometimes, after a series of arsphenamine-injections, the spirochaetae become more dangerous by

attacking vital tissues. Apparently they have been dislodged from the surface, from skin, mucous membranes and lymphatic glands. In the ordinary course, without arsphenamine, they would have been contained there, subjected to lymrhocytic inflammation and meanwhile time would have been allowed for immunity reactions to develop and to take their part in the defence. Driven into the circulation, while adequate protection has not yet been provided, they appear more virulent; but it is not necessary to assume that they have acquired new invasive and aggressive properties. Absence or breakdown of natural defences could have the same effect. Wherever the interference took place, it must have been due to arsphenamine. It would follow that in some cases arsphenamine is unsuitable and should be replaced by another, better fitting remedy. The advice to prolong and combine the course of injections appears not to be the wisest, but emerges from the difficulty of appraising any peculiar situation properly so as to assign to it the remedy which has appropriate sphere of action. This is where comparative observation of the individual signs and symptoms comes in.

Any clinical appreciation of arsphenamine has further to take into account, how it affects the chances of the syphilitic patient to develop syndromes of the cardio-vascular and central nerve system. Some fifteen years ago the general impression was that these sequels had become more frequent and occurred earlier after the infection since the introduction of arsphenamine than before that era. Several competent authors

were of the opinion that this was due to inhibition of natural defence, particularly immunity processes. Modern clinicians do not deny the fact, but ascribe it to insufficient treatment, another reason for prolonged and combined treatment. As this method has been in extensive use for barely twenty years, it is perhaps too early to form a definite opinion on that question. In days of old, when mercury was the mainstay, we were taught that mental paralysis and locomotor ataxia had an approximate interval of fifteen to twenty years from the infection. In view of what has been said about early meningo-neuritis, some reservation as to the effect of arsphenamine alone on the frequency of late sequels appears not unreasonable.

Let us now examine the experimental evidence. A few years ago it seemed impossible to bridge the gap between the concentration of arsphenamine needed to kill spirochaetae *in vitro* and that obtainable without danger *in vivo*. That seemed to exclude a strictly chemotherapeutic action. Recently, however, a product, mapharsen, obtained by splitting arsphenamine under oxida-



ARSPHENAMINE MAPHARSEN

tion, was shown to fulfil the requirements for direct parasiticidal action. It is assumed, therefore, that this oxidation and splitting of arsphenamine takes place *in corpore*. Mapharsen has been administered also directly; being approximately ten times more toxic than arsphenamine, it is given in a tenth of the usual arsphenamine dose. It is too early to say whether it has any advantage apart from being easier to administer. Assuming that the simpler compound is the active agent, it has been suggested that it acts via the essential sulphydril-compounds of the cells like glutathione (cysteine-form). For once it is known that similar phenyl-arsinoxides form dissociable compounds with glutathione which annul their trypanocidal action *in vitro* and *in vivo*. *In vitro* addition of small quantities of glutathione (cysteine-form) protects the parasites from being killed by otherwise deadly concentrations of mapharsen. In infected animals previous introduction of such sulphydril compounds either considerably delays or prevents destruction of the parasites by arsinoxides. Lastly, also the toxic effects of large arsphenamine doses in the non-infected animal can be delayed or prevented by reduced glutathione. That explains the old observations that otherwise sufficiently high concentrations of organic arsenicalia do not kill the parasites *in vitro* if serum or tissue mash is added. Apparently the sulphydril compounds of the organic matter compete with those of the parasite cell. How much more must this competition occur in the living body where all the cells possess these SH-compounds necessary for their respiration? If,

therefore, the respiration of the parasites should be inhibited by the arsenicalia before that of the body cells, obviously special conditions have to be assumed ; none are known so far. Surely the susceptibility of different parasites and body cells to arsenicalia varies considerably. Streptococci, cholera vibrio and typhoid bacilli succumb under very small amounts of arsenic, while staphylococci, coli bacteria and some proteus types even thrive in those concentrations. Very low concentrations of arsenic promote the fermentative capacity of yeast, larger amounts depress it and finally kill the yeast cells. Certain fungi, far from being destroyed by solid arsenic, even convert it into gaseous compounds. On the other side, the cells and organs of the human body, though all susceptible to arsenicalia, show varying degrees of resistance to the poison. The potentially universal action of arsenic is emphasized when it is designated as protoplasma-poison or as capillary-vascular poison. In general, the low organized tissues, like connective tissue and lymphatic glands, are much less affected. Which cells or organs manifest signs of defence or of succumbing in a particular case will depend not only upon the circumstances, approach, time, quantity and form, under which they are reached by the poison, but also upon their individual reactivity.

Any adequate conception of the antisyphilitic action of arsenicalia has, therefore, to take account of the competition of the adversaries, microbe and body, not only to die under the poison, but also to react against it. Whether the mode of action of the arsenicalia via the sulphydril com-

pounds proves to be the cardinal one or not, the issue appears not as simple as the alternative, who dies first from the arsenicale. We have touched on some results of resistance by the spirochaetae ; the reactions of the highly organized system are, of course, immeasurably more complex and variated. For that, a great amount of knowledge about their manifestations has accrued from arsenic poisonings and has been enriched in distinctive details by intentional " provings." Whether these body reactivities against arsenicalia turn out to be inimical to the spirochaetae by themselves, or through throwing a fuller weight of the poison on to the microbes, or both, we shall have to scrutinise them for similarity with syphilitic manifestations.

Considering the location only, surely the battle-grounds of body reactivity against spirochaetae and arsenicalia should correspond ; so should the general rhythm and further particular means and modes of reactivity against the living and the inorganic aggressor. No better guidance offers itself than to study the totality of manifestations in a given case of syphilis with a view to finding out whether they have the characteristics of arsenic effects or fit better into the sphere of another agent, say, mercury or iodide. In short, if the body defences play any part in the curative action—and for arsenicalia in syphilis this is strongly emphasized by observations—the homoeopathic aspect comes into the fore.

