Hepatocellular carcinoma and African iron overload

EDITOR.—Gangaidzo and Gordeuk (Gut 1995; 37: 277-270) postulate that iron overload may be a risk factor for hepatocellular carcinoma (HCC)—a subject of obvious interest to workers in Africa. It is especially so to one of us (AW) who, originally, in 1953, proposed the iron overload hypothesis. This sought to explain the abnormal iron deposition (siderosis) present in many Africans, caused by a high adventitious intake of the element arising from food preparation in iron utensils.1

In comment, firstly, the above authors state that HCC is probably the commonest malignancy occurring in men worldwide. Actually it ranks eighth in numerical importance on a worldwide basis, accounting for 3-3% of new cancers in men and 2-6% in women.2

Next, it is insufficiently appreciated that its incidence in men in Africa is highly variable, ranging from 47.9 per 100 000 world population to 7.5-10 per 100 000 in Uganda and South Africa.3 In agreement with the latter, recently, in three rural widely separated hospitals, responsible for the needs of about 400 000 Africans, we found an average of five admissions of HCC per 100 000 annually. Interestingly, the latter rates are much the same as those of Afro-Americans, 5.0-6.6 per 100 000.3 The citing of 100 cases per 100 000 in Mozambique is inappropriate as no well-defined transfusorsing type made in Uganda,4 has been pursued in Mozambique—a country at war for 20 years. We know of no present day excessively high rates for HCC in African countries south of the Sahara.

Turning now to the noxiousness of iron overload, in the original hypothesis, also in a subsequent local study based on 296 postmortem examinations at Baragwanath Hospital, Soweto, Johannesburg,5 the pathogenicity of iron overload was doubted, for no constant correlation was found between the degrees of fibrosis and cirrhosis and the amount of iron pigment in the liver. Later, in a hospital, as recently detailed by Lynch,6 associations were reported of siderosis with osteoporosis, diabetes, oesophageal cancer, and heart failure. The findings in these studies, however, made over 20 years ago, have not been currently confirmed. More to the point, over the decades, no attempt has been made at the village level to learn whether iron overload contributes significantly to morbidity and mortality, that is, is it disadvantageous to 1 per 100, or 1 per 1000?

In an investigation made in 1985 by Gordeuk et al7 in Zimbabwe, it was estimated that 550000 were at risk of iron overload. In the same year, it was stated that in that country there were 14 587 cases of malaria, 2956 of tuberculosis, and 144 of cholera. Surely, were iron overload as pathogenic as suggested, there would have been a plethora of evidence incriminating it. This does not seem to be the case.

Gangaidzo and Gordeuk regret that in Africa, only about half of the cases of HCC are attributable on the basis of HBV infection. It must be recognised that apart from the cause and effect of classic deficiency diseases, the above proportion or less is common with cirrhosis in Africa—dental caries, coronary heart disease, and certain cancers. In brief, the balance of knowledge and ignorance regarding the causation of HCC is the usual.

We entirely support the authors in their urge that prospective studies should be undertaken to examine the possible role of African overload in the pathogenesis of HCC. However, at the village level, in the requisite studies, major difficulties will be encountered regarding participation, especially regarding blood taking and the fear of AIDS. A complicating factor for HCC, as Kew and associates5 have shown, is the high rate of HBV, an important aetiological factor, varies not only from region to region, but from village to village. Additionally, there will be the usual difficulties in seeking to resolve whether iron overload, if implicated, is a causative or an associated factor. Not least of perplexities is the situation whereby a given parameter, for example, serum ferritin concentration, can have a differing significance according to the context. As a recent example of this phenomenon, at Belfast and Toulouse, there is the same average serum cholesterol value but a fourfold difference in mortality from coronary heart disease.

Finally, should iron overload be meaningfully incriminated, the authors say ‘it is evidently preventable through changing the practices of preparation and consumption of traditional beer', by phlebotomy therapy to remove iron from the body.7 In our view, both of the suggested procedures, in the rural context, are non-starters.

To reiterate, while we are unconvinced of the clinical importance of iron overload, the issue must be resolved—whether it is or is not of public health significance within the context of impoverished Africa.

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Analysis of biological variables in Crohn's disease

EDITOR.—We wish to comment on the paper by Sahmoud et al (Gut 1995; 37: 811–8) where the authors suggested the following factors to predict relapse: disease, interval since previous relapse, and colonic involvement as powerful prognostic factors to predict relapse in quiescent Crohn's disease. We also followed up for 18 months 107 patients with Crohn's disease in Remission 1 and used laboratory tests enhanced by clinical characteristics for predicting relapse.

Interestingly, our results about clinical characteristics were, for some aspects, similar to the results from the preparation of traditional beer in place of the newer and more convenient, but probably more dangerous, iron drums. For the past two years our research team has conducted a rural based trial on the presence of dietary iron overload. We have been struck by the overwhelming level of cooperation that we have been able to obtain through close and regular contact with the rural communities. Despite the need for veneration and a high awareness of the problem of HIV, it has been unusual for subjects to refuse to take part.

In summary, we believe the available data point to both HCC and dietary iron overload as major health problems in rural Africa. There is a strong body of evidence to suggest an association between the two conditions. Major initiatives are needed to combat these diseases beginning in the communities where the people live.

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