

## 6 THIOSEMICARBOZONES IN TUBERCULOSIS

Occasionally of late there have been seen titles and abstracts of reports of the use in Germany, during the past two years and more, of a new type of sulfur-containing chemotherapeutic agents for tuberculosis, drugs of a class called thiosemicarbozones. In the January 1950 issue of the *American Review of Tuberculosis* there are no less than four articles on the subject which, taken together, constitute a comprehensive review of the chemical features of these drugs and of animal and clinical experimentation with them, with particular reference to one which has been given the trade name of "conteben." Three of these articles emanate from the laboratories of the Elberfeld Works of the Farbenfabriken Bayer, at Leverkusen. The fourth is a report of a special survey of the results of the clinical use of conteben in 10 of the 300 institutions in the western zone of Germany where, it is said, this drug has been employed in the treatment of a total of far more than 10,000 patients with various forms of tuberculosis. This survey, made possible by the Schenley Laboratories and the Bayer Company in the United States, was carried out on behalf of the American Trudeau Society, the medical section of the National Tuberculosis Associ-

ation, by Drs. H. Corwin Hinshaw and Walsh McDermott, two of the leading investigators in the field of chemotherapy of tuberculosis.

Impressive as are the reports from the German source, the indications of the value of conteben<sup>1</sup> will be given all the more attention because of the agreement of the American investigators on virtually all essential points, and their conclusion that the drug can no longer be ignored in the United States and should promptly be subjected to thorough experimental and clinical trials there—which of course does not imply—restriction to that country.

Because effectiveness of any chemotherapeutic agent in clinical tuberculosis may well have implications regarding leprosy which should not be overlooked, these articles are abstracted at some length elsewhere in this issue (p. 129). Of interest from the theoretical point of view is the conclusion of Behnish, Mietzsch and Schmidt that, while the activity of the whole class of drugs to which the thiosemicarbozones belong depends on the sulfur atom, it does not depend on the sulfone or other groups; they hold that an open, chain-like arrangement of nitrogen and sulfur atoms as in the thiosemicarbozones is a much more active principle. Of interest to leprologists, and familiar to those who have been using the sulfones and especially the base substance diaminodiphenyl sulfone, are the small quantities employed, the slow attainment of maximum dosage and the individualization of patients as regards that maximum, the nature of the toxic effects (which, however, include apparent effects on the liver not as yet reported in connection with the sulfone treatment of leprosy), the prompt and striking effects on lesions of the mucous membranes, and the apparent usefulness in cutaneous affections.

Also of interest are the conclusion that the effects are due to a direct influence on the bacilli and not some hypothetical indirect action, and the changes of staining capability of the bacilli described by Domagk and in part also by Mertens and Bunge. It is said that they first lose their acid-fastness but—this by implication—persist as gram-positive forms; then gram-positiveness is lost, but still they may persist for a long time and be demonstrated by fluorescence microscopy. So far as we are

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<sup>1</sup> This is the Bayer name. Proposed proprietary names of other manufacturers in the United States, according to Hinshaw and McDermott, are "tibione" (The Schenley Laboratories) and "myrizon" (E. R. Squibb and Sons).

aware, no such observations have been made with respect to the leprosy bacilli in lesions.

— H. W. Wade

We are informed by the Schenley Laboratories, Inc., 350 Fifth Ave, New York 1, N. Y., that reprints of the articles referred to—which they had translated from the German for publication—are available for interested leprosy workers on request.

—H. W. W.