If the accepted standards of medical practice are not to become those of the Stock Exchange then some evidence is required from the GMC that it is prepared to enforce its code of ethics, otherwise there will be similar justification in seeking to end self-regulation in medicine, as in the financial markets.

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ATRIAL NATRIURETIC PEPTIDE CONCENTRATIONS DURING PREGNANCY

SIR,—Dr Rutherford and colleagues (April 18, p 928) report that the concentration of atrial natriuretic peptide (ANP) does not increase during pregnancy but that it rises during the early puerperium. Because pregnancy is associated with an increase in circulating volume, an increase in ANP concentration would have been expected. Nevertheless, the puerperal increase in ANP was associated with marked natriuresis.

Testing the hypothesis that an increase in plasma volume during the latter part of pregnancy would cause plasma ANP concentrations to be greater in the third trimester than in the first trimester, we have obtained results similar to those of Rutherford and colleagues. ANP concentrations in samples from 29 women with normal pregnancies (median 2·5 pg/ml, range 1·2–10·4) were similar to those in 12 age-matched and sex-matched controls (median 3·2 pg/ml, range 1·4–8·6). Furthermore, ANP concentrations in the third trimester ($n = 13$, median 2·4 pg/ml, range 1·0–7·5) were similar to those in the first trimester ($n = 16$, median 3·0 pg/ml, range 1·2–10·4).

However, Cusson et al[1] have demonstrated that plasma ANP concentrations increase during pregnancy. This increase is consistent with the hypothesis that expansion of plasma volume during normal pregnancy stimulates the secretion of ANP.[2] The only explanation for the discrepancy between the results of Cusson et al and those of Rutherford et al and ourselves probably lies in the radioimmunoassay method for ANP, because it is unlikely that the expansion of circulating volume in pregnancy is not associated with an increase in ANP, especially after Cusson et al have convincingly demonstrated such an increase. Cusson et al developed their own assay and their control reference range is 58·5–102·5 pg/ml. Our assay is based on that used by Sagnella et al,[3,4] with reagents from Amersham International. Also, our reference range is different. Thus the assays measure ANP in two forms. It is relevant that, using the Amersham assay, MacGregor's group[5] and ourselves (unpublished) have observed increases in ANP in cardiac failure. We have also observed increases in ANP in patients in chronic renal failure, who have a rapid decrease in plasma ANP concentrations after dialysis. We do not know why ANP, when assayed by Cusson et al, responds to the hypervolaemia of pregnancy with an increase, whereas that measured by Rutherford et al and ourselves does not.

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SIR,—Dr Rutherford and colleagues report a rise in plasma atrial natriuretic peptide (ANP) 3–5 days after delivery. No measurements were reported, however, during the puerperium.

We have compared plasma concentrations of ANP before and after birth up to the sixth puerperal week in seven healthy normotensive primiparae (diastolic blood pressure under 85 mm Hg). They had uneventful pregnancies and were not restricted in dietary sodium. The mean age of the women was 27 (SD 5) years and the mean gestational age at birth was 282 (7) days. Six patients gave birth vaginally and one had a caesarean section because of cephalopelvic disproportion.

ANP was measured weekly from week 35 of pregnancy until birth, and on days 1, 2, 4, 6, 10, 14, 21, 28, and 42 of the puerperium. In our radioimmunoassay ANP was extracted on silica-C-18 cartridges before assay in a non-equilibrium system with a sheep anti-human-ANP serum and a second antibody separation procedure. The intra-assay and inter-assay variations were 7% and 10%.

In all seven patients the mean ANP values during the first two days postpartum were higher (98 [SD 44] pg/ml) than those during late pregnancy (57 [21] pg/ml; paired t-test, $p < 0·02$). The mean ANP level from day 4 to day 42 decreased (52 [20] pg/ml; $p < 0·05$ compared with the first two days postpartum).

Thus ANP was nearly doubled during the first few days post partum compared with plasma levels in normal late pregnancy and the puerperium. A possible explanation is the shift in fluid post partum from the extravascular space to the circulation, leading to increased atrial wall tension. The significance of the increased plasma concentrations of ANP post partum in relation to the enhanced volume diuresis after birth remains to be determined.