It may be questioned, whether arsphenamine and inorganic arsenious acid (arsenicum album) are at all comparable in antisyphilitic action.

Important differences there are, no doubt, but they do not concern the essential points. One remembers the old empiric use of Donovan's solution combining mercury and arsenic. Indeed, *Ehrlich* aimed at perfecting the arsenic virtues by trying out one organic compound after another; he started with cacodylates (aliphatic arsen compounds) which proved less toxic than arsenic. Atoxyl (p-amino-phenyl-arsinic acid) was even more effective against trypanosomes and certain spirillae, though it did not kill them *in vitro*. Finally, *Ehrlich* found the salvarsan, as he named his product obtained by reducing an amino-phenyl-arsinic acid, the most suitable for the syphilitic infection. For our reflections we need not dwell upon further modifications like neo-, silver- and neosilver- arsphenamine.

Nothing in the toxic effects of arsphenamine is alien to those known from arsenic; but some occur less frequently and less intensely from the organic compound. Such detoxication, to a greater or lesser extent, by phenyl-bonds is by no means limited to arsen. It may have to be ascribed to easier dissociation, diffusion and elimination of the products formed by their interaction with cell constituents as compared with the products from inorganic compounds. Indeed, it is not at all unlikely that some kind of arsenic detoxication *in vivo* is done by going through similar organic bonds. Thus arsphenamine, or mapharsen for that, would anticipate certain intermediary measures and so quicken and concentrate the arsen-action, offering conditions more suited to the host organism. This sort of closer, more immediate

aiming is a feature often encountered with organic, as against inorganic, bonds ; for certain purposes to great advantage, but by no means for all.

It appears, therefore, justifiable to view the arsphenamine actions, so far as they involve the body defences, under the wider aspect of arsenic actions. The broad lines of similarity between arsenic poisoning and syphilis have already been mentioned. Arsenic and spirochaetae, both acting as universal protoplasma- and cell-poisons, bring about manifestations, potentially from every organ or tissue, so numerous and multiform that the subjects of comparison abound almost embarrassingly. Indeed, it is far more important to point out the limitations in the similarity and to search for characteristics which would allow one to distinguish a case of syphilis bearing such features as would peculiarly indicate arsenicalia.

On skin and mucous membranes the primary syphilitic ulcer has its counterpart in the phagedaenic, necrotic ulcers of arsenic. If it were not for the demands of social hygiene, one would reserve arsphenamine for the rapidly progressing infections which do not linger in the lymphatic glands but tend to invade the blood at once via the capillary vessels.

Amongst the whole host of secondary syphilitic eruptions, there is hardly any which is not simulated by arsenic poisonings—the ordinary roseola and maculo-papulous exanthema being less characteristic for arsenic, the herpetiform, vesiculous, the lichenoid and psoriatiform eruptions and the abnormal pigmentations more so. The skin plays an essential part in the defence processes

of syphilis. It has frequently been noticed that the subsequent course of the infection is more favourable, if the first exanthema is intensely developed, and especially that visceral syphilis then occurs less frequently and is milder. Intense exanthema of the secondary phase does not call particularly for a vehement capillary poison like arsenic.

The rapid and malignant progress of the infection, involving the capillary vessels, into the bloodstream corresponds far more to the ways and rhythm of arsenic. The endo-meso and peri-vascular alterations from syphilis and arsenic can produce very similar pictures. Some authors (*Fr. Lesser* i.a.) have attributed to the cell processes in the walls of the blood vessels a main rôle in the defence against the spirochaetae. One might deem that to be rather a second chance, after the less vital skin and lymphatic gland defences have been by-passed. So long as an early stage of inflammation is active in the walls of the vessels, and cell degeneration or substitutive tissue proliferation has not set in, there is a good chance for arsen stimulation. The danger of a violent arsphenamine stimulus in gummatous lesions of vital tissues has already been pointed out. The same reflections apply to the cell processes in the various organs which may be affected. There is no need to enumerate them here. They can all be similarly produced by syphilis and arsenic. Suffice it to mention only the polyneuritis which in syphilis has not seldom arsenic features and yields to its use. The atrophic end-effects (opticus, etc.) occurring both from the infection and from arsenic

intoxication are, of course, beyond the stage curable by stimulation.

Not much more than general indications, such as the nature, location and rhythm of the pathological processes, can be given for or against a short-term therapy with massive arsphenamine doses. Only if circumstances permit, a more discriminating choice of the therapeutic agent, based on the more functional details up to psychic symptoms, comes into consideration for the individual case.

After all, syphilis is only one field amongst many where arsenicalia may be called for as suitable stimulants on grounds of similarity of reactions. A discussion, however cursory, of the wider sphere of arsenic indications appears, therefore, not out of place in order to bring our main theme into a better perspective.

In the far progressed structural changes of carcinoma the arsenic effects can be compared generally on that broad level only; seldom can indications be enhanced by individual characteristics. Arsenic has been used from time immemorial for malignant tumors. On the other hand, it is one of the carcinogenic substances. We need not go into the very limited successes of cancer treatment with arsenicalia. But it is interesting in this context to recall the action of arsenic on cell mitosis; further, that in carcinomatous cells anoxybiotic, fermentative processes have the upper hand against the oxidative ones (*O. Warburg*), while arsenic again is known to be able to depress the oxygen consumption in cells.

This inhibition of oxidation by arsenic has been

studied chiefly on erythrocytes. Very low concentrations in the range of the 4-5 decimal potency in homoeopathic terminology, such as are present in the natural arsen spas, show this effect. Atoxyl can produce a blood picture similar to that of pernicious anaemia : diminished erythrocytes and haemoglobin, with poikilocytosis and anisocytosis. Again, what little benefit could be derived in pernicious anaemia before the introduction of the substitutive liver therapy, was achieved by arsenic medication.

