Africans, notably in West Africa.¹ It would have been of interest to have had an account of erythrocyte morphology, sickling tests, Hb electrophoresis, and Hb F determinations in the pregnant patients studied.

But to accept for the purpose of further criticism that the cells whose origin I hold in question were derived from the fetus. Though the time of appearance of Rhesus antigenicity in fetal tissues has, to my knowledge, not been accurately determined, it cannot be at an earlier stage in embryonic development than the start of haemopoiesis. Since angioblastic tissue differentiates in only the third week of life and blood cells become recognizable only sometime thereafter, it is hardly likely that even the total blood volume of a 6-10-week embryo after intraperitoneal dilution, as the authors propose, in what is often several litres of maternal blood could account for the scores given for acid-resistant cells in the intraperitoneal and maternal peripheral venous blood. Such an effectively infinitesimal volume of fetal blood cells coupled with probably incompletely expressed Rhesus antigenic determinants can scarcely be described as a potential stimulus to maternal isoimmunization.

Furthermore, it should be pointed out that though ectopic pregnancy is a commoner occurrence in some groups of Africans than in Europeans, probably owing to the high prevalence rate of gonorrhoea in the former,² only some 5 per cent of South African Bantu are Rh negative.³ Drs. Katz and Marcus unfortunately omit any comment on the Rhesus phenotypes of their patients. It was my recent experience in Kenya, where the prevalence in the indigenous population of Rh(D)-negative phenotypes is very similar to that in the South African Bantu, that haemolytic disease of the newborn was infrequently encountered and when it did occur it was more often due to ABO than to Rhesus incompatibility. A very low incidence of haemolytic disease of the newborn due to Rhesus incompatibility has been described in other populations in which the incidence of the Rh(D)-negative phenotypes approximates to 5 per cent.⁴ Indeed, not all Rh(D)-negative women who suffer fetomaternal haemorrhage from a Rh(D)-positive fetus will become immunized.

In the light of these comments it is surely small wonder that Drs. Katz and Marcus have discovered only one record of Rh isoimmunization supposedly resulting from tubal pregnancy.—I am, etc.,

RONALD D. BARR

Department of Medicine,
University of Aberdeen

- 1 Lehmann, H., 1972, personal communication.
- 2 Carty, H. J., Nzoiki, J., Verhagen, A. R. H. B., and McGlashan, H. E., *East African Medical Journal*, 1972, 49, 376.
- 3 Mourant, A. E., *The Distribution of the Human Blood Groups*. Oxford, Blackwell, 1954.
- 4 *Obstetrics and Gynaecology in the Tropics and Developing Countries*, ed. J. B. Lawson and D. B. Stewart, p. 295. London, Arnold, 1967.

Hereditary Nephritis

SIR,—I should like to expand on your leading article on hereditary nephritis (12 August, p. 367) since more recent information is available on several points it emphasized. With regard to the natural history of the syndrome, we have recently analysed the ages at death (or terminal renal failure) of males with Alport's syndrome and found a high degree of concordance within families with regard to this parameter.¹ Moreover, two populations of affected families could be distinguished—one in which males invariably develop terminal renal failure between 16 and 28 years of age, and the other in which the renal failure develops between

33.5 and 52.5 years. Statistical analysis suggests that these two groups differ by a single gene of large effect rather than by multifactorial phenomena. Both types of Alport's syndrome appear to be inherited in an autosomal dominant manner. Both our study¹ and that of Feingold and Bois² indicate that the prevailing notion of an excess of affected offspring of affected parents is the result of the bias of ascertainment of earlier studies. Segregation ratios for all but possibly male offspring of affected males are not statistically different from unity, as expected in simple autosomal dominant inheritance.¹⁻³

With regard to therapy and counselling, a sizeable number of individuals with Alport's syndrome (at least 83) have undergone renal transplantation.⁴ Short-term rates of patient survival and kidney function are certainly no worse than those in other groups of patients treated similarly for other causes of renal failure.⁴ In addition, it has been our experience that their usual lack of debilitation facilitates their rehabilitation. Certainly these data, in addition to the results of long-term follow-up studies of transplanted patients, must be considered when providing genetic counselling. The genetic counsellor must also remember that not all affected males develop renal failure at a young age, and that he can frequently use the family history to predict the approximate age at which transplantation will be necessary. Moreover, our ability to determine the fetal sex permits a possibly more rational alternative (for example, aborting all male fetuses) for an affected parent than having no children at all.—I am, etc.,