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GROUP SPECIFIC COMPONENT AND HIV INFECTION

SIR,—In their paper on group-specific component phenotypes and human immunodeficiency virus (HIV) infection Dr Eales and colleagues (May 2, p 999) state: "It is of interest that in an area where HIV infection is very common—namely, in some parts of Central Africa—the Gc 1f allele predominates in the indigenous population", and they cite Constans et al.[1,2] On May 3 one of the authors of this paper was interviewed on the BBC World Service's *Science in Action* about their research which "may explain why the epidemic has spread faster in central Africa than even in the United States". The whole interview sounded as if a fact about central Africa had been discovered yet it concluded with the statement "We have not yet tested this hypothesis ourselves about central Africa". So Eales et al used the data of Constans et al, which are not about AIDS-afflicted central Africa at all but about a group of pygmies[2] (in whom AIDS is notable for its absence) and about the Peuhl Fula in Senegal[1] where AIDS is not much of a problem. Yet they broadcast to the world and leave the impression that there was something genetically wrong with Central Africans, hence their plight vis-à-vis AIDS. The Bi-Aka pygmies, 267 of whom were described by Constans et al[2] (cited by Eales et al in table IV) form a tiny group of at most 60 000 pygmies in the former Central African "Empire" with a total population of 2700 000. To use genetic data from this anthropologically distinct group, who do not even have AIDS, to cover "central Africa" leaves a lot to be desired.

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SIR,—The suggestion by Dr Eales and colleagues that genetic constitution may influence the development of AIDS, and that the presence of the allele *Gc1F* promotes susceptibility while *Gc2* is protective, is not easy to reconcile with epidemiological data. Tables

TABLE I—FREQUENCIES (%) OF Gc ALLELES IN VARIOUS RACIAL GROUPS[1]

	Gc1F	*Gc1S*	*Gc2*
European	15–16	56–58	27–32
American (whites)	10–16	54–63	26–31
American (blacks)	68	20	12
African	49–68	19–36	11–15
Mongoloids	40–61	20–30	11–30

TABLE II—RACE-SPECIFIC INCIDENCE (PER 100 000 POPULATION) OF AIDS[2] IN FOUR US CITIES

	New York	Manhattan	Los Angeles	San Francisco
A whites	80·4	216·2	62·4	303·8
A blacks	71·9	142·0	29·4	67·0

I and II show the frequencies of the Gc alleles[1] and the incidence of AIDS[2] in various racial groups.

Despite the high frequency of the *Gc1F* in American blacks (similar to that in Africa), the incidence of AIDS is consistently lower in the black population of the United States than in the whites. In certain regions the incidence in blacks is only one-fifth of that in whites. Similarly, mongoloid peoples have high frequencies of the *Gc1F*, but the incidence of HIV infection in Japan is very low.[3]

Besides genetic constitution, therefore, regional environmental factors, especially duration of exposure to infection, are likely to be important contributors to the full-blown disease. The Gc association is based on a small sample of whites, and, in view of the conflict with the epidemiological data, obviously requires validation on a larger sample taking into account the considerable variation in gene frequencies in the Gc system from one population to another.

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1. Papiha SS, Constans J, White I, McGregor IA. Group-specific component (Gc) subtypes in Gambian and Transkeian populations: A description of a new variant. *Ann Hum Biol* 1985; **12:** 17–26.
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SIR,—Dr Eales and colleagues report an interesting association between HIV infection and different allelic forms of group specific component. They propose a possible role during cell binding which may enhance surface receptor cross-linking and the movement of attached virus into the cell, and they refer to work (now published[1]) which shows that the presence of CD4 induces HIV binding to both human and mouse cells but productive infection only in human cells. However, this does not necessarily mean that other human cellular components affect HIV infectivity. Indeed not only is there little evidence that the human T4 molecule is endocytosable in the mouse cells used but also the transfected HIV genome does not replicate well in mouse cells so far studied. Further studies on these two topics are in progress. Furthermore, whereas Gc is present in the serum as well as on lymphoid cells, hela cells expressing the CD4 antigen are readily infectable and these are non-lymphoid.[1]

What is of interest, however, is the constant number of exposed individuals who remain HIV antigen and antibody positive.[2] The amount of exposure that some of these individuals have had suggests that there must be some serum component or other immunological mechanism whereby the virus is killed before it has an opportunity to bind to a T4 molecule, as the lymphocytes from these patients are readily infectable in culture.[2]

Early studies suggest that complement would appear not to have a significant role in controlling HIV infection.[3]

It is thus tempting to interpret the results of Eales et al as evidence for a component which is directly or indirectly associated with control of viral infection before virus binding. This hypothesis could also explain the lower incidence of disease in those patients who eventually become infected.