On the skin the hyper- and parakeratosis of chronic arsenic poisoning is well known ; again, arsenic is widely used, sometimes with success, in psoriasis and lichen ruber. The more acute eruptions from arsenic are multifarious, as already mentioned ; dermatologists use arsenic on occasion for dermatitis herpetiformis and pemphigus. All these empirical uses conform to the homoeopathic principle of remedy selection, but they are homoeopathy on a low level, as it were ; the similarity applies to pathological tissue changes only. Still, some cases offer no better distinctive symptoms and one has to work on that level. If a dermatitis of any kind be qualified by predominant burning and by itching, worse from cold and from scratching, the homoeopath would have greater confidence in his choice of arsenicum album.

What has been said about the necrotic, phagedaenic character of ulcers as indicating arsenic, applies not only to syphilis. Such ulcerations may be due to other infections or be of trophoneurotic origin, even transgress into gangrene, as particularly under the deteriorated tissue con-

ditions of diabetes; always the acrid, offensive, even cadaverous secretions would call special attention to arsenic.

The inflammatory degenerative processes in the inner organs which can be caused by arsenic are so multifarious that, if diagnoses like nephritis, hepatitis, etc., were the only and sufficient grounds for choosing the simile as the appropriate remedy, arsenic would appear well nigh a panacea. The chances are slightly improved when the nature of an infection is taken into account. For the violent cell poison arsenic emulates more especially such processes as are encountered from the most virulent toxins of microbes, e.g., cholera vibrio, typhoid and botulismus bacillus and streptococcus. Incidentally, these species show themselves *in vitro* particularly sensitive to arsenicalia. Incidental, indeed? After what has been said of arsen action in syphilis, one would rather take such a special affinity both to certain microbes and to the tissue and organ cells more rationally as a clue to a similar kind of competitive action in the defence play of the two antagonists.

Yet, diagnoses, even if specified by the causative germs, are still too wide a frame to fit the arsenic case sufficiently. The similarity of acute arsenic poisoning to cholera has often been emphasized. It goes beyond the pathological findings and the clinical syndrome from the toxic gastro-enteritis. Great restlessness and anxiety with fear of death, extreme thirst quenched by frequent, but small draughts, cold drinks being badly tolerated and readily vomited, chilliness and general aggravation from cold in any form (with one noteworthy

exception referred to below) ; a periodicity in the recurrence of such symptoms as cramp-like and burning pains and fever, aggravation during the night, more specially in the hours immediately after midnight—these are characteristic features of the arsenic case. They would determine the choice of arsenic not only in cholera, but equally in many acute diseases, whatever the diagnosis may be.

These modalities are abstracted from the observations in poisonings and " provings." With the appropriate adaptation (for not all need be present in every case) they apply also to neuritis. Here a great sensitiveness to touch would present nothing peculiar, and is, therefore, insignificant for the choice of the remedy. But the arsenic patient bears his periodically exacerbated pains particularly ill ; they make him furious ; he is not at all patient.

This intolerant attitude assumes, under less provoking circumstances, a form of mental peculiarities which, when noticed, may lead one to presume that person, also under more trivial afflictions or even in his normal health, to be particularly susceptible to the arsen stimulus. He reacts unduly, without proper sense of proportion, to slight untidiness or irregularity in his wonted environment ; this makes him appear somewhat pedantic.

It would be misleading to think of arsenic only in terms of its poisonous effects progressed to structural alterations. The precursory functional symptoms are not less important. They can indicate an arsenic medication, then to be more

delicately adjusted, in a great number of syndromes of the allergic and vasomotor type. Many of the pertinent symptoms are met occasionally also under arsphenamine treatment. Then they have been described as " nitroid crises," nitroid because the vasomotor symptoms are similar to those produced by nitrites. It seems somehow ludicrous to find these occurrences interpreted by various hypotheses excepting the obvious and simple one offered by toxicological knowledge, namely that these " side effects " are due to the arsenicale. They come on with flushes, palpitation, precordial anxiety, headache, giddiness, then progress to cold perspiration, cyanosis with extreme anxiety and restlessness and fear of death. Equally, attacks similar to allergic conditions may be provoked by arsenic ; hay fever or asthma-like, urticaria or circumscribed oedema, not omitting the accompaniment of leukopenia and eosinophilia.

The asthma-brochiale-like symptoms of arsenic are characterized by aggravation from lying down. The same modality applies to the headaches which may be of the megrim type. More distinctive for arsenic in headaches is that they are relieved by cold ; that is in marked contrast to the feature mentioned above, namely, that the chilly arsenic patient is generally worse from cold in any form.

Enough has been said of the wide sphere of arsen-compounds. The organic arsenicalia, sponsored by the chemotherapeutic conception, have certainly an important place in it, though the theory had to be modified. Within the limitations given by the course of such infections as syphilis, there seemed room for improving on the present

short-cut therapy on diagnosis of the disease by individualizing, i.e., by selecting amongst the potential remedies that one which fits best in the situation of the diseased person.

The brief summary of the use of arsenic on homoeopathic lines may be inapt to encourage a trial of its suggestions, but perhaps it may transmit something of the satisfaction which accompanies every synthetic attempt to find the sectional integrated by a fuller aspect.

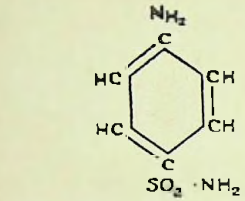
Chapter IV

Coccal Infections—Sulphanilamides.

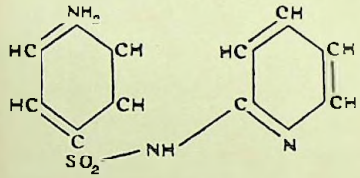
Our third example illustrating medicinal therapy in homoeopathy as compared with chemotherapy has to deal with recent research and experience and it might be argued that it is too early to assess properly the action of the organic sulphur compounds of the sulphonamide type. However, what is known so far of the actions of these preparations will be found hardly lagging behind what little knowledge there is regarding the two other chemotherapeutic agents which have been discussed.

