QUALITY OF EMBRYOS FROM IN-VITRO FERTILISATION

SIR,—In their paper on in-vitro fertilisation and embryo transfer (IVF/ET) Dr Edwards and Mr Steptoe (Dec 3, p 1265) describe the delivery of 139 infants in the five years since their first success and a pregnancy rate improved to almost 30% of embryo transfers, figures that establish the technique as a highly suitable option for the management of infertility. Our IVF/ET programme, which has a record of 16 healthy infants after a first successful outcome in July, 1982,[1] has been developed from the techniques of Edwards and Steptoe and experience with Prof Ian Craft when he was at the Royal Free Hospital School of Medicine.

Edwards and Steptoe comment that the major remaining difficulty is the proportion of embryos which implant (23% in our hands[2]). We too have tried to analyse the efficiency of various aspects within the system to explain the failure of implantation when the techniques appear satisfactory and the transferred embryos are morphologically normal. Is there a maternal factor preventing the implantation of normal embryos or are the embryos of poor quality despite their normal morphological appearance and rate of cellular division? Most pregnancies in our series are derived from the transfer of more than one embryo (table I). All cases were stimulated with clomiphene or clomiphene/human menopausal gonadotropin (hMG), and ovulation was triggered with 5000 units of human chorionic gonadotropin. 70 embryos developed from 79 preovulatory oocytes collected (table II). Ultrasound estimations were undertaken between 5 and 6 weeks post-transfer and revealed that 28 of 70 transferred embryos had developed into gestational sacs (40%). 6 of the 23 clinical pregnancies aborted (26%). No significant differences were observed in the implantation rates for the two stimulation regimens although embryo development per oocyte recovered was less in those with added hMG ($\chi^2 = 4 \cdot 8$: $p < 0 \cdot 05$).

TABLE I—RELATION BETWEEN EMBRYOS TRANSFERRED AND NUMBER OF GESTATIONAL SACS

No of embryos transferred	IVF pregnancies with gestational sacs numbering: 1	2	3	Total
1	3	—	—	3
2	9	1	—	10
3	3	—	1	4
4	1	—	—	1
5	5	—	—	5
6	—	1	—	1
Total	21	2	1	24

TABLE II—SUMMARY OF EMBRYO DEVELOPMENT, IMPLANTATION SUCCESS, AND PREGNANCY OUTCOME IN 24 IVF PREGNANCIES

Category	Clomiphene		Clomiphene/hMG		Total
	Ongoing	Aborting	Ongoing	Aborting	
Patients pregnant	10	5	8	1	24
Oocytes collected	26	12	36	5	79
Embryos transferred	25	11	29	5	70
Gestational sacs	10	5	12	1	28
Embryos implanting	40%	45%	41%	20%	40%

On the assumption that the maternal and uterine features which favour the successful implantation of an embryo apply for each embryo transferred, table II implies that 60% of embryos do not possess the potential for successful implantation.

The probability of pregnancy arising after multiple embryo transfer has been set out in a mathematical model, which takes embryo and uterine factors into consideration,[3] but for any successful case the uterine factor is constant and favourable. The chance of any one embryo implanting, assuming that the transfer technique is the same for all embryos in each successful transfer, is dictated by an embryo factor. Edwards and Steptoe discuss the possibility of one implanting embryo helping its twin. This idea is interesting but lacks corroborative evidence. Our view is that any proportionately increased likelihood of multiple pregnancies from multiple transfers relates to the quality of embryos developed. Whilst the figures reveal that only 40% of embryos in our system have the potential to implant, we are more likely to produce a number of high-quality embryos together because of the simultaneous effect of optimal technical factors within the laboratory and the recovery of oocytes in an individual case. We believe that this is the more likely explanation for the successful implantation of all three embryos in our triplet pregnancy.

We also believe that IVF/ET technology can be applied effectively to many types of infertility[4] and that a success rate of greater than 50% for embryo transfer is possible, but will require the development of techniques for assessing embryo quality before transfer—and that means experiments on human embryos to assess the infrastructure of blastomeres, chromosome make-up, and integrity of metabolic pathways.

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VIP AS BRONCHODILATOR

SIR,—We were interested to see the letters (Jan 14, p 112; Jan 21, p 162) commenting on our Nov 26 paper. We agree with Dr Altiere and Dr Diamond that previous studies with nebulised vasoactive intestinal peptide (VIP) have revealed little or no effect. This has been our experience also. In four asthmatic subjects nebulised VIP in the dose range 50–200 μg produced no change in lung function whereas intravenous infusion produced bronchodilatation in all subjects (mean increase in FEV_1, 0·2 litres after 15 min infusion). No systemic effects of VIP were noted during nebulisation, in contrast with the obvious flushing and tachycardia seen during intravenous infusion.

VIP is a peptide containing twenty-eight aminoacids and has a molecular weight of about 3300. Although the matter is not yet settled[1] it is unlikely that large molecules penetrate the lung epithelial membrane very rapidly, and we think that this is the most likely explanation for the lack of efficacy of nebulised VIP.

Both Altiere and Diamond and Dr Barnes and his colleagues point to the possibility that vasodilation produced by systemic administration of VIP may have reflexly caused a rise in plasma catecholamines which indirectly caused bronchodilatation. Indeed Diamond and Altiere feel that this is a probability, despite their own evidence[2] which showed intravenous VIP to be an effective bronchodilator in the cat in the presence of propranolol pretreatment and sectioning of the vagosympathetic trunk.

In our study, venous blood was withdrawn from the right antecubital fossa immediately before completion of each experiment, during the last minute of the infusion (VIP or vehicle), and placed into pre-chilled tubes. The tubes were then centrifuged and the plasma stored at −70°C for subsequent assay of plasma catecholamines by a radioenzymatic technique.[3] There was no significant difference in plasma adrenaline between placebo and VIP treatment groups; although plasma adrenaline was higher in three out of the seven subjects, mean plasma adrenaline was 0·15 (±0·06 SD) on placebo, compared with 0·24 ±0·19 nmol/l on VIP treatment. Plasma noradrenaline was significantly higher on VIP treatment (mean plasma noradrenaline 1·14±0·40 on placebo

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