study, necropsies were performed on 604 adult blacks from southern Africa and one of five grades of hepatic and splenic iron was assigned based on the Prussian blue reaction obtained when a piece of tissue was dipped in a mixture of potassium ferrocyanide and hydrochloric acid.¹¹ Using logistic regression models, we found that iron overload was strongly associated with the findings of cirrhosis ($p < 0.0001$), HCC ($p = 0.0002$), and tuberculosis ($p < 0.0001$).¹⁰ Secondly, we reviewed all 320 diagnostic liver biopsy specimens processed at the University of Zimbabwe from 1992 to 1994. HCC was present in 19% of the evaluable specimens, cirrhosis in 21%, and high grades of iron in 19%. We found significant associations between the presence of iron overload and the histological diagnoses of cirrhosis and HCC.

We do not completely share the pessimism of Drs Walker and Segal with regard to changing the method of preparation of traditional beer and to instituting a phlebotomy programme. The iron drums that are now used to prepare traditional beer replaced clay cooking pots around the turn of the century, but these clay utensils are still used in most rural communities to prepare food and other forms of beverages. It seems feasible to us to encourage the use of these clay pots for 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 study 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 venesection 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.

INNOCENT TICHAONA GANGAIDZO
Department of Medicine and the
Clinical Epidemiological Unit,
University of Zimbabwe School of Medicine,
PO Box A178,
Avondale,
Harare,
Zimbabwe

VICTOR ROLAND GORDEUK
Department of Medicine,
George Washington University Medical Center,
Washington DC,
USA

- 1 Sackett DL, Hayes RB. Bias in analytic research. *J Chron Dis* 1979; 32: 51-63.
- 2 Kew MC. Hepatocellular carcinoma: epidemiology. In: Watters D, Kiire CF, eds. *Gastroenterology in the tropics and subtropics*. London: Macmillan, 1995: 184-6.
- 3 Cook GC. Hepatocellular carcinoma: one of the world's most common malignancies. *Q J Med* 1985; 57: 705-8.
- 4 Gordeuk VR, McLaren G, Samowitz W. Etiologies, consequences and treatment of iron overload. *Crit Rev Lab Clin Med* 1994; 31: 89-133.
- 5 Bothwell TH, Bradlow BA. Siderosis in the Bantu. A combined histopathological and chemical study. *Arch Pathol* 1960; 70: 279-92.
- 6 Bothwell TH, Isaacson C. Siderosis in the Bantu. A comparison of incidence in males and females. *BMJ* 1962; i: 522-4.
- 7 Isaacson C, Seftel HC, Keeley KJ, Bothwell TH. Siderosis in the Bantu: the relationship between iron overload and cirrhosis. *J Lab Clin Med* 1962; 58: 845-53.
- 8 Bassett ML, Halliday JW, Powell LW. Identification of homozygous hemochromatosis subject by measurement of hepatic iron index. *Hepatology* 1986; 6: 24-9.

9 Friedman BM, Baynes RD, Bothwell TH, Gordeuk VR, MacFarlane BJ, Lamparelli RD, et al. Dietary iron overload in southern African blacks. *S Afr Med J* 1990; 78: 301-5.

10 Gordeuk VR, MacPhail AP, McLaren CE, Deichsel G, Bothwell TH. Associations of iron overload in Africa with hepatocellular carcinoma and tuberculosis: Strachan's 1929 thesis revisited. *Blood* 1996; 87: 3470-6.

11 Strachan AS. *Haemosiderosis and haemochromatosis in African natives with a comment on the aetiology of haemochromatosis*. [MD thesis]. Glasgow: University of Glasgow, 1929.

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 features: age, duration of 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 clinical remission¹ and we used laboratory tests enhanced by clinical characteristics for predicting relapse.

Interestingly, our results about clinical characteristics were, for some aspects, similar to those obtained by the French group. A Cox regression analysis indicated interval since previous relapse, previous surgery, location (ileum versus non-ileum), and occurrence of postsurgical clinical recurrence as predictors of relapse; however an intercorrelation was found among these characteristics and particularly between previous surgery and location (but simultaneous Cox regression indicated that surgery would be more predictive than location). Thus two groups of risk of relapse according to clinical characteristics were defined: (a) favourable group consisted of patients in clinical remission after last relapse for at least 24 months or patients with less than 24 months but who had undergone surgery without subsequent post surgical clinical recurrence; (b) unfavourable group consisted of patients in clinical remission for less than 24 months not included in the favourable group.