The protagonists in the new field are organic sulphur compounds on the one hand and, on the other, a whole group of bacteria, prominently of the coccus type, strepto-, pneumo-, meningo-, gono- and staphylo-cocci. For our purpose we may restrict our discussion to these cocci. Characteristic of the infections of this kind is that the host organism reacts chiefly by the leucocytic-endothelial tissues, manifesting purulent inflammation.

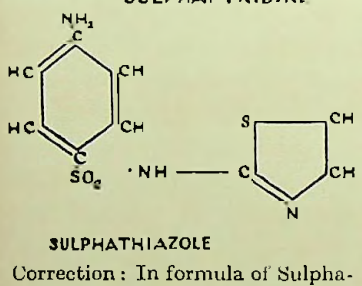
The hundreds of sulphonamides so far investigated can be represented for our immediate purpose by the simplest, sulphanilamide, which has the characteristics of all of them, viz., the sulphonamide, $\cdot SO_2NH_2$ - group linked to



SULPHANILAMIDE



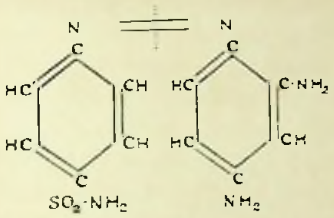
SULPHAPYRIDINE



SULPHATHIAZOLE

Correction: In formula of Sulphapyridine, in first ring, linked to NH_2 : add a "C."

the benzene ring, with another amino- (NH_2) group in para- (opposite) position, thus p-amino-benzene-sulphonamide. A few further preparations call for attention in so far as they enhance activity in special bacterial infections. They have one H of the $\cdot SO_2NH_2$-group replaced by various rings, e.g., by the pyridine-ring to form sulphapyridine, i.e., pyridyl-sulphanilamide, or by the thiazole-ring to form sulphathiazole, i.e., thiazole-sulphanilamide (in which again one H of the thiazole group may be methylated so as to form sulphamethyl-thiazole). The preparation from which this chemotherapeutic branch originated, prontosil, can be disregarded. It is now established that it becomes active only after its azo-bond has been split by reduction *in corpore* and thus free sulphanilamide has been formed. That accounts for the inactivity of prontosil *in vitro* against bacteria. Originally this whole field of re-



PRONTOSIL

search started from the observation that introduction of the essential $\cdot SO_2NH_2$ -group into the diazo-dyes was seen to give a firmer fixation of the colour to the proteins of wool and silk. The idea was to fixate organic compounds by means of the same group on to bacteria. It remains to be seen whether a similar "fixating" property plays any part in the anti-bacterial action. Almost certainly it is not solely responsible for it. Immediately the question arises, why bacteria should be affected in preference to the cell proteins of the system. Furthermore, it is not the $\cdot SO_2NH_2$-group only which has anti-coccal action, but such action is known to appertain to many other incompletely oxidized sulphur compounds, namely disulphides (SH), e.g., mercaptans (aliphatic hydrosulphides) and sulphoxides (SO), beside sulphinic (SO_2H) and sulphonic (SO_2) compounds. So, if a bacterial receptor group specific to (SO_2NH_2) were responsible for the action, the other incompletely oxidized sulphur compounds would have to be transformed *in corpore* to sulphonamides, before becoming active. As ·SH-compounds are present in every cell and their progressive oxidation is in the course of normal katabolism, it would be difficult to conceive, why this chemical transformation should not be brought about also by the host cells in their defence. Again, if that were the case, the part played by the medicinal sulphur compounds

could be understood to be stimulation of such defence mechanism, that is to say, on homoeopathic lines.

However, what evidence there is so far regarding the sulphanilamides seems to point to other modes of action in which the systemic defence plays only a secondary part. Nor, on the other hand, is a direct bactericidal effect in the original chemotherapeutic sense supported by present opinion on the known facts. The interpretation of these facts, which we shall discuss more fully, lies in between those two theories ; it is briefly that the sulphanilamides compete with certain metabolites, especially p-amino-benzoic acid, which are essential for the growth and mobility and possibly the reproduction of the bacteria in question.

Assuming this theory is confirmed no theory will be satisfactory unless it accounts also for the wider issue, that other and simpler, incompletely oxidized, sulphur compounds are similarly effective. The cardinal point to be kept in mind is that the *sulphur* is indispensable in these compounds for the anticoccal action. We may, therefore, expect to gain a broader view on the problem by including in our survey the old homoeopathic use of sulphur preparations in comparable infectious processes. Eminent amongst these is *Hepar sulphuris calcareum*, a mixture mainly of calcium-polysulphides, obtained by exposing a mixture of oyster-shell chalk and sublimated sulphur to white heat. In experiments on healthy persons, " provings," this preparation has been seen to promote purulent inflammation, like boils ; triturations of it have, in the experience of more than

a hundred years, proved very efficient in bringing furunculosis and other strepto- and staphylo-coccal infections to a speedy end. For another sulphur-compound, sulphur iodide, *Bier* and his co-workers more recently have confirmed both the pharmacodynamic and the curative effects in the same sphere.

Certainly it is a far cry from these localized purulent inflammations to generalized septicaemia or meningitis, and it has never been claimed by homoeopaths that infections of that advanced stage were cured by their usual sulphur preparations. Nevertheless, the high tribute paid to the simple calcium sulphide in small doses by *H. J. Thomson* (*Brit. Med. Journ.*, II, 1935, p. 1070) in puerperal sepsis hardly yields to sulphanilamide results; the sulphide reduced the death-rate in sepsis from 5.3 to 0.7 per 1,000 cases of confinement. All the same, it can hardly be disputed that the introduction of the organic sulphonamides is a great advance in reducing the mortality in a number of the most dangerous generalized coccal infections and in shortening the course of others. It would be sheer doctrinairism for the homoeopath not to avail himself of the sulphanilamides in appropriate cases for which he has no equally potent remedies, on the ground that the new preparations have not been discovered and proven on homoeopathic lines. Non-homoeopaths may at least plead ignorance as excuse while neglecting the simpler sulphur preparations in cases where they are indicated and prove helpful on homoeopathic indications.