PETER V. TISHLER

Harvard Medical School,
Boston City Hospital,
Boston, Mass

- 1 Tishler, P. V., and Rosner, B., *Birth Defects Original Article Series* (the Fifth Conference on the Clinical Delineation of Birth Defects, 1972), in press.
- 2 Feingold, J., and Bois, E., *Humangenetik*, 1971, 12, 29.
- 3 Preus, M., and Fraser, F. C., *Clinical Genetics*, 1971, 2, 331.
- 4 Advisory Committee to the Renal Transplant Registry, *Journal of the American Medical Association*, 1972, 220, 253.

Cannabis and Recurrent Herpes Simplex

SIR,—A variety of stimuli are known to trigger a recurrence of latent herpes simplex infection. A rise in temperature, physical trauma, exposure to ultraviolet light, steroids, and anxiety with a presumed liberation of adrenalene are well-known provoking factors. Cannabis smoking has not, to my knowledge, previously been noted as a provoking agent causing recurrent herpes simplex.

A 30-year-old man was first seen in October 1971 complaining of recurrent herpes of the shaft of the penis. The attacks lasted for five to eight days. For the past two years they had occurred much more often. During that period he had been smoking cannabis, and within two to three days, never less, never more, of having a "reefer" he would get a recurrence of his genital herpes. The attacks were unrelated to intercourse. In the spring of 1971 almost continuous attacks had made him give up smoking cannabis for a while and the attacks became much less frequent. When he later started smoking cannabis again the attacks recurred. When seen in October at the beginning of a new recurrence Type 2 herpes simplex virus was isolated, confirming the diagnosis of genital herpes. The lesion healed quickly with

antiviral treatment and he had only one recurrence, in a different site and equally short-lived, until January 1972. During the interval he had not smoked cannabis. He thought the antiviral drug had solved his problem and started smoking cannabis again (2-3 cigarettes per day),—and within 48 hours of starting he had an attack in yet another site. Though the attacks were aborted by antiviral chemotherapy he had another outbreak in August 1972 after smoking a lot of cannabis. He had had only two recurrences in the interval, both very slight.

I have since seen three other cannabis smokers with genital herpes who gave a very similar history. I have asked colleagues who see a large number of students whether they had had a similar experience. Two had had patients who were heavy cannabis smokers in whom distressing recurrent genital herpes had been an outstanding feature which had puzzled them greatly. MacCallum and I have speculated¹ that a possible common mechanism for provoking a reactivation of herpes simplex virus may be vasodilation. I asked Professor W. D. M. Paton whether cannabis had properties which might provoke recurrent genital herpes. I am grateful for his comments which were: (1) Cannabis produces vasodilation, the best-known example being conjunctival injection, now known not to be due to irritant smoke but apparently, from animal work, to a reduction of sympathetic tone. (2) The psychically active principles are intensely lipophilic and could well be taken up by nervous tissue (where it is possible the dormant virus resides, in whatever form, between attacks). It is also known that tetrahydrocannabinol (the main principle) affects the fine nerve fibres (Auerbach's plexus) in the intestinal wall. (3) Crude cannabis in experiments investigating the question of chromosome damage has been found to reduce the mitotic index. It may interfere with local or general immunity.—I am, etc.,

B. E. JUEL-JENSEN

Radcliffe Infirmary,
Oxford

- 1 Juel-Jensen, B. E., and MacCallum, F. O., *Herpes Simplex Varicella and Zoster*, p. 61. London, William Heinemann, 1972.