In the French study surgery was not identified as a prognostic factor; this could be explained because in that study quiescent disease induced by surgery seems to be excluded and ileal location (and for this reason also previous resection) is present in a small number of patients in comparison with colonic location. In our experience duration of illness was not a useful predictor of relapse; we did not study age of patients.

In the study by Sahmoud *et al* biological indicators such as albumin and erythrocyte sedimentation rate did not result in predicting the course of the disease; in contrast, in our experience, laboratory tests seem to be extremely useful for this aim. In a previous study² a prognostic index based on laboratory tests was proposed. In our last study¹ the ability of this index to predict relapse was validated and a simplified application was proposed; patients with at least one of the laboratory tests changed (α_1 acid glycoprotein > 130 mg/dl, or α_2 globulin > 9.0 gm/l or erythrocyte sedimentation rate > 40 mm/h, or all three) presented within 18 months a relapse rate of 75% whereas in patients with normal tests it was 13%. In our study nine among 18 false-negative (normal laboratory tests with subsequent relapse) were represented by patients with previous remission < 3 months who had recently stopped corticosteroid treatment. Usually, however, values of laboratory tests are rapidly normalised by a period of

corticosteroid treatment and it is shown^{3,4} that these tests, performed during or immediately after corticosteroids have poor ability in discriminating the clinical outcome. In our opinion the French investigators were unable to show a prognostic ability of sedimentation rate and albumin because at least 64 patients among 167 included were treated with corticosteroids at the entry of the study (placebo group of the trial about usefulness of prednisolone treatment in patients in clinical remission after prednisolone treatment for an acute attack).

We agree, however, with Sahmoud's conclusions about the necessity of identifying patients with different risks of relapse in quiescent Crohn's disease. In our study, at the end of 18 months of follow up, the predicted proportion of patients with relapse was 13% and 31% in the subgroup with normal laboratory tests and favourable and unfavourable clinic characteristics respectively, and 87% in patients with abnormal tests and unfavourable characteristics. Thus risk of relapse varies substantially among different subgroups of patients with clinical remission; prediction of this risk is helpful not only for a correct design of clinical trials, but also, in clinical practice, for timing subsequent clinical visits and for selecting groups of patients where preventive treatment could be justified.

C BRIGNOLA
C BELLOLI
G DE SIMONE
M CAMPIERI
P GIONCHETTI
A BELLUZZI

Istituto di Clinica Medica e Gastroenterologia,
Polichinico S,
Orsola, V,
Massarenti 9,
40138 Bologna,
Italy

- 1 Brignola C, Iannone P, Belloli C, De Simone G, Bassein I, Gionchetti P, et al. Prediction of relapse in patients with Crohn's disease in remission: a simplified index using laboratory tests, enhanced by clinical characteristics. *European Journal of Gastroenterology and Hepatology* 1994; 6: 955-61.
- 2 Brignola C, Campieri M, Bazzocchi G, Farruggia P, Tragnone A, Lanfranchi GA. A laboratory index for predicting relapse in asymptomatic patients with Crohn's disease. *Gastroenterology* 1986; 91: 1490-4.
- 3 Landi B, N'Guyen Anh T, Cortot A, Soule JC, Rene E, Gendre JP, et al. Endoscopic monitoring of Crohn's Disease treatment: a prospective, randomized clinical trial. *Gastroenterology* 1992; 102: 1647-53.
- 4 Brignola C, De Simone G, Belloli C, Iannone P, Belluzzi A, Gionchetti P, et al. Steroid treatment in active Crohn's disease: a comparison between two regimens of different duration. *Aliment Pharmacol Ther* 1994; 8: 465-8.

Reply

EDITOR.—Thank you for referring the interesting comments of Brignola *et al* to us concerning our article. The Italian group has considerable experience in investigating the value of biological parameters in Crohn's disease and has published several research results in that field. One of their earliest publications¹ suggested a prognostic index for predicting relapse in quiescent Crohn's disease patients using the baseline blood values of α_1 glycoprotein, α_2 globulin, and the erythrocyte sedimentation rate. This was based on data from 41 patients who had been in remission for at least six months. The same study suggested that the blood values of C-reactive protein and α_1 antitrypsin were of borderline significance and the predictive value of some other biological variables were much less important, namely the haemoglobin concentration, the white blood cell count, serum iron, albumin, and γ globulin blood values.