The homoeopathic and the chemotherapeutic

way of obtaining and applying knowledge about sulphur compounds are originally separate in historical development as well as in theoretical approach. It is, however, highly probable that both schools would benefit from each other by future contact, so deplorably lacking at present. After all, it is facts that count and they will be found congruent in the end, no matter how they were approached or interpreted.

Homoeopathy makes no assertions on the intersystemic chemical mechanism of drug action. It is concerned with the interaction of drug and person as a whole. So far as modes of drug action are elucidated by physico-chemical analysis, they come in handy for interpreting factual knowledge about the whole by facts disclosed about parts. For applied knowledge, however, as medicinal therapy is, it would be unsound and pseudo-scientific indeed, to take the " partial " instead of the " whole " as a basis. For one thing, we cannot know the total of relevant processes, as long as the complexity of the reacting organism surpasses the sphere of physico-chemical analysis; and even if we knew, the whole is something more than the sum of its parts. Obviously, therefore, a therapy dealing with persons can do no better than rely on facts observed on that same level of wholeness. Whatever needs for analysis and explanation one may have, they are secondary in sequence and rank. It is surely not more but less rational and scientific to mistake or even reverse this precedence.

For chemotherapy the relations between relevant facts seem at first different. Of course, this

therapy too cannot, and does not, wait for clarification of the modes of action so as to become "scientific." But its objects, at least at the outset, are the microbes and, therefore, the experimental search for facts can be pursued for a while with simplified models, infected animals or even bacteria cultivated *in vitro*. The real test, though, comes with application to man. Supposing the difficulties inherent in transferring observations from one level of complexity to another have been overcome and fallacious conclusions have been avoided, so that the simplified model represents the essential processes between germ and drug action in the human system; that in itself is not yet an explanation, but only preparatory experimental investigation under simpler conditions. The mere fact that observations on infected mice have preceded those on infected man, makes the latter observations not more correct or scientific, though it serves to diminish the risks of tentative trials on man. Only if and so far as new facts, relevant to the drug actions on man, are disclosed, therapy becomes more "scientific," at least potentially so. Extension of knowledge may be obtained in pursuance of any therapeutic hypothesis, though the latter be found untenable in the further course of investigation.

To come back to our example : the sulphanilamide research started under the strictly chemotherapeutic hypothesis that it would kill certain bacteria *in vivo* without essential interference or assistance from the host organism ; that was the original intention for using it. If that were

confirmed, no connection could be conceived between such a mode of sulphanilamide action and that of other sulphur compounds which, like the homoeopathic preparations already mentioned can obviously have no effect against those cocci without assistance of the body defence.

The assumptions with which chemotherapy started have, however, not been supported by the facts as they have become known. Once more in the case of the sulphanilamides, too, the chemotherapeutic theory had to be modified to conform with the findings. As already mentioned, in anticipation of the discussion to follow, the opinion at present generally accepted is that the sulphanilamides compete with certain metabolites which are essential for the growth and mobility of the cocci in question. (Our discussion on the organic arsenicalia came to a similar assumption of competitive antagonism.) Again, if sulphanilamides are only one link in a chain of possible processes leading to the defeat of bacterial aggression, then a similar action of simpler sulphur compounds, like inorganic hydrosulphides, through stimulation of the body defences is perfectly reconcilable with that modified version of chemotherapy. Stimulation of the normal sulphur metabolism by suitable sulphur preparations could furnish body-made sulphanilamides or similar compounds to the same effect. The direct supply of an intermediary product useful in defence against bacteria could not be called stimulation of the defence ; we should not expect symptoms of intensified defence activities from the infected system or similar symptoms in deliberate

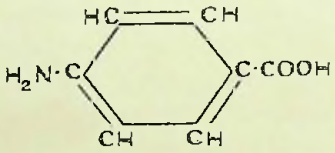
"provings" of such a substance on healthy persons. All the same, such a "progressed" sulphur could be said to assist the defence. So conceived, the two methods, supplementive chemotherapy and stimulative homoeopathy, would neither contradict nor exclude, but definitely complement each other. Indeed, we should understand the reasons for using the sulphanilamide drugs in cases where extent and *tempo* of the infection call for the direct subsidy of a metabolite-like compound, but we should choose the simpler and less risky sulphur preparations, like hepar sulphuris, where stimulation of the available defence—means appears to meet the case.

These reflexions on the methods do not settle the issue, but are made to clarify the problems. We shall have to see now whether the known facts support or conform with such conceptions.

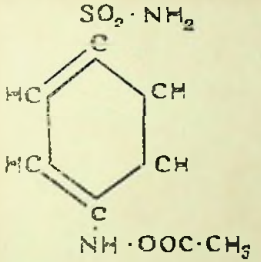
For the sulphanilamides, the observations *in vitro* speak against direct bactericidal action *in vivo*. Even bacteriostatic effect, by sulphanilamide concentrations comparable to those obtained *in vivo*, requires *in vitro* a favourable medium, e.g., the presence of certain peptons. Addition of whole blood facilitates bacteriostasis; it may even conduce to bactericidal effect. In this case it is doubted whether active phagocytosis plays a similar role *in vitro*, as it does *in vivo* where it completes the work of bacteriostasis. Anyhow, measured by the concentrations needed *in vitro*, the bacteriostatic or bactericidal effect of sulphanilamides appears to be favoured by several normal constituents of the system. How they co-operate against the bacteria is not known. The fact itself

is further evidence against the direct bactericidal mode of action, but on the other hand does not imply stimulation of normal tissue functions by sulphanilamides; it is equally conceivable as an additional deterioration of the terrain for the bacterial activities.

