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CORRESPONDENCE

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Delayed cerebellar ataxia: a new complication of falciparum malaria?

SIR,—Professor Nimal Senanayake's observation of cerebellar ataxia as a possible delayed complication of falciparum malaria has been made by others in Sri Lanka over the past few years.[1,2] In these series, however, there was no parasitaemia during the cerebellar illness, and a documented attack (blood film positive for ring forms of the parasite) of falciparum malaria, which was successfully treated with chloroquine, preceded its onset. Cerebellar ataxia occurring during an attack of falciparum malaria has been reported previously.[3]

Ring forms of *Plasmodium falciparum* were seen in blood films from five of Professor Senanayake's 12 patients, and in four the parasite was resistant to initial treatment. This may suggest that the ataxia occurred during an attack of inadequately treated, resistant malaria and that his series had two subgroups of patients: those with and those without evidence of infection during ataxia. Therefore, the word delayed may not be relevant in all 12 cases.

All of the patients had visited or were resident in the northern, central, or eastern parts of Sri Lanka, which are endemic for malaria. Professor Senanayake has not, however, taken into account the epidemic of Japanese encephalitis that affected these areas during the period in which many of his patients would have presented. As this virus may produce cerebellar ataxia[4,5] I believe that it deserved more specific exclusion by serology, particularly as Professor Senanayake himself admits to the presumptive nature of the diagnosis of falciparum malaria in some of his patients.

Reports of ataxia associated with malaria seem to have originated solely from Sri Lanka. I wonder whether this phenomenon has been observed in the countries of South East Asia and Latin America where falciparum malaria is a major problem?

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Treating Paget's disease

SIR,—Dr David Heath viewed the place of medical management of Paget's disease of bone somewhat pessimistically in the sense that the "almost exclusive" indication offered was for the treatment of bone pain (25 April, p 1048). In contrast, we believe that the development of the diphosphonates has revolutionised the potential for treatment of Paget's disease.

Whereas the effects of the calcitonins and mithramycin do not persist long after stopping treatment, diphosphonate treatment consistently results in a reduction of disease activity for many months or even years after stopping treatment.[1] The question arises whether long term control of disease activity confers important advantages. Dr Heath concedes that this may be so in the case of bone pain, but there are other instances that suggest that the long term or more complete control of disease activity confers clinical benefit. The calcitonins, disodium clodronate and aminohydroxypropylidene diphosphonate, have been shown to halt the advance of Paget's disease.[1-3] Moreover, the decrease in bone turnover at affected sites seems to be associated with a resumption of lamellar rather than woven bone formation.[4-6] These observations suggest that progressive deformity of Paget's disease might be prevented but do not help to determine whether a deformity may be reversed. Our preliminary observations in Paget's disease of the facial bones suggest that not only may progressive deformity be arrested but adequate modelling of bone may also occur with long term treatment.[1]

Improvements in skeletal architecture are difficult to assess, but objective evidence for the efficacy of medical treatment is available for the neurological syndromes that may complicate Paget's disease. There is now considerable evidence to suggest that effective medical management may improve or halt the progression of some of these syndromes.[7-9] Irrespective of the agent used, substantial clinical improvement occurs in most patients with spinal root and cord syndromes. In patients with slowly progressive lesions the response rate is comparable with that observed after laminectomy but without the hazards of surgical intervention.[8,9] After medical treatment the duration of clinical improvement correlates remarkably with the degree of disease activity, as judged by biochemical estimates of bone turnover, and provides perhaps the most convincing evidence for the relation between clinical and biochemical indices of disease activity. Though these studies are uncontrolled, it is unlikely that improvements are the result of the natural history of the disorder as spontaneous recovery from cord compression due to Paget's disease has not been reported. Responses in bone pain, neurological syndromes, the formation of lamellar bone, radiographical improvements, and changes in skeletal shape suggest that the long term control of Paget's disease is likely to yield clinical dividends.

We have suggested that high doses (20 mg/kg/day) of disodium etidronate for one month were as effective as a six month course using recommended doses (5-10 mg/kg/day).[10] We have confirmed these observations in a larger number of patients and shown the responses to be more consistent than with the low dose regimen.[11] Moreover, the duration of remission (62% relapse free at 12 months) was similar to that achieved with high or low doses of disodium etidronate used for six months and to that achieved with oral disodium clodronate. In this study it was particularly interesting that the more complete biochemical suppression was associated with more prolonged responses, irrespective of the regimen used or the pretreatment disease activity. Indeed, some of our patients remained in symptomatic and biochemical remission after six years without further treatment.