INTERNATIONAL JOURNAL OF LEPROSY

PUBLISHED AS THE OFFICIAL ORGAN OF THE INTERNATIONAL LEPROSY ASSOCIATION WITH THE AID OF THE LEONARD WOOD MEMORIAL

Postal Address: Dept. of Preventive Medicine, School of Medicine, 2109 Adelbert Road, Western Reserve University, Cleveland 6, Ohio.
Entered at the Post Office at Cleveland as second-class matter.

Vol. 15, No. 3 1947

EDITORIALS

Editorials are written by members of the Editorial Board and opinions expressed are those of the writers.

LET US ALSO HAVE PRELIMINARY EVIDENCE

After many years of study with chaulmoogra derivatives in the treatment of leprosy, the results with this one drug do not permit one to make any simple statement concerning its effect on the parole rate or other objective yardstick. A recent editorial by Dr. Doull presents the challenge that *this time we must have proof!* Final proof can be gotten by properly planned clinical study, and by that method alone. This means that both the Governments and the Committee involved must be prepared for prolonged and expensive undertakings, and that once committed to the testing of a certain drug there can be no turning back during a period of less than several years.

There are not enough patients under the supervision of careful investigators to justify the hope that more than a very few drugs can be properly evaluated within our generation. It will be a misfortune, therefore, if these skilled leprologists are permitted to undertake this arduous task without every assurance that the drugs to be tested are indicated and justified by every criterion available.

The synthesis of sulfa and sulphone drugs and the discovery of the antibiotics provide the methods and the principles required either to manufacture or to search for agents effective against all infectious diseases. The new drugs studied thus far are "hand-me-downs" from investigations in tuberculosis. All recognize, nonetheless, the fundamental differences in the physiology of tubercle

and leprosy bacilli and in the biology of tuberculosis and leprosy. One of the great dangers in relying upon a related disease as the screening agent is the possibility that drugs which are not effective in tuberculosis may be discarded and forgotten without ever having been tried in leprosy. With the large and carefully classified group of patients and the prolonged and meticulous observation required to evaluate drugs by clinical trial, this will surely result if chemotherapeutic plans are confined to the clinic.

Chemotherapy and antibiosis depend on the principle of interference with specific metabolic peculiarities of the parasite. Only the specific parasite can serve as a screening agent. It follows that cultivation of the causative agent has never before been so urgent as it is today. Though *in vitro* inhibition does not prove therapeutic effectiveness, it does permit rapidly sifting out those compounds which are not worthy of more extended work, and is the most practical tool for directing the synthesis of, or the search for, active agents.

In the meantime how shall we screen drugs so as to bring to clinical trial those which impede the metabolism of the type which characterizes leprosy bacilli? Let us not forget that the rat leprosy bacillus possesses many if not all the metabolic peculiarities of the human leprosy bacillus, that it readily infects mice, that mice are a standard test animal for which there is likely to be tolerance data on practically every drug developed, and that these animals can be used in such numbers as to provide statistically significant data.

Dubos and co-workers have recently demonstrated remarkable differences in the susceptibility to tuberculous infection of the different families of mice developed in cancer research, and have shown their suitability for virulence testing.

If in a susceptible mouse family one were to use a test dose of leprosy bacilli producing cutaneous lesions (or perhaps death by the intracerebral route) within one to two months, it is probable that drugs failing to inhibit lesions during this short period could be regarded as not sufficiently active, and that only those which meet this criterion would need to be followed for longer intervals.

Certain advantages of carefully planned mouse screening arise from the fact that in a central testing laboratory a single group of control mice can serve as a base line against which to compare simultaneously as many drugs as the number of mouse groups which can be handled. With a standard mouse family, test dose and diet, and the advantage of using organisms which are visible and

countable, one could hope for a system with fewer difficulties than those which continually beset investigators in virus work.

Clinical trials could then be conducted with the probability that useful drugs have not been overlooked and that the selected drugs are those most likely to interfere with the metabolism of the human leprosy bacillus. *Let us also have preliminary evidence.*

JOHN H. HANKS