The latter course has been substantiated by observations on antagonism of certain protein fragments to sulphanilamides. The rôle of p-amino-benzoic acid

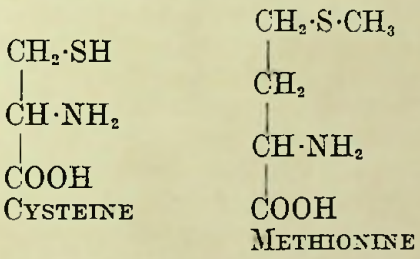


has attracted particular attention. This metabolite became known to be essential to the mobility and growth of the cocci (it seems to have certain vitamin-like functions in mammals, too). Further it has been noticed that the presence of this simple aromatic amino-acid in the medium hampers the anti-bacterial action of sulphanilamides. This antagonism is interpreted as one between competitors for the same groups or receptors. Sulphanilamides would block up the bacterium receptors for p-amino-benzoic acid and that would account for the inhibitory sequels to the bacteria. Such competitive antagonism appears the more probable from the similar chemical constitution of the two compounds, both being p-amino-benzene derivates. That would explain why the para-position of the amino group is so essential for the sulphanilamide action. If that group is acetylated, the compound acetyl-sulphanil-



amide becomes ineffective. Such "detoxication" of sulphanilamides occurs *in vivo* in varying proportions so that the curative and the noxious doses are subjected to considerable fluctuations.

The antagonism of p-amino-benzoic acid to sulphanilamides is by no means the only one which can be demonstrated *in vitro* and may also



be assumed *in vivo*. Purines and thio-amino acids, like methionine and cysteine, also inhibit the anti-coccal action of sulphanilamides. But no definite conclusions as to the mode of action can be drawn from the antagonism of these metabolites any more than from the synergism of certain peptones. All the same, it is of great interest to note that sulphydril compounds of normal metabolism should act as protectors of the bacteria. As they are powerful reductors and the action of the cocci on proteins is prominently reductive too, similar decomposition products may result. In the artificial medium, where no defensive actions such as

adequate detoxication and elimination can be assumed, this synergism with the cocci would antagonize the sulphanilamides and favour the cocci.

The competitive antagonism of sulphanilamides to p-amino-benzoic acid is probably an essential factor in their mode of action, but it does not follow that it tells the full story. *In vitro* experiments cannot exclude concurrent modes such as stimulation of the body defences. For that we have to examine the sulphanilamide reactions in living systems.

In mice infected with haemolytic streptococci, sulphanilamide is found more effective against types of high than of low virulence. Significantly, too, the most virulent strain of β-haemolytic streptococci (group A *Lancefield*) responds best to sulphanilamide therapy. One has tried to explain the observation in mice experiments in terms of a mass equation ; streptococci of low virulence would require a greater size of inocula to bring about infection or death, hence a given sulphanilamide dose would be spread over a greater number of cocci and, therefore, not suffice to inhibit all. That explanation might be plausible, if the sulphanilamide molecules were used up in irreversible processes such as permanent fixation to bacterial tissue, hardly compatible with continuation of life. But all evidence points to temporary, reversible reactions with the bacteria. The drug is highly diffusible and rapidly excreted, the cocci are seen to survive even prolonged sulphanilamide medication, but their aggressiveness is temporarily diminished. Besides, the preference for the most virulent strain of haemo-

lytic streptococci in human infection and the fact that generalized infections at the height of the destructive struggle respond comparatively much better to sulphanilamide than localized and mild ones, indicate that it is the intensity of the aggression rather than the number of aggressors affected which counts in respect of the inhibitory effect of sulphanilamide. Whether special weapons of the cocci, "aggressines," are frustrated by direct interference with the bacteria or by stimulation of specific defence measures, "anti-bodies," can not be deduced from these observations.

Virulence and terrain are closely inter-related and as they are the conditions of bacterial activities which, to all appearance, are chiefly altered by sulphanilamides, it is well to recall the relations of the cocci, with which we are here mainly concerned, to the host body under a wider perspective. The species most susceptible to sulphanilamides, certain strains of haemolytic streptococci, pneumococci and meningococci, are as often as not found on mucous membranes without their interfering with normal body functions. Normal secretions provide the cocci with conditions in which "to live and let live." When, however, the terrain is altered, say, a sudden and insufficiently compensated deprivation of animal heat leads to stasis of circulation, to impeded oxidation, accumlation of katabolic products, disturbance of the ionic equilibrium, in short, to the pre-stage of inflammation, the cocci, for survival, have to adapt themselves to the new conditions. They become invasive, aggressive, virulent. To call the new conditions

favourable to the cocci, because they are unfavourable to the body, is obviously a misnomer. After all, the cocci are forced to employ and develop new means of self-defence in the altered medium. Their chances are by no means good. If the body succumbs, these aerobic microbes die with it; if the host recovers, the bulk of the cocci fall victim to the body defence, are assimilated by leucocytes and macrophages, and finally eliminated; at best, the surviving few find themselves again on the mucous membranes, the old conditions being restored there.

