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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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Reply to Dr. Bergel's Letter to the Editor

TO THE EDITOR:

The results on pharmacological and toxicological effects of dapsone (DDS) obtained and discussed by M. Bergel in his Letter to the Editor might be of great interest; they have, however, nothing to do with the antibacterial mode of action of DDS on the enzymatic level of the bacterial cell. The action of DDS is highly specific on the 7,8-dihydropteroate synthetase, i.e., the inhibition of bacterial growth occurs via depletion of dihydrofolate. It can be totally antagonized by p-aminobenzoic acid (PABA), which competes with DDS for the binding site on 7,8-dihydropteroate synthetase.

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The Fingers in Non-lepromatous Leprosy

TO THE EDITOR:

Dr. McDougall ([4]) comments on Dr. Pearson's finding of inflammatory cells in the skin of the fingers of patients with non-lepromatous leprosy in the absence of skin lesions. He concludes that the fingers may be a focus for leprosy bacilli similar to the observations in patients with lepromatous leprosy. However, in describing Dr. Pearson's findings, he states that although inflammatory cells were present "*no acid-fast bacilli were seen.*" Previously, I described inflammatory cells in the skin of the hand of a patient who had severe edema of the hands and feet and acute sensory loss. There was no hypopigmented skin lesion at this site, and in spite of inflammatory cells, no acid-fast bacilli were found ([1]). At the X International Leprosy Congress at Bergen in 1973, I described two further non-lepromatous leprosy patients who had edema of the hands and feet in which skin biopsies showed inflammatory cell infiltrates at these sites ([2]). Dr. Pearson's observations in patients with swollen extremities would be consistent with these findings.

The significance of these findings lies in the fact that this inflammatory cell infiltrate is associated with sensory loss which may be acute and is of glove and stocking distribution, i.e., a sensory polyneuritis probably occurring in the *absence* of leprosy bacilli. If unrecognized and untreated, sensory loss will be irreversible, leading to the inevitable sequelae: mutilation of the fingers and toes, ulcers of the feet, osteomyelitis, and Charcot's joints. Current descriptions of "reversal reactions" emphasize the pain and swelling in the hypopigmented skin lesions and also in the peripheral nerve trunks but infrequently mention the edema of the hands and feet. In my opinion, it is the edema of the hands and feet which is much more important in indicating nerve damage, and it usually occurs in the absence of visible changes in the skin lesions and pain in the nerve trunks ([3]). Furthermore, the experimental finding of foot pad swelling, mononuclear cell infiltration, and cutaneous nerve damage in thymectomized and irradiated mice which have been given injections of lymphocytes is similar to this clinical syndrome ([5]).

Dr. McDougall's suggestion of the need for further investigation of this syndrome is welcome. The dose and timing of corticosteroid therapy could be monitored by performing serial skin biopsies in the hands and feet.

—C. L. Crawford, M.B., M.R.C.P., D.T.M.&H.