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.,

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1 Lehmann, H., 1972, personal communication.
2 Carty, H. J. Nzoiki, J., Verhagan, 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 study[1] and that of Feingold and Bois[2] 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.,

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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 adrenaline 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 speculated[1] 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 chromosone damage has been found to reduce the mitotic index. It may interfere with local or general immunity.—I am, etc.,

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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 carpingly to criticize the letter of Dr. W. Jones Williams and others (7 October, p. 47) detail by detail, but the evidence presented by Doniach[2] 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