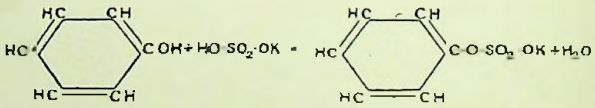
The main trend of life-processes is to free energy by oxidation; that applies to the bacteria as well as to the human system. Numerous reductive reactions are, however, interwoven in this course of processes to make it possible at all. In our context two reductive agents are of particular interest: (1) the normal cell constituent cystein which, by autoxidation to cystin (di-cystein), makes the H of its sulphydril group available for reductive processes. (We may ignore here its bond with glutamyl and glycine forming the tripeptide glutathione. The functions of another sulphydril compound, thioneine, in the red blood corpuscles may have similar important functions but they are not yet sufficiently known.) The respiratory cysteine-cystine system is, by means of the ·SH— group, probably the main one working independently of thermolabile enzymes. (2) Bacteria, too, whether anaerobic or aerobic, are principally reductive agents. In providing for their O_2-needs they reduce i.a. peptons. While the products may be harmless on excreting surfaces, or even of assistance,

as in the intestines for absorption and assimilation, others, when absorbed, put at least an additional strain on the detoxicating mechanism, e.g., the phenols (indoxyl, etc., arising from reductive de-amination). Produced inside the system in quantities, and even more when they are fragments altogether alien within the normal processes, those products of bacterial life provoke vehement reactions: the complex sequence of inflammation and fever, aiming at elimination with the least delay. If cocci of the endotoxic type, with which we are dealing here, extend their activities further and come into the circulation, then a new danger to the body arises out of its very defence; outright destruction of the cocci would set free their endotoxic fragments, cells are poisoned to degeneration and death, and the mutual destruction, without intervention, usually ends fatally on both sides. In septicaemia more streptococci are found in the blood before than during the attacks of rigour and fever. Once the life-and-death struggle is at its height, both sides employ their utmost resources of defence, though that may complete the fatal cycle. We need not detail the weapons and their handling on both sides; for the coccisome of their "aggressines" are known and named from their effects only, such as haemolysines and leucocidines.

With regard to the action of sulphanilamides, it would appear anything but helpful if the cocci in the bloodstream were killed outright. Inhibition of their immediately aggressive and acutely dangerous activities, however, giving the body defences time to overpower and eliminate the living but helpless cocci, would be just the thing

to be looked for. And that is what appears to happen in the successful cases.

As to the normal sulphydril constituents of the cells, their legitimate reductive action might well lead to useless and even undesirable and potentially dangerous by-products, say, phenols. But in doing so, they themselves supply the detoxicating remedy; oxidized to sulphate, they conjugate with phenols to form ethereal sulphates. (It is worth noting that normally only three-quarters is excreted as fully oxidized sulphate, one quarter



remains incompletely oxidized, thus the oxidation after the conjugation is more likely.) The conjugation product, as Na- or K-salt, is easily soluble and speedily eliminated. The same qualities account for the comparatively low toxicity of sulphanilamides, though they are aniline compounds. Assuming an increased reductive activity of the normal sulphydril-peptides, such as may be provoked by inorganic hydrosulphides, like hepar sulphuris or mercaptans, undesirable pepton fragments would accumulate and, under certain conditions, lead to defence reactions of the inflammatory type. "Provers" susceptible to these substances would show the corresponding symptoms, as actually they did more frequently than could be attributed to incident. On the other hand, such artificially promoted and skilfully controlled reactions would increase a similar defence against

coccal action—in short, conform to the homoeopathic plan of assisting the body defence.

Now, where do the sulphanilamides come in? We shall presently examine the known facts as to whether they lend themselves to assuming direct stimulation of defensive reactions, and we may here anticipate that there is no proof and no probability of it. We assume no further mode of action than what has emerged from recent research, viz., that by means of their p-amino handle, as it were, they keep the p-amino-benzoic acid, essential to the cocci, away from them. If sulphanilamides were formed in the system and their production increased by sulphur stimulation, that would solve the problem. The sulphanilamides would be an important link in the defensive mechanism without being themselves capable of setting that mechanism into motion. Artificial addition of that ready-made link, when it is most needed, would enormously ease the task of the other defence measures. Of course, the body-made compound would not necessarily have to be identical with sulphanilamide, if only it had the same inhibitory action. It is suggestive to think of the normal phenol-conjugation with sulphite or sulphate in this connection. If p-amino-phenol were detoxicated *in vivo* in the same manner to form sulphanilic acid or its easily soluble alkali salts, such, or a slightly modified, intermediary product might be found to have the same temporary emergency function which is ascribed to sulphanilamide. However, the missing link in the chain of processes is not known and probably has not so far been looked for.

There we must leave, for the time being, the biochemical problem. It remains to examine the facts for or against the probability that sulphanilamides stimulate, and not only add to, the body defences against coccal infection. Provings of sulphanilamides on homoeopathic lines would give the best material on which to form an opinion; but the only one made so far with sulphamidochrisoidine (prontosil rubrum)* has, besides the known toxic effects, revealed only a number of sulphur- and sulphide-similar symptoms which, however, are not very distinctive. One has to rely mainly on experience with patients treated with these drugs. Such observations have the drawback that they make it difficult to discern drug reactions from the signs and symptoms of the infection. For the toxic effects of sulphanilamides, one should remember that they are aniline (p-amino-benzene) compounds. It is, therefore, not surprising that not infrequently toxic effects are incurred which are well known from poisoning with, or as "side effects" of aniline and its derivates, e.g., acetanilide (antifebrin). The sulphon-amide group apparently renders the anilide less toxic as may be deduced from the far greater doses usually employed with impunity than, say, of acetanilide. The latter, we may recall, is transformed *in corpore* to p-amino-phenol and excreted as such; we mentioned this product as possibly subject to detoxication by sulphate. Tentatively we may thus ascribe any aniline-like effects to the anilide becoming separated from the sulphonamide group and oxidized to p-amino-phenol.

* *Sutherlands and Roberts* (cf. journ. Am. Inst. of Hom. 1944, 37, 305).