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**These letters have been shown to Dr Eales and her colleagues, whose reply follows.—ED. L.

SIR,—We are not suggesting that genetic factors are the sole determinants of the epidemiology of HIV infection and AIDS. Exposure to the virus is the primary determinant of infection, and behavioural factors have a key role in determining virus spread within any population.[1] Furthermore, the worldwide distribution of HIV must also reflect its rate of spread to different populations as well as within them. Nevertheless, having presented evidence that Gc subtypes appear to influence susceptibility/resistance to HIV infection and disease amongst homosexual men in London, it was natural to propose that these observations could be relevant to other populations affected by HIV. Therefore, in discussing our novel findings, we speculated on the possible implications for the HIV pandemic as well as for the biology of HIV infection. Naturally such hypotheses will be tested and falsified or not in the normal way.

For the purposes of our discussion, we chose Gc data on African populations that were representative of the pattern of subtypes found in affected areas, pending direct studies on African HIV cohorts (which are now underway). As pointed out by Dr Papiha, the increased frequency of *Gc 1f* and the decreased frequency of *Gc 2* that we quoted for comparison with Caucasian populations are indeed representative, and a recent report[2] includes data from several other African peoples (central, south, and west), with ranges for *Gc 1f* of 0·58–0·88, for *Gc 1s* of 0·08–0·19, and for *Gc 2* of 0·02–0·16. The emerging epidemic of HIV-2 (HTLV-IV) infection in Senegal and neighbouring countries means that the west African figures are likely to be directly relevant. Gc subtype patterns among Asian populations include some resembling Caucasians (eg, Indians) through to others not dissimilar to those in Africa (eg, Malays); Japanese are intermediate.

The under-representation of blacks in the US AIDS epidemic almost certainly reflects a white predominance amongst the most affected homosexual populations. However, heterosexual spread in the USA seems more common among blacks than among whites and the rate of progression to AIDS seen in blacks appears to be more rapid; this is of interest since they have a higher frequency of *Gc 1f* (0·67–0·79) and a lower frequency of *Gc 2* (0·08–0·13).

Broadly speaking, populations with black and yellowish skin have higher frequencies of the *Gc 1f* allele than white populations, and Kamboh and Ferrell[2] have suggested that "during the course of evolution *Gc 1f* allele products, having a greater affinity for vitamin D3, might be selectively favoured in dark skinned peoples by more efficiently transporting vitamin D3 from the skin to target tissues". Dr Konotey-Ahulu quotes accurately from a radio interview given by one of us (A. J. P.) but his interpretation of these comments is at fault. There was no suggestion that there is something genetically wrong with Central Africans, just that they are genetically different in a way that may explain why HIV has spread so rapidly in the region. We cannot see how this can be taken as impugning anyone; rather it seems a plausible hypothesis that may help to explain how the tragic situation that affects that region could have arisen. It would be improper not to draw attention to this possibility which, while consistent with the known facts, must of course be tested formally.

If the Gc subtype association does indeed apply more widely, then such genetic factors must be taken into account when evaluating rates of spread of HIV in any population, along with other factors such as the prevalence of HIV and sexual behaviour. Similarly they must be included in any assessment of natural history, along with co-factors for disease, such as sexually transmitted infections.[3,4] It is just this type of information that Anderson et al[5] require to allow more accurate predictions of the future size of the AIDS epidemic.

We thank Dr Dalgleish for his illuminating comments but would emphasise that Gc is present on the surface of a wide variety of cells

other than lymphoid cells, although we are unaware of the status of hela cells. One possible implication of this widespread cellular distribution is that Gc binding of HIV exerts its effect through epithelial cells by increasing the probability that HIV is approximated to T4(CD4)-bearing target cells. Apart from extending our serological studies in HIV-risk populations, we are assessing the effect of Gc subtype on cell binding of HIV and on lymphoid cell function.

