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EDITORIAL

LEISHMANIASIS : AN INCREASING THREAT

Leishmaniases comprise a group of diseases with a spectrum of clinical manifestation ranging from self-healing cutaneous ulcers to severe disease with high mortality. Leishmaniasis is now endemic in 88 countries, including southern Europe, with some 350 million people living in endemic areas. An estimated 12 million people are infected each year including 1.5 million new cases. Leishmaniasis has been included amongst the six entities on the World Health Organization/ Tropical Disease Research list of most important diseases. The current interest in the disease arises from a number of reasons. New foci of disease have been reported, viz. visceral leishmaniasis in Nicaragua, and insect and vertebral hosts have been reported from the Sudan and Saudi Arabia. Two major ongoing epidemics of visceral leishmaniasis have occurred in recent years, one in Bihar (India) and the other in southern Sudan during 1997-1998. In the Indian epidemic widespread failure of treatment with antimonials, which have been the mainstay of treatment for decades, has been reported. Visceral leishmaniasis is emerging as an important opportunistic infection among subjects with HIV, and 1.5-9.0 per cent of patients with AIDS develop the visceral form of the disease. Establishing a definitive diagnosis has depended on finding the parasite in bone marrow or spleen macrophages by light microscopy. Pentavalent antimonial agents given parenterally for 20 days has been the mainstay of treatment, but there are signs of emerging resistance. Amphotericin B that was hitherto relegated to the second line of treatment because of toxicity has now been reintroduced in another format. Lipid formulations of amphotericin B (amphotericin B lipid complex; amphotericin B cholesteryl sulphate; liposomal amphotericin B) are undergoing dose optimization studies and offer much promise. Another possible drug is paromomycin, usually administered jointly with the antimonials. Miltefosine which was also developed for the treatment of visceral leishmaniasis has proved to be first orally active drug against kala azar including antimony resistant cases. But drug is very expensive and contraindicated in pregnancy.

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In the years following 1858, when the British Raj formally assumed power over the whole of British India, the first report on its epidemic was recorded. This epidemic was due to Kala-azar. Once *Leishmania donovani* had been identified as the causative organism of Kala-azar, news of its existence came from other areas where the disease was endemic.

Pentavalent Antimony treatment of Kala-azar was introduced by Sir U.N. Brahmachari. The great success of the organic arsenic complex atoxyl gave Brahmachari the inspiration that an antimony compound obtained by replacing arsenic of atoxyl with antimony would be specific against Kala-azar. This is the story of discovery of Urea Stibamine, the urea salt of p-stibanilic acid. The timely

discovery of the drug prevented the spared in other parts of the country the horrors witnessed earlier in Assam (1890-1925). In the chemotherapy landscape of Kala-azar, the discovery of urea stibamine is certainly a landmark. The work is a monument of labour and knowledge, and was amply rewarded by the clinical success it attained.

Wallace Peters in his lecture in 1978 in connection with the lady U.N. Brahmachari Memorial Oration at the University of Calcutta stated, "Urea Stibamine was a compound that could never have seen the light of the day had it been invented in the past decade. Preclinical toxicity tests carried out prior to the first administration of this new drug to the man were the simplest, and of such a nature that the compound would not have been contemplated for clinical testing for a moment in our modern age of superconscientiousness and highly sophisticated drug toxicity testing regulations. Nevertheless, urea stibamine, produced by Brahmachari in the research institute that he was later able to form from his private means, was administered to hundreds of sufferers from kala-azar".

We still do not know the exact cause of antimony resistance in Kala-azar and until now an effective vaccine against Kala-azar does not exist. Thus there is a great deal of resurgence of interest in Leishmania research as the disease is widening its base not only in our country but also else where. This special issue of the Science and Culture devoted towards Leishmania research will hopefully provide with some glimpses of current trends in this area. ❐

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