which block meiosis at metaphase I. We postulate that lesions within the oocyte's developmental programme are major causes of embryonic mortality. For example, alterations to pre-ovulatory steroid profiles selectively disrupt protein reprogramming and individual components of the fertilization process. Similarly, some proteins secreted during maturation appear to facilitate early embryogenesis, whilst the role of others is at present unknown, although they bind to specific oocyte receptors. We postulate that it will be through a more complete understanding of somatic signals and developmental responses that early embryonic viability will be enhanced.

Hormonal and non-hormonal male contraception

Wednesday 25 June 1997
Hall B: Sidlaw Suite

08.30–09.05

O-159. Hormonal male contraception

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Abstract not submitted

09.05–09.40

O-160. Male contraception: alternative strategies

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Infertility in men can be produced by a wide variety of drugs and chemicals. Several have been considered as male contraceptives (α-chlorohydrin, win 18446 and gossypol) but none have reached clinical acceptance. The therapeutic ratio must be extraordinarily high for a compound used for social rather than medical reasons. Whilst hormonal contraception remains a favoured route and immunological approaches hold great promise, they are certainly not ideal and other targets should be sought. The goal is to find a compound which will produce safe, rapid, reliable and reversible infertility. One route is to empirically screen compounds and hope that serendipity takes a hand, as in the search for the contraceptive constituents (diterpenes) of the plant *Tripterygium wilfordi*. However, modern drug development harnesses the powerful techniques of molecular biology and, after identifying the target, millions of compounds from traditional or combinatorial chemical libraries can be screened in a very short time. If progress is to be made, then targets must be identified and evaluated. The search is encouraging as the testis and epididymis carry out many unique processes to transform the spermatogonial stem cell into a fertilizing spermatozoon. Some of these can illustrate the potential for contraceptive intervention. Programmed cell death (apoptosis) is an important regulator of germ cell numbers, particularly the meiotic spermatocyte. Chemicals such as methoxyacetic acid precipitate germ cell apoptosis, demonstrating that the signal transduction systems are in place although they are unknown. The Bcl-2 gene family, a target for cancer chemotherapy, may be involved and leads may arise from this arena. Another target is spermiation, when the Sertoli cell releases the mature germ cell into the tubular lumen. That this approach is possible can be shown by the antifertility effects of boric acid, which occur before any disruption of spermatogenesis. The epididymis is perhaps the most desirable target for male contraception because here the onset and recovery of infertility will be the fastest. Infertile men often possess mutations in the cystic fibrosis gene, which codes for a transmembrane conductance regulator involving a chloride channel, which suggests that secretion is a good target. Blockade of an ATPase proton pump neutralizes the pH of the epididymal fluid and renders the spermatozoa infertile. In conclusion, the possibility of the development of a non-steroidal male contraceptive remains. Progress is dependent on identifying molecular targets (enzymes, receptors) against which chemicals can be screened. This will only be achieved by appropriate financial investment, which may have to be driven by social and demographic priorities.

Trophoblast–uterine interaction

Wednesday 25 June 1997
Hall C: Fintry Suite

08.30–09.05

O-161. Modulation of trophoblastic invasion by the endometrium

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Mammalian embryos will initiate implantation-type reactions in many different non-uterine sites. Thus the embryo expresses an intrinsic invasive potential. Most of the time this is not true for the endometrium because it protects itself from implantation, except during a limited period known as the implantation window. After the initial steps of implantation, trophoblast invasion is also controlled by endometrial signals. Medium conditioned by decidual cells inhibits the invasion of trophoblast cells in the amnion invasion assay. These effects seem to be caused by cytokines. We examined the effects of decidual cell-conditioned medium