M.I.F. Test in Halothane Jaundice

SIR,—A cause and effect relationship between halothane and postoperative liver dysfunction has not yet been established.¹ We do not wish carpishly to criticize the letter of Dr. W. Jones Williams and others (7 October, p. 47) detail by detail, but the evidence presented by Doniach² does not withstand careful scrutiny and the "use of lymphocyte transformation tests for detecting hypersensitivity," reported by Paronetto and Popper,³ has not been confirmed.⁴

We contend that normal subjects are unacceptable as controls for the investigation by Jones Williams and his colleagues. We suggest that appropriate controls would be, firstly, postoperative patients, since lymphocyte responsiveness is known to be abnormal during this period,^{5,6} and secondly, patients suffering from liver dysfunction who have not been given halothane. Alteration in cell-mediated immune reactivity has been shown in various liver diseases^{7,8} and these changes may reflect an autoimmune response to liver damage, the implication being that liver damage releases liver specific antigen to which the subject may not have acquired full immunological tolerance. In

the absence of appropriate controls and other information it would be regrettable if the communication by Dr. Jones Williams and his colleagues added to the confusion which already exists on this controversial subject.—We are, etc.

B. R. SIMPSON
B. WALTON

Anaesthetic Unit,
London Hospital,
London E.1

L. STRUNIN

Anaesthetic Department,
King's College Hospital,
London S.E.5

- 1 Simpson, B. R., Strunin, L., and Walton, B., *British Medical Journal*, 1971, 4, 96.
- 2 Doniach, D., *New England Journal of Medicine*, 1970, 283, 315.
- 3 Paronetto, F., and Popper, N., *New England Journal of Medicine*, 1970, 283, 277.
- 4 Walton, B., et al., *British Journal of Anaesthesia*, 1972, 44, 904.
- 5 Riddle, P. R., *British Journal of Surgery*, 1967, 54, 882.
- 6 Park, S. K., Brody, J. I., Wallace, H. A., and Blakemore, W. S., *Lancet*, 1971, 1, 53.
- 7 Bacon, P. A., Berry, H., and Brown, R., *Gut*, 1972, 13, 427.
- 8 Mella, B., and Lang, D. J., *Science*, 1967, 155, 80.

Gastrin and Gastrointestinal Disease

SIR,—We were interested in your leading article on this topic (9 September, p. 604), but we think your statement that gastrin may affect intestinal motility needs qualification.

In doses producing near-maximal gastric-acid secretion both gastrin and pentagastrin were found to stimulate motility in the gastric antrum, but no effect on colonic motor activity could be detected.^{1,2} As you point out, serum gastrin levels are high in patients with pernicious anaemia but are likely to be low after total gastrectomy. Colonic pressure activity, however, especially after a protein-containing meal, is greater after total gastrectomy than in pernicious anaemia.³ It would therefore seem unlikely that gastrin is involved in the colonic motor response to meals.³—We are, etc.,

J. J. MISIEWICZ
SHEILA L. WALLER

Central Middlesex Hospital,
London N.W.10

D. J. HOLDSTOCK

Ashford Hospital,
Middlesex

- 1 Misiewicz, J. J., Holdstock, D. J., and Waller, Sheila L., *Gut*, 1967, 8, 463.
- 2 Misiewicz, J. J., Waller, Sheila L., and Holdstock, D. J., *Gut*, 1969, 10, 723.
- 3 Holdstock, D. J., and Misiewicz, J. J., *Gut*, 1970, 11, 100.

Psychiatrists in Training

SIR,—May I express concern at some current thinking in the training of psychiatrists? I feel that it is essential when applying for a consultant post to have as wide an experience as possible of different specialties, consultants, and types of unit. I also accept that rotation between units should be freely available, as desired by junior staff and advised by their senior colleagues. May I, however, express the view that if rotation to a reasonable extent has been achieved by the time the junior doctor has reached senior registrar level there are important advantages in spending the whole senior registrar period in one hospital and making up the deficiency by the process of secondment on a regular sessional basis to other units and by attending courses. This allows a senior registrar to learn skills that would be com-

pletely neglected by the senior registrar who had at the most spent one year in one place. It forces him to have continuing long-term exposure to the patient who will not get better. It allows him to become an important and powerful member of the Cog-wheel structure and to take part therein in the developments of a hospital and its policies. And it allows him to create long-term plans for the establishment of new units with the supervision of a consultant and to work through all their administrative and staff problems to full fruition. This view is at variance with the currently popular one, which seems in the main to hold that the best training is offered by wide rotation.—I am, etc.,

J. A. FLOWERDEW

Shelton Hospital,
Shrewsbury

Candidates for Coronaries

SIR,—It seems the ivory towers of the research workers are getting taller or we on the ground are being obscured by a deepening mist. Any general practitioner of reasonably long experience could join in the discussion of coronary personality types under consideration in your leading article, "Life Pattern for Coronary Arteries" (14 October, p. 63). They would generally be in agreement with the personality type of the Dunbar profile¹ and that not all people falling within this profile suffer from coronary artery occlusion. That is to say that coronary occlusion occurs in people who are conscientious, responsible, and lead stressful lives but that not all such people suffer coronary artery disease. There must be another consideration to be taken into account.

