HOMŒOPATHIC PROVINGS IN THE LIGHT OF THE NEWLY FORMULATED "HUMAN PHARMACOLOGY"

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As far as direct applicability to medical practice is concerned, it is quite certain that experiments made on man are always the most conclusive. No one has ever denied this.—CLAUDE BERNARD.

The first organized study of pharmacology in the West was not, as is generally believed, the animal pharmacology of Bucheim of Dorpat, Germany, in 1848, but rather the human pharmacology of Samuel Hahnemann of Meissen, Germany, fifty years earlier. Although there had been superficial investigations of human pharmacology throughout medical history, particularly in the latter half of the eighteenth century (J. Lind on scurvy, 1753; Menghini on camphor, 1755; Fontana on snake venoms, 1765; William Alexander on many drugs, 1767; Daries on Belladonna, 1776) nothing further was done by non-homœopathic pharmacologists until 1930's when Evans and Hoyle[1] and Gold[2] both published studies of the effectiveness of various substances in reducing cardiac pain. In fact, the re-awakened interest in this field is so recent that the first symposium of human pharmacology[3] was held in 1958 in London, and the first journal has just been published (January 1960).

Thus, it has been the privilege of homœopathic physicians to hold the science of human pharmacology in trust for all physicians for nearly 150 years. Their work has been based on Hahnemann's original criteria, best described, interesting enough, not by Hahnemann but by Drysdale,[4] the father of the British Homœopathic Association, in his classic paper of 1843 on the proper method of testing medicines on healthy humans. This has remained the standard for homœopathic physicians up to the present time and, as a result, homœopathic provings have not kept pace with the forward surge of medical dis-

coveries. The newly formulated science of human pharmacology however, contains the very best of the recent discoveries in clinical pharmacological techniques and because they bear so significantly on the conduct of homœopathic provings this paper has been prepared.

Since all sciences are basically mathematical, the changes in mathematical techniques in the past 150 years have naturally had a reflection in medical thought. This is particularly true in the field of statistics—founded by Süssmilch of Prussia in 1761.[5] Among other things, statistics elaborate the mathematical techniques by means of which controls of one sort or another help reduce experimental bias to a minimum. J. Lind[6] in 1753 used well-conceived placebo controls in his study of the effect of oranges and lemons on scurvy. (Hahnemann and Drysdale did not recommend the use of controls of any kind). Apparently the first use of controls in the nineteenth century biological sciences was that of Koch[7] in 1882. In his work on tuberculosis he left part of each group of experiments untouched as an "environmental control" on the possible action of variables other than those he was consciously manipulating. During the next 50 years, various investigators applied statistical concepts to experiments on animals, culminating in the work of Ronald Fisher[3] in 1935. He stressed the need for the proper pairing of control and experimental subjects for such variables as age, sex, race, religion, etc., and of the need to assign subjects to control and experimental groups by mathematical randomization. Fisher usually required hundreds of test subjects in his control and experimental groups in order to establish statistically valid results. One of his students Mainland[9] applied his work to the field of pharmacology, in particular to the design of experiments requiring fewer than 100 test subjects in each group. Rinzler[10] has drawn significant conclusions from samples as small as 25 in number. Evans and Hoyle[1] re-introduced into human pharmacology Lind's[6] use of placebo controls (or the "singleblind" test). Shortly thereafter Gold[2] introduced the "double-blind" test in which bias on the part of the supervising physicians is reduced by keep-

ing them in ignorance as to which medicine is the placebo and which the test substance.

Because of the increasing importance of placebos in human pharmacological research a number of investigators have studied the "placebo response" in some detail. Beecher[11] demonstrated in 1955 that 35.2±2.2% of 1,082 patients noted a marked improvement in their symptoms after receiving placebos. In addition to the improvement in existing symptoms Beecher[11] and Wolf and Pinsky[12] reported the development of toxic reactions to placebos varying in severity from difficulty in concentrating and fatigue, to palpitations, urticaria, diarrhoea and vomiting, in from 8-56% of control groups of various types of medicines.

Thus it would appear the Drysdale's[14] excellent experimental design of medicine testing needs to be further refined by preventing incorrect conclusions due to one or more of the following errors:

1. Contemporaneous errors resulting from short term epidemic contagions, mass atmospheric poisonings, mass emotional states, etc. These can be reduced by an unmedicated control group.
2. Toxic placebo symptoms. These could be discovered by a period on placebo before the experimental medicine is administered.
3. Amelioration of minor sub-clinical symptoms by the act of treatment itself, separate from the clinical agent. This could be discovered by a placebo before and during the administration of the active ingredient.
4. Errors of sampling due to age, sex, race, religion, health, and other difference between the control and experimental groups. They could be reduced by correct pairing and randomization of the variables.
5. Bias on the part of the subject if he knows when the test medicine has been administered. This could be controlled by the "single-blind" technique.
6. Bias in the part of the supervising physician in his descrip-

tion of the test subjects if he knows which are controls. This can be controlled by the double-blind technique.

7. Paucity of test subjects for statistically significant results. This can be corrected by having at least 25 members in each group of subjects.

To be specific, Drysdale's[1] instructions could be modified by interposing the following paragraph after his section on "idiosyncracy":

The test subjects should be assigned by randomization into three groups of at least 25 subjects each in such a manner that each group contains approximately equal numbers of every type of subject as classified by age, religion, sex, race, etc. After whatever diagnostic procedures as seem indicated have been completed, all the members of the groups will start their daily diaries. After a period of at least two weeks, two of the groups will be started simultaneously on placebo, the third remaining untreated throughout the course of the experiment. After a period of at least two weeks on placebo one of the two placebo groups will, without the knowledge of the subjects or supervising physicians, receive the experimental substance. All physicians who come in contact with the provers shall be kept in ignorance as to the contents of the medicines they administer. When the final evaluation of the test is made only those symptoms will be considered significant which

1. Differ from the symptoms experienced before any active ingredient was given.
2. Differ from the symptoms of the placebo control group and the unmedicated control group.

This paper is, of course, strictly suggestive. It is hoped, however, that some of the suggestions contained herein may help stimulate a much-needed re-organization of the criteria for homœopathic medicine testings.

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