(DCM), IGFBP-1 (the major secretory product of decidual cells) and different cytokines of endometrial origin on the secretion of trophoblastic gelatinases [matrix metalloproteinase (MMP)-2 and MMP-9] and their inhibitor (TIMP-1). First-trimester cytotrophoblastic cells were obtained from abortions and cultured *in vitro* in presence or absence of DCM, IGFBP-1 or different cytokines. Secreted gelatinases were analysed in the culture supernatants by zymography and measurement of the total gelatinolytic activity. TIMP-1, HCG and fetal fibronectin (fFN) were measured using commercially available immunoassays. DCM inhibited the total gelatinolytic activity of cytotrophoblastic cells but increased trophoblastic MMP-9, TIMP-1 and fFN. In contrast, IGFBP-1 increased the total gelatinolytic activity, and TIMP-1 had no effect on MMP-2, MMP-9 or fFN. TGF-β inhibited the total gelatinolytic activity of cytotrophoblastic cells and this effect was mainly due to an inhibition of MMP-9. In contrast, TNF increased the total gelatinolytic activity and MMP-9 but decreased MMP-2 and fFN. Macrophage colony-stimulating factor had no effect on the parameters studied. We conclude that decidual cells exert a profound effect on the proteolytic activity of trophoblast cells. Although these results explain the effects of decidual cell supernatants on trophoblastic invasion, a complete understanding of how endometrial cytokines interact to modulate trophoblastic invasion is still lacking.

09.05–09.40

O-162. Immunology of human implantation

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Successful implantation of the placenta is dependent on the correct degree of trophoblast invasion into the uterine decidua. The extent of this invasion is tightly controlled. Under-invasion will lead to inadequate transformation of the decidual spiral arteries, resulting in clinical conditions such as miscarriage, intrauterine growth retardation or pre-eclampsia. Over-invasion is exemplified by placenta percreta. The factors that control trophoblast invasion are not known. Because placental trophoblast cells are derived from the antigenically 'foreign' fetus, it is likely that there could be an immunological mechanism of control similar to that which occurs between a transplanted allograft and recipient. Surprisingly, recent evidence indicates that the immunological mechanism in implantation appears to be based on a population of maternal natural killer (NK) cells rather than T cells, as in organ transplantation. Furthermore, these NK cells probably interact with a classic human leukocyte antigen (HLA) class I antigen (HLA-C) and a non-classic HLA class I antigen (HLA-G) expressed by invading trophoblast, instead of the usual HLA-A and HLA-B expressed by other somatic cells. This would appear to be a novel allo-recognition system unlike that seen in transplantation immunology, and is now a major focus of research interest.

Assisted reproduction 09

Wednesday 25 June 1997
Hall A: Pentland Suite

10.15–10.30

O-163. Success of ICSI in couples with male and/or female chromosome aberrations

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Introduction: To assess the genetic consequences of ICSI in male subfertility couples, most centres perform routine cytogenetic analyses of the male patient. In our ICSI programme, chromosome investigations are performed in all male patients and their wives prior to the initiation of ICSI treatment. Here we report on ICSI results in patients where constitutional or single cell chromosome aberrations were detected in the male and/or female partner.

Materials and methods: In a collaborative approach, all patients are counselled to undergo an extended andrological, gynaecological and cytogenetic examination prior to ICSI. This study was based on the evaluation of 434 couples who received ICSI treatment. The selection for ICSI was based on severe male factor infertility and/or previous fertilization failure in an IVF attempt with the absence of a female factor.

Results: Out of 434 couples treated by ICSI, 16 were affected by constitutional chromosome aberrations (eight male and eight female patients) and 96 by single cell chromosome aberrations (22 males, 59 females and both partners in 15 couples). In all, 322 couples were unaffected and were regarded as the control group. In the group with constitutional chromosome aberrations we performed 30 treatment cycles. When compared with a matched control group, couples with the male affected (20 cycles) showed significantly lower fertilization, implantation and pregnancy rates. In the female group (10 cycles), fertilization, implantation and pregnancy rates were comparable with the control group but a high abortion rate (two out of three pregnancies) was noted. Couples affected by single cell chromosomal aberrations received 166 treatment cycles with 48 male-affected cycles, 96 female-affected cycles and 22 cycles where both partners showed an abnormality. Fertilization and transfer rates were significantly lower when compared with the remaining (unaffected) 322 couples (394 cycles), whereas implantation and pregnancy rates proved to be comparable. In all couples suffering an abortion mainly parental autosomal aberrations were involved (six out of eight).

Conclusion: An unexpectedly high number of infertile couples in our ICSI programme are affected by chromosome