Time and time again patients who have suffered from their first or subsequent attack of myocardial infarction admit to have felt absolutely tired out for days, weeks, or months before the infarction episode. Often the more perceptive will say "I had felt so tired for weeks that I had come to accept this as a normal state of affairs." It is this acceptance of fatigue as being something to put up with, the trying to ignore it, and the trying to carry on normally despite its presence which I believe to be the common factor which has been missed in the coronary profile.

This accommodation to an abnormal strain may be useful in seeing a patient through a difficult time. If the attempt is unsuccessful the patient breaks down one way or another and serious physical harm is averted. It is in the stage of neither the strain being cleared nor the battle lost that the danger of coronary occlusion lies. Parallels may be drawn with the body's reaction of inflammation to infection or antigen/antibody abnormal reactions.

The significance may not lie so much in the prediction of an occurrence of myocardial infarction in an individual as in the education of a person recovering from such an episode in the prevention of further coronary occlusion. Unfortunately, I have no facts or figures to back the above but clinical impressions will do for me when research fails to produce an answer.—I am, etc.,

LEONARD SMITH

Preston, Lancs

- 1 Dunbar, F., *Psychosomatic Diagnosis*. New York, Paul B. Hoeber, 1943.

Predicting Coronary Artery Disease

SIR,—Your interesting leading article on the prediction of coronary artery disease (7 October, p. 3) perpetuates two false premises that I feel have made both the research into and discussion of this important subject more difficult. The first is the assumption that the aetiologies of atheroma and of overt myocardial infarction are the same. Atheroma develops chronically, is lipid-dependent, and occurs in many parts of the arterial tree. The events preceding an infarct of the myocardium probably involve the short-term disturbance of a complex thrombotic equilibrium, this disturbance being made more likely by the presence of atheroma in the coronary arteries. Why does a man suffer an infarct at a specific time when risk factors may have been present for years? What determines the sudden catastrophe? Do we wish to predict atheroma or the liability to myocardial infarction?

The second false assumption brings me to the analogy of the horse and the stable door. Should we expect the lowering of a raised serum lipid level or a raised diastolic blood pressure to prevent the occurrence or extension of coronary artery disease? It may be too late. We may lower these levels but leave the primary cause of their rise unaffected. The primary rise above the accepted norms of these factors is more likely to be the important target for future prevention, and this prevention may be important far earlier in the patient's life than we have so far considered, perhaps in the second decade.

As you say, we know little of the prediction or prevention of this greatest single cause of death in Britain. We need to attack on two fronts. We need to prevent atheroma in those still young enough or lucky enough not to have developed it. We need to prevent those who now have atheroma and risk factors from developing clinical coronary artery disease. I do not believe that these two fronts are identical.—I am, etc.,

MARGARET HAIGH

London S.E.26

Mechanisms of Rosette Formation

SIR,—Mr. M. Bewick and others (26 August, p. 491) do not distinguish between rosettes formed by the spontaneous adherence of human lymphocytes to sheep red cells and rosettes known to be formed by immune mechanisms. Recent studies have indicated that rosettes may occur through at least three different mechanisms: (a) specific antibody or antibody-like molecules at the surface of lymphoid cells;¹ (b) the affinity of non-specific lymphocytes to antigen-antibody complexes;^{2,3} and (c) non-immune mechanisms of the types required for the formation of tissues and organs of multicellular organisms.

Thymocytes and to a lesser extent non-thymic lymphocytes adhere through non-immune mechanisms to a variety of autologous and heterologous cell types. Thus guinea-pig thymocytes adhere to autologous macrophages,^{4,5} rabbit and rat thymocytes adhere to autologous red cells,⁶ and rat thymocytes adhere to autologous mast cells. Similar non-immune mechanisms may result in the adherence of guinea-pig thymocytes to rabbit red cells and mouse thymocytes to rat red cells.⁸ The main characteristics of