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Using ovarian tissue from fetuses

EDITOR,—S R Brennan writes that the BMA's medical ethics committee has rushed to support the idea of donation of ovarian tissue by fetuses.¹ The committee began its discussions on this issue last September, when a presentation was made by Dr Roger Gosden, a leading researcher into the use of fetal ovarian tissue; all the issues were carefully explored. At its meeting on 10 February the committee discussed at length the use of fetal ovarian tissue for treatment purposes and the other issues raised in the Human Fertilisation and Embryology Authority's consultation document on donated ovarian tissue in embryo research and assisted conception. Contrary to press reports earlier this year, the committee concluded that use of ovarian tissue from fetuses for treatment purposes was unethical, although it accepted use of such tissue in research. Concern was expressed about the safety of the techniques and the long term effects on children who found out about their genetic origins. The difficulties of obtaining ethically acceptable consent were also highlighted.

These conclusions and the BMA's response to the Human Fertilisation and Embryology Authority's consultation will be debated fully by the BMA's council in May, when the views of other committees in the BMA are known. Any policy decision taken by the council will also require ratification by the representative body at the BMA's annual representative meeting in the summer.

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Management of preterm labour

Safety of hormone treatment unproved

EDITOR,—Gerald J Clesham reports a case in which antenatal corticosteroids and thyrotrophin releasing hormone were used in an attempt to accelerate fetal lung maturity in a twin pregnancy with imminent preterm delivery.¹ Randomised controlled trials have shown that corticosteroids given to mothers before preterm delivery can reduce the odds of neonatal death by about 40% and of periventricular haemorrhage and the respiratory distress syndrome by half, with no known side effects.² Analysis of the trials should be based on "intention to treat." This is especially important in preterm labour as our experience shows that as many as half of pregnancies judged to be at sufficient risk of preterm delivery to warrant a course of corticosteroids will continue for at least 10 days after the course is completed. Evidence from randomised controlled trials based on intention to treat analysis and long term follow up studies is reassuring, indicating that antenatal corticosteroids are safe not just for those babies born within 10 days but also for babies in pregnancies that continue.

Although the methodological safeguards described above have been followed in the trials of corticosteroids,² they have not been in the trials of a combination of corticosteroids and thyrotrophin

releasing hormone. Although the data from the five small randomised controlled trials suggest potential benefits (particularly for the respiratory distress syndrome) from such combined treatment, the effects are still far from certain.³ Only two of the trials used an intention to treat analysis. In the others the outcome for babies resulting from pregnancies that continued for more than 10 days after administration of thyrotrophin releasing hormone is not known.

Current scarcity of reassuring evidence that thyrotrophin releasing hormone is safe cannot be disregarded, particularly when evidence of effectiveness is weak. There are certainly maternal side effects, and thyrotrophin releasing hormone might conceivably be harmful to a fetus with compromised placental supply.

We believe that the temptation to try new treatments outside properly designed trials should be resisted, particularly in fetal medicine, until clear evidence emerges. We hope that the publication of two recently completed trials, from New Zealand and Australia, will help in this respect.^{4,5}

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Avoid ergometrine in the third stage

EDITOR,—As Gerald J Clesham mentions,¹ fluid overload is generally accepted as being probably the most important factor in the development of pulmonary oedema associated with the use of β agonists in the treatment of preterm labour. Every step, therefore, should be taken to reduce the risk of fluid overload. This includes giving the drug in small volumes of 5% dextrose with a syringe pump.¹

Another step, which is often ignored, is the choice of oxytocic drug used in the active management of the third stage of labour in these patients.² The two most widely used oxytocic agents are oxytocin and ergometrine-oxytocin (Syntometrine). Ergometrine has both α and β adrenergic properties, causing widespread peripheral vasoconstriction and leading to a sudden diminution of the vascular compartment.³ The pulmonary vessels, on the other hand, seem to be less susceptible to adrenergic stimulation and are controlled mainly by a metabolic autoregulatory mechanism.⁴ Intense adrenergic activity (for example, the effect of ergometrine) causes widespread constriction of the peripheral vessels and shifts a relatively large volume of blood to the pulmonary circulation, thus creating a local pul-

monary fluid overload.^{4,5} This effect, coupled with the normal increase in the circulating blood volume due to the autotransfusion that follows uterine contraction after delivery,⁶ can further contribute to the development of pulmonary oedema.²

When there are other risk factors, such as multiple pregnancy (with increased plasma volume) and the use of steroids (with their fluid retaining mineralocorticoid activity), it is worth considering using oxytocin instead of ergometrine-oxytocin in the management of the third stage in patients who have recently received β agonists.

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Antimalarial prophylaxis

Manufacturers recommend more stringent guidelines for halofantrine

EDITOR,—Current advice on prophylaxis against malaria for travellers from the United Kingdom was published in the *BMJ*.¹ Halofantrine hydrochloride was among the drugs recommended if standby treatment of malaria is necessary—that is, to be carried by travellers to malarious areas who will be out of reach of prompt medical advice for self treatment only in an emergency. The British position on this was consistent with that of the World Health Organisation.

In the light of further experience of cardiac adverse effects, the manufacturers have recommended more stringent guidelines for use of halofantrine. These have been endorsed by the World Health Organisation, and the British recommendations have therefore been modified. In particular, halofantrine should be used only for emergency self treatment by people who have a normal QTc interval (one not exceeding 0.44 s). The drug should be taken on an empty stomach. It is unsuitable for those with a family history of congenital QT prolongation, for those with electrolyte imbalance or cardiac disorders, or in combination with drugs that prolong the QT interval. The dose should not exceed the recommended 1500 mg given as 500 mg (two tablets) three times every six hours for adults, or 24 mg/kg given as 8 mg/kg three times every six hours for children. Halofantrine should also not be given as a standby antimalarial to those taking mefloquine prophylaxis.

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Mefloquine not first choice in aircrew

EDITOR,—N J White's editorial on mefloquine¹ quotes a recommendation by Bradley that for all British people except pregnant women mefloquine is the drug of choice for short term antimalarial prophylaxis in resistant areas.² White omits the other exclusion group mentioned in Bradley's article—namely, aircrew. Until more is known about the risk of serious side effects, mefloquine is