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Reply to Dr. Harboe's and Dr. Closs' Letter to the Editor

TO THE EDITOR:

We have no explanation why Harboe and Closs were unable to reproduce our lithium acetate extraction procedure to obtain an extract containing antigens with reactivities that we described as *M. leprae* "specific" in 1979 ([2]). We have reproduced this extraction procedure with comparable results more than 15 times and would welcome Harboe or Closs trying the same procedure in our laboratory. Perhaps small but relatively important differences in technique would prove responsible for their inability to detect the antigen(s) that we described.

Harboe and Closs state that our "antigen" cross-reacts with *M. avium* and BCG. These authors have demonstrated that our antigenic extract reacts with antiserum to *M. avium* and BCG without demonstrating that the antigen(s) with *M. leprae* "specific" activity react with the BCG and *M. avium* antiserum. We have never claimed antigenic purity of the lithium acetate extract, and an SDS polyacrylamide gel of this extract reveals that more than ten separate proteins as well as carbohydrate and glycolipid molecules are present. One would estimate therefore that there may be 10 to 20 separate antigens in this extract, considerably more than just the antigens 4, 5, and 7 recognized with CIE by Harboe and Closs. The basis for the claim of "specificity" of protein antigenic determinants for *M. leprae* was the use of a pool of sera from LL patients adsorbed by Abe, *et al.* ([1]) with BCG, *M. vaccae*, cardiolipin, and lecithin. This adsorption made the serum pool "specific" for *M. leprae* in an IFA test and specific for *M. leprae* as compared to four other mycobacterial species using double diffusion in gel. The proof that the *M. avium* or BCG antisera recognized the same *M. leprae* antigen(s) in our extract as that recognized by Abe's adsorbed serum pool would require using Abe's adsorbed serum pool in the same double diffusion in gel experiment. This critical experiment was not performed by Harboe and Closs. Therefore, their claim of cross-reactivity between the antigen(s) that we described and antigens of *M. avium* and BCG, while potentially correct, is not proven.

We have extended our studies by reacting Abe's adsorbed serum with lithium acetate extracts from 21 species of mycobacteria in double diffusion in gels. In September 1979 we reported that Abe's adsorbed serum recognized a shared antigenic determinant between *M. leprae* and *M. lepraemurium* ([3]). Subsequent studies with Abe's adsorbed serum also showed shared reactivity between *M. leprae* and *M. bovis* (BCG), *M. gordonae*, *M. nonchromogenicum*, *M. flavescens*, and *M. gastri* and no shared reactivity with 15 other mycobacterial species including significant human pathogens such as *M. tuberculosis*, *M. intracellulare*, *M. scrofulaceum*, *M. kansasii*, and *M. marinum*. These results are summarized in an abstract ([4]) which has appeared since the letter of Harboe and Closs was written.

It is our opinion that definite proof of whether or not *M. leprae* contains unique antigenic determinants will require monoclonal antibodies or extensive antigen purification. It cannot be answered by double diffusion in gel or CIE experiments.

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Mechanism of Action of Sulfones

TO THE EDITOR:

In an editorial in the INTERNATIONAL JOURNAL OF LEPROSY ([2]), in a work of Seydel, *et al.* ([4]), and in a work of McDougall ([3]), the possible mechanisms of action of sulfones in leprosy are analyzed.

We have worked on this subject and published a very extensive monograph, dealing with the pharmacology and toxicology of sulfones ([1]). Our work has proven experimentally that sulfones have the following pharmacological properties:

1) The sulfones are powerful biological antioxidants. As a class, they are perhaps one of the most powerful known up to the present time. They can replace vitamin E biologically in white rats fed pro-oxidant diets. Sulfones have high activity in the formation of ceroid pigment, showing activity in a concentration of 1:100,000. Also, they prevent the decolorization of the upper central incisors and the renal autolysis postmortem in the animals.

2) The sulfones have radiosensitizing activity in white mice subjected to LD 50/30 of X rays.

3) The sulfones have hepatic enzymatic inductive activity in white rats, as determined by barbiturate sleep.

4) The sulfones have hepatoprotective activity in acute intoxication by carbon tetrachloride in white male rats. It is known that the toxicity of carbon tetrachloride and of ethanol is related to a mechanism of lipoperoxidation.

5) The sulfones are powerful carcinogens in white male rats, able to induce malignant tumors of the spleen and the thyroid.

We believe that the mechanism of action of sulfones involves its very powerful antioxidant capacity, which can explain all the pharmacological activities mentioned above.

It would be highly advisable that those who study the problem of the mechanism of action of sulfones take into account the experimental facts described in this letter, which have been summarized in the monograph concerning the sulfones ([1]) already discussed.

It should be noticed that the properties described for the sulfones are shared in major or minor degree by other antileprotics such as clofazimine, the phenylthioureas, and the antileprotic thiosemicarbazones.

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