judgment, but the thought crosses my mind that, apart from some criticisms on points of detail, which I am happy to accept, the reasons for rejection of these papers might in themselves be matters for comment. I imagine that Minerva, in her wisdom, will not overlook the Athenian principle that truth is most likely to emerge in temples whose columns are open for entry.

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Stress after amniocentesis for high serum alpha-fetoprotein concentrations

SIR,—In his review of maternal serum α-fetoprotein (AFP) screening in pregnancy (17 May, p 1199) Rodney Harris concludes that one potential benefit of population screening might be the identification of fetuses at risk of spontaneous abortion, low birth weight, or perinatal death. He bases this conclusion on the increased incidence of these problems among women who have a high maternal serum AFP concentration but a normal result on amniocentesis. The possibility that the prenatal diagnostic intervention may have caused the subsequent problems is discounted by reference to the significantly better pregnancy outcome of women who have amniocentesis for other reasons.

An outcome measure which receives no attention in Harris's review, but which I have found to be significant in differentiating women with high serum AFP concentrations from those with other indications for amniocentesis, is the woman's emotional reaction to the diagnostic intervention.[1] The data in the table are based on interviews with 90 women who had a normal result on amniocentesis. Although nearly all women were worried about the test outcome, the anxiety of the high serum AFP group was more generalised and more disabling. Sixty-eight per cent of this group, as compared with 22% of those who had amniocentesis because of their age or their obstetric or family history, felt that their health had suffered during the period of waiting for results ($p < 0.001$). This was sometimes a cause of further anxiety, in that women worried about the effect that their stress might have on their unborn child: "If they're inside you and you're worrying terrible it must affect them somehow"; "My husband's greatest worry was that the baby was perfectly normal but I would miscarry because I was so worried"; "I was worried about not eating—thinking I will miss the nutrition for the baby"; "I smoked a lot more and I was worried that it was not good for the baby."

Emotional reaction to the experience of waiting for the result of prenatal diagnosis, according to indication for amniocentesis

	Indication for amniocentesis	
	High serum AFP	Other
Found the experience:	(No = 33)	(No = 57)
Not distressing	3% } 21%	17% } 86%
A little distressing	6%	39%
Moderately distressing	12% } 79%	30%
Very distressing	21%	12% } 14%
Extremely distressing	58%	2%
Could stop self worrying:	(No = 33)	(No = 56)
Yes	33%	87%
No	67%	13%
Suffered from:	(No = 31)	(No = 55)
Depressed mood	71%	24%
Crying	71%	9%
Irritability	57%	20%
Poor concentration	53%	7%
Headaches	35%	16%
Sleep disturbance	61%	16%
Loss of appetite	65%	5%
>3 of the above	71%	9%

All differences between groups are significant at the $p < 0.001$ level (χ^2, 1 df).
AFP = α-fetoprotein.

Eight women (seven from the high serum AFP group) said they smoked more during the period of waiting for results. Four (three from the high serum AFP group) took tranquillisers. One woman with a high serum AFP concentration mentioned that although she normally drank alcohol only in moderation and on special occasions, she was drinking up to half a bottle of spirits a day during the time of waiting for the results.

There is evidence to suggest that stress during pregnancy is associated with both fetal death[2] and low birth weight.[3] The hypothesis of the women just quoted, that the stress reaction to a false-positive result on a serum AFP screening test might contribute to poor pregnancy outcome, would seem no less reasonable than the assertion of Harris and his colleagues[4] that "the greater fetal loss and low birth weight associated with pregnancies complicated by high maternal serum AFP concentrations appear to be an inherent feature of these pregnancies, rather than the result of amniocentesis."

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[1] Farrant W. *Mims Magazine*, 15 June 1980, 55-63.
[2] Myers RE. In: Zichella I, Pancheri P. eds. *Psychoneuroendocrinology in reproduction*, Amsterdam: Elsevier/North Holland Biomedical Press. 1979, 555-73.
[3] Newton RW, *et al. Br Med J* 1979;ii:411-3.
[4] Read AP, *et al. Br J Obstet Gynaecol* 1980;**87**:372-6.

Plasma exchange in severe rhesus haemolytic disease

SIR,—Intensive plasma exchange is now becoming a recognised and effective form of treatment for antibody and immune-complex mediated disease.[1 2] Mr G R Barclay and others in their report (28 June, p 1569) suggest that the maternal concentration of anti-D increased despite intensive plasma exchange and that the procedure may have been deleterious by removing maternal "inhibitory" activity.

Although they feel that they were unable to control the secondary antibody response, it appears from the graph that each significant rise in anti-D concentration occurred during the two to three-day gaps in the exchange programme. When regular exchange occurred there was either a decrease in the rate of rise or an actual fall in the concentration of anti-D.

The immunoglobulin produced in the secondary response is in the IgG class, of which only 44% is in the vascular compartment. When the balance between the intravascular and extravascular space is disturbed by rapid reduction in the intravascular concentration of IgG then equilibration will occur when plasma exchange is withdrawn. In addition, immediate rebound in antibody synthesis may be expected owing to feedback stimulation of the clone of lymphocytes producing the antibody.[3]

Graham-Pole *et al*[4] demonstrated reduction of anti-D concentration with intensive plasma exchange in severe rhesus disease but there was a rapid return of antibody between courses of exchange. This also accords with our own experience in treating patients with factor VIII inhibitors following essential surgery. These inhibitors are also IgG antibodies and plasma exchange is required daily to control the inhibitor level until such time as the clinical state resolves (data to be published, available on request). Our patients also receive high-dose factor VIII concentrates daily, which may provoke further antibody stimulation but by contrast may have led to immunological tolerance.[5]

Haemolytic disease of the newborn differs from other antibody-mediated disease in that the fetus can benefit only indirectly from plasma exchange. The beneficial effects depend on the free passage of antibody between fetus and mother. IgG levels in the newborn infant are frequently higher than in maternal serum.[6] The level of anti-D may vary from 2% to 30% of that in the mother.[7] The level in the latter is not, therefore, an accurate assessment but is only a guide to the severity of the disease. The placenta does not act as a simple filter but bears Fc receptors and appears to be the rate-limiting point in antibody transfer.[8] It selectively and directionally transfers IgG against a substantial concentration gradient. The rate of transfer is relatively slow[9] but better from mother to fetus than from fetus to mother, and acute changes of antibody concentration in the mother due to plasma exchange will not be reflected in the fetus unless the improvement is sustained by frequent exchange. If the problem in haemolytic disease of the newborn is purely related to antibody production then on theoretical grounds we have not yet been treating affected women sufficiently intensively to expect significant benefit.

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[4] Graham-Pole J, Barr W, Willoughby MLN. *Br Med J* 1977;i:1185-8.
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[6] Kohler PF, Farr RS. *Nature* 1966;**210**:1070-1.
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Social environment and relapse in schizophrenia

SIR,—Your recent leading article on social environment and relapse in schizophrenia (19 July, p 173) gave an accurate and useful summary of the research carried out by members of this unit. It is difficult, however, in presenting the results of such work to avoid an emphasis on factors that predict relapse, while factors that predict a good outcome receive less attention. In particular, the fact that a majority of the families we have studied provide a helpful and supportive environment, associated with a low relapse rate, tends to be left out of consideration. Professional people concerned with the long-term management of