Under sulphanilamide medication symptoms from the central nervous system are quite common —headache, dizziness, tinnitus, feeling of intoxication and depression ; the gastro-enteric syndrome of anorexia, nausea, vomiting and diarrhœa is also attributed to this central action. We encounter very similar side effects from numerous aniline derivates, like acetanilide, when they are employed as antipyretics and analgesics. Cyanosis due to methaemoglobinaemia is a far more distinctive feature ; it occurs from sulphanilamides as from many other aniline compounds. The rarer but more serious sequel from sulphanilamides, acute haemolytic anaemia, too, is shared by aniline and its oxidation products, equally as jaundice and toxic hepatitis are. The even rarer and most dangerous sulphanilamide sequel, agranulocytosis, is seen more often from benzene, dinitrophenol and amino-pyrine. Fever, often accompanied by a rash and mild eosinophilia, can be distinguished as due to sulphanilamide and not to the infection when it occurs after several days of medication and the fever from the original infection has already subsided. It is of a type familiar from the toxicology of acetanilide and similar aniline compounds. The manifold skin eruptions, besides allergic types as urticaria and angioneurotic oedema, those imitating exanthemata (morbilliform, scarlatiniform), erythematous, erysipeloid, petechial, purpuric, are also not distinctive for sulphanilamide ; they all occur, perhaps not so frequently, from sulphur-free aniline compounds. Considering the close connection of sulphur to the skin and its inflammatory disorders, the severer

dermatitis exfoliativa appears more characteristic for the sulphonamide ; it is not noted from other anilines ; but we recall that it occurs as toxic effect of arsphenamine, and there again we see the arsen affinity to the skin made more vehement by the aromatic bond.

Our brief summary of the toxic effects of sulphanilamides leaves the impression that they have much in common with septicaemia: fever, the central nervous and gastro-enteric syndromes, the whole series of skin eruptions, haemolysis, jaundice, hepatitis and the rare final development,- agranulocytosis. Thus, at first sight, sulphanilamide seems a remedy in septicaemia indicated on the homoeopathic principle. Yet, all these symptoms are, as we saw, not characteristic for sulphanilamide, but are shared by a great number of aniline compounds. Indeed, it is suggestive to ascribe them all to incidentally liberated aniline or its oxidation products. These are similar, partly perhaps identical, with poisonous products of katabolism which are normally quickly detoxicated and eliminated; it is, therefore, not surprising that they should arouse syndromes similar to septicaemia where these cell and bacteria fragments accumulate so that even intensified detoxication and elimination is no longer a match for them. The intact sulphonamide bonds, however, meet this precarious situation, partly through their rapid excretion. Furthermore, the syndromes as enumerated are either very common events or destructive final effects ; the first allow no distinction for selecting a homoeopathic remedy and the second signify the absence of reactions on

which a stimulative therapy would have to rely. True, advanced septicaemia, meningitis, etc., are just of that kind, all the available defence reactions are engaged, even overtaxed and exhausted. So they are not distinctive of any individual effort and do not indicate a peculiarly fitting stimulant : one may even say there is, at such a stage, no longer a call for any stimulant. We have to acknowledge certain limitations to homoeopathic therapy, and exhaustion of all body defence activities is a very definite one.

In these extreme conditions of body activities and interference with them by medicinal substances, we find ourselves approaching a borderline. And in matters biological such borderlines are not defined exactly. It would be easy to stretch the principle of similarity between remedy and disease far enough to comprise the relation of the effects of aniline compounds to coccal infections. Indeed, the similarity even of chemical constitution, identity of essential groups, between poison and antidote is often striking. We met it in the case of p-amino-benzoic acid and sulphanilamide. For any competitive antagonism on chemical lines this has to be expected. Similar intermediary reaction takes place, but it is isolated and not accessible to direct observation. To extend the principle of similarity, as conceived and applied in homoeopathy, to such extremes serves no useful purpose ; and that for the simple reason that the remedy fitting the case cannot be found by using isolated or indistictive criteria for the comparison on similarity. As a matter of fact, the virtues of sulphanilamides have not

been discovered with a view on any similarity but under the assumption that they would kill the bacteria *in vivo*. That proved faulty, but many things, like America, have been discovered under wrong premises. Sulphur, too, was used on vague ideas of its cleansing properties against purulent inflammations long before *Hahnemann* submitted it to scientific provings and found it, especially in the sulphide form, most suitable to promote similar reactions in man. Sulphanilamides might never be used in infectious diseases if they had to wait for the theory of depriving certain cocci of p-amino-benzoic acid by a similarly constituted compound unhealthy to them.

From the data so far reviewed, having not sufficient provings to judge from, we would conclude that the reactions to sulphanilamide do not show that degree of similarity to coccal infections which would suggest its curative effects to be due essentially to stimulation of the defence. There is another criterion : if sulphanilamide therapy should leave the patient after recovery in a state of improved defence, with some measure of immunity, it would be a forcible argument for the stimulative mode of action. Experience has shown that it is not so. The impression so far is that the same infections, notably pneumonia, recur even more frequently after sulphanilamide cures than was seen before that therapy, but it is too early to form a definite opinion on this point at present. Surely one would not expect creation of complete immunity through stimulation in these types of coccal infection which leave behind no natural immunity.

We recall that soluble exotoxins, provoking specific antitoxins, play only a secondary part in the activities of these cocci ; the main threat comes from the endotoxins, against which the more general, less specific, defence measures of detoxication and phagocytosis are called up. Thus the failure to promote immunity is no argument against stimulative action of sulphanilamides, but a lowered state of defensive preparedness after sulphanilamide therapy, if confirmed, would be so.

Our discussion of the problem must certainly not be understood as establishing the competitive antagonism for which some evidence has been revealed so far, as the only mode of action of the sulphanilamides. Nor should the tentative explanations, how such intermediary links may fit into a chain of defensive processes, be taken to be more than a first attempt to reconcile two apparently related fields of experience.

It is beyond the scope and purpose of our present discussion to follow up the whole range of sulphur actions which determine its use in homoeopathic therapy, indeed, make it the remedy perhaps most frequently called for. Even for the more acute actions of the sulphides, represented by hepar sulphuris calcareum, we have had to confine ourselves to that part of its sphere which best lends itself to comparison with sulphanilamide effects in coccal infections.

Thus, if, within the given limitations, your demand for learning about homoeopathy has not been satisfied, let us hope that it has been stimulated.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