

than that in peripheral venous blood in ruptured acute ectopic pregnancy,¹ and in the former situation the haemoglobin appears to be largely intracorpuscular.² For a peripheral fetal cell score of 14 per 150,000 maternal red cells in a woman with a circulating blood volume of 3 l. and a red cell count of $2.5 \times 10^6/\text{mm}^3$ some 1.5 ml of fetal blood would require to enter the maternal circulation. But, as Drs. Katz and Marcus rightly point out, the fetal blood is shed almost entirely into the peritoneal cavity, in which it is commonly diluted in at least 1 l. of maternal blood.³ Certainly 1.5 ml of fetal blood in 1 l. of maternal blood of red cell count $2.5 \times 10^6/\text{mm}^3$ could result in a fetal cell score of 44/150,000 in the intraperitoneal blood. However, to produce a score in the maternal peripheral blood of 14/150,000 the mother would have to reabsorb this total volume (which she does not, as much of it is present at laparotomy), have it autotransfused (which was presumably not the case in the authors' patients), or selectively reabsorb all the fetal red cells from the peritoneal cavity (hardly a likely eventuality). Even if one of these three possibilities was to occur, how could any of the fetuses in the series described by Drs. Katz and Marcus, all of which by their own admission would weigh 1 g or less, provide 1.5 ml of blood (weighing more than 1.5 g) or even 0.5 ml, the minimum volume they propose?

In support of my original contention that the acid-resistant cells in the maternal circulation of the South African Bantu patients could well be of maternal and not fetal origin, it is of interest to note that McConnell *et al.* (quoted by Mollison⁴) found that 24% (the same figure as that given for their patients by Drs. Katz and Marcus) of healthy non-pregnant adults had acid-resistant cells in the circulation and in the smaller number in whom intensely stained cells were found these were shown mostly to be of maternal and not fetal origin.

Mollison⁴ has recently stated that "it is now clear that the acid elution method is unsuitable for detecting small numbers of fetal red cells in the maternal circulation during the first few months of pregnancy." The "small numbers" referred to are scores of less than 1/10,000, which was the maximum recorded in the South African patients.

It was my supposition that in embryos there were "probably incompletely expressed rhesus antigenic determinants." In the reference⁵ cited by Drs. Katz and Marcus to point to the early detection of rhesus antigens, the data completely support my supposition (the fetal red cells failed to agglutinate with anti-e, although the red cells of both parents grouped with this antibody and failed to agglutinate with anti-E, being of the probable genotype R₁r).

Finally, if it was not the intention of Drs. Katz and Marcus, as they state, to consider the possibility of the development of rhesus antibodies as a result of the rupture of acute ectopic pregnancies, why entitle their original article "The risk of Rh Isoimmunization in Ruptured Tubal Pregnancy"?—I am, etc.,

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¹ Pathak, W. N., and Stewart, D. B., *Lancet*, 1970, 1, 961.

² Carty, M. J., and Barr, R. D., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1972, 79, 1131.

³ Carty, M. J., Barr, R. D., and Ouna, N. In preparation.

⁴ Mollison, P. L., in *Blood Transfusion in Clinical Medicine*, 5th edn., p. 295. Oxford, Blackwell 1972.

⁵ Bergström, H., Nilsson, L. A., Nilsson, L., and Ryttinger, L., *American Journal of Obstetrics and Gynecology*, 1967, 99, 130.

Thiocyanate Metabolism in Human Vitamin B₁₂ Deficiency

SIR,—Dr. Douglas McAlpine (24 February, p. 486) writes that my recent letter (27 January, p. 231) reminded him of an article published jointly by Dr. Goldsmith and himself in 1951.¹ He states that "its publication in an obscure and short-lived journal (under my editorship) provides ample reason why this article has passed unnoticed."