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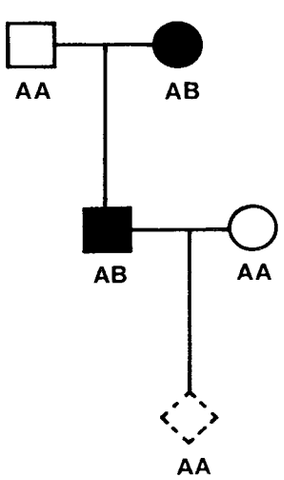
FIRST TRIMESTER PRENATAL EXCLUSION OF TUBEROUS SCLEROSIS

SIR,—The suggestion of a linkage between tuberous sclerosis (TS) to ABO blood group[1] has been confirmed in the collaborative UK study reported by Dr Fryer and others (March 21, p 659). This maps the locus for TS to 9q34. We have identified[2] linkage between TS and a DNA polymorphism from 9q34 and have utilised this information for first trimester prenatal exclusion in a pregnancy at risk.

DNA analysis was undertaken in the six Scottish families whose ABO and adenylate kinase-1 data were included in the UK collaborative study. Unaffected individuals at risk were rigorously investigated, and all affected individuals conformed to the diagnostic criteria of Gomez.[3] DNA from each family member was digested with *TaqI* and, after electrophoresis and Southern transfer, was probed with pSA-19, which is a 1·9 kb fragment of v-*abl*.[4] No recombinants were observed in 13 informative meioses (4 phase known) giving a maximum lod score of 3·18 at zero recombination with confidence limits of 0–0·15.[2] The human oncogene c-*abl* is the cellular homologue of the transforming sequence v-*abl*. With v-*abl* or c-*abl* probes, c-*abl* has been localised to 9q34 by in-situ hybridisation and somatic cell hybrid panels.[5-9]

A couple at risk in one of these families asked about the possibility of prenatal diagnosis in their current pregnancy. In this family (GLA4136) the husband and his mother (and other relatives) have TS. The couple had previously been counselled that on average half of their offspring would receive the mutant gene and that about half of their children with this gene would be mentally retarded.[3] They were further counselled that with the use of this linked DNA marker the risk of error might be as high as 15% (the upper confidence interval), and that confirmation of the diagnosis might not be possible in the event of termination of pregnancy. Nevertheless, the couple asked for prenatal diagnosis. Fetal DNA was extracted from a transabdominal chorionic villus sample taken in the 13th week of pregnancy. The husband was known to be heterozygous (informative) and to have inherited TS along with the fragment of size B from his mother. The wife is homozygous for the fragment of size A. The fetus is predicted to be unaffected since it has received the paternal A fragment (figure).



Partial pedigree indicating DNA results for *TaqI*/v-*abl* restriction fragment length polymorphism with allelic fragments indicated A or B.

Further family studies will help to determine the frequency of recombination between this DNA polymorphism and TS but it should prove more useful for early prenatal diagnosis than the ABO blood group or the adenylate kinase-1 loci and will aid attempts to clone the structural gene for TS.

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COMPUTED TOMOGRAPHY OF CHEST IN DIAGNOSIS OF MILIARY TUBERCULOSIS

SIR,—Miliary tuberculosis can be difficult to diagnose, especially in its early stages. We report two cases of this disease in which computed tomography (CT) of the chest appeared to be much more sensitive than the plain chest X-ray in detecting miliary shadowing.

A 50-year-old woman was admitted with a history of fever, malaise, shivering attacks, and severe headache. The fever had not responded to treatment with erythromycin. She had been born in India but had lived in the UK for 18 months. There was no history of tuberculosis and she had not been in contact with any sick person. Her white blood cell count (WCC) was $9{\cdot}8 \times 10^9$/l and erythrocyte sedimentation rate was of 21 mm/h[1]. A blood film was negative for malarial parasites and blood cultures were sterile. A plain chest X-ray was normal. 5 days later a repeat chest X-ray showed fine parenchymal infiltrate. A CT scan the following day clearly showed fine miliary mottling throughout the parenchyma of both lung fields (figure). 1 month later typical miliary shadowing was seen on plain chest X-ray. Miliary tuberculosis was confirmed by liver biopsy and culture.

A 21-year-old woman was admitted with malaise, weakness, night sweats, and weight loss. She had not responded to oral amoxycillin. She was born in Kenya but had lived in the UK from the age of 3 years. There was no history of tuberculosis or recent foreign travel. WCC $1{\cdot}5 \times 10^9$/l and ESR 20 mm h. Blood cultures grew no pathogen. The chest X-ray suggested early miliary