I am happy to assure Dr. McAlpine that this article has certainly not passed unnoticed. In my letter I referred to a paper by Dr. J. M. Heaton and myself entitled "The Aetiology of Retrobulbar Neuritis in Addisonian Pernicious Anaemia" which was published in 1961.² This contained a historical review of previous work, including a commentary on the two case-reports of optic atrophy and pernicious anaemia presented by Drs. McAlpine and Goldsmith. We also laid particular emphasis on their finding that this rare complication of pernicious anaemia predominantly affects males and quoted and commented on their statement that "at the present time the evidence pointing to tobacco as a contributory cause is slight but may increase as more observations are made" in the light of our thesis that tobacco amblyopia and retrobulbar neuritis in pernicious anaemia and other vitamin B₁₂ deficiency disorders were, in fact, similar neuropathological states.^{2,3}

Dr. McAlpine and other earlier workers in this field will have noted with particular interest that during the past 15 years the role of chronic cyanide toxicity in relation to the pathogenesis of neuro-ophthalmological disorders and degenerative neuropathies has merited considerable clinical research and laboratory study in many centres. In my view there is now sufficient evidence in support of current opinion that tobacco amblyopia retrobulbar neuritis in pernicious anaemia, and Leber's optic atrophy are neurological manifestations of chronic cyanide intoxication in persons with an acquired or genetic error of cyanide or vitamin B₁₂ metabolism.—I am, etc.,

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¹ McAlpine, D., and Goldsmith, A. J. B., *Archives of the Middlesex Hospital*, 1951, 1, 109.

² Freeman, A. G., and Heaton, J. M., *Lancet*, 1961, 1, 908.

³ Heaton, J. M., McCormick, A. J. A., and Freeman, A. G., *Lancet*, 1958, 2, 286.

Children of Anaesthetists

SIR,—Reports of an increased incidence of abortion, stillbirth, and fetal malformation among women anaesthetists¹⁻³ may reflect other, more subtle effects from prolonged exposure to inhalational anaesthetic agents. One suggestion is that male anaesthetists tend to have more female children than

would normally be expected,³ and we carried out a pilot study to test this belief.

All anaesthetists of registrar grade and above employed in the Sheffield Hospital Region were asked to complete a postal questionnaire giving their age and sex, the date of their starting regular anaesthetic practice (with periods of absence), and the sex and dates of birth of their offspring. Other information requested concerned past and present use of various inhalation anaesthetics, and comments were invited. The use of randomly-numbered envelopes for returning the questionnaires, the key correlating these numbers with named individuals being held by a third party not involved in the survey, ensured confidentiality.

Out of 156 questionnaires sent 117 (75%) were answered. Of those who replied 21 were childless men and nine were women. The remaining 87 men had between them 157 live-born children conceived while they were in regular anaesthetic practice (children whose dates of birth were less than 42 weeks after the date of their father taking up, or returning to, anaesthetics were excluded). Of the children admitted to the survey 89 (56.8%) were girls. These findings were compared with those for the general population of England and Wales and for the Sheffield Hospital Region for the eight years 1963-70 inclusive.⁴ In these there was no significant variation in the proportion of female live births either from year to year or between the Sheffield Hospital Region and England and Wales as a whole (see table). The difference between these groups and the study group, applying binomial distribution, is significant ($P < 0.05$).

| Population | Total No. of Children | Female (%) | S.D. (8 Years) | P |
|---|-----------------------|------------|----------------|-------|
| Male anaesthetists Sheffield Region (1963-70) | 157 | 56.8 | | |
| England and Wales (1963-70) | 652,288 | 48.6 | 0.16 | <0.05 |
| | 6,876,035 | 48.6 | 0.04 | <0.05 |

Because of the wide geographical area of the Sheffield Hospital Region and the un-complicated nature of our questionnaire our results are unlikely to be biased. Indeed, with several replies was a comment that more male children were to be expected among anaesthetists. The comments, nevertheless, also reflected the concern you recently expressed (15 April 1972, p. 123) about the effects on anaesthetists of the agents they use. Our findings also underline the advisability of reducing to a minimum the exposure of anaesthetists to inhalational agents.⁵

We would like to thank all the anaesthetists who completed questionnaires, Professor J. A. Thornton for help with the survey, and Dr. R. A. Dixon for statistical assistance.—We are, etc.,

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¹ Knill-Jones, R. P., Rodrigues, L. V., Moir, D. D., and Spence, A. A., *Lancet*, 1972, 1, 1326.

² Cohen, E. N., Bellville, J. W., and Brown, B. W., *Anesthesiology*, 1971, 35, 343.

³ Askrog, V., and Harvald, B., *Nordisk Medicin*, 1970, 83, 498.

⁴ Registrar General, *Review of England and Wales*, 1963-1970, London, H.M.S.O.

⁵ Forrester, A. C., *Practitioner*, 1971, 207, 533.