unclear, several suggestions have been proposed such as premature resumption of meiosis results in aged oocytes and alterations in the steroid environment of the antrum. In this study, pituitary suppressed patients undergoing IVF treatment were exposed to differing concentrations of LH, and the effects on oocyte maturation and fertilization were evaluated.

Materials and methods: A randomized prospective assessor-blind group comparative study was performed. Couples undergoing their first IVF treatment cycle were recruited to the study. Pituitary down-regulation was achieved using the long protocol GnRH analogue regime prior to randomization to one of four gonadotrophin preparations. The amount of FSH was kept constant at 75 IU/ampoule, while the LH dose in the gonadotrophin preparations varied (0, 1, 25 and 75 IU/ampoule; group A, FSH/LH 75:0; group B, FSH/LH 75:1; group C, FSH/LH 75:25; group D, FSH/LH 75:75. Gonadotrophin preparations were controlled for batch variation.

Results: Group A showed a significantly lower percentage of mature and fertilized oocytes and a correspondingly higher percentage of immature and unfertilized oocytes. The frequencies of atretic and abnormally fertilized oocytes were too small for any valid comparison to be made.

Total fertilization failure by group

	Group			
	A (75:0)[a]	B (75:1)[a]	C (75:25)[a]	D (75:75)[a]
No. of cases failed to fertilize	6 (17.6)	3 (13.0)	3 (11.1)	0 (0)
No. of cases fertilized	28 (82.4)	20 (87.0)	24 (88.9)	26 (100)
Total (n = 128)	34	23	27	26

Kruskal–Wallis exact test, P = 0.03. Values in parentheses are percentages.
[a]FSH:LH doses.

Conclusion: A dose-related trend in total fertilization failure was observed, with group A, containing no LH, showing the highest rate of total fertilization failure.

Reproductive endocrinology 02

Tuesday 24 June 1997
Hall C: Fintry Suite

14.00–14.15

O-113. A possible interaction between embryo and endometrium via activin and its receptors

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Introduction: Our objective was to study the role of inhibin/activin in early embryo development. To do this, the expression of inhibin/activin subunits, activin receptors (types I and II) and follistatin in human granulosa luteal cells, endometrial stromal cells and preimplantation embryos was assessed to evaluate the possibility of interactions between the embryo and the endometrium.

Materials and methods: Transcripts of inhibin/activin subunits, activin receptors and follistatin were detected by a reverse-transcriptase PCR in human granulosa luteal cells, endometrial stromal cells treated with or without progesterone and preimplantation embryos.

Results:

Cell numbers (n) of the embryo samples studied and their gene expressions (+/–)

	α-subunit	β_A-subunit	β_B-subunit	Activin I receptor	Activin II receptor	Follistatin
4- to 6-cell pre-embryo	– (7)	– (5)	– (5)	– (5)	+ (6)	– (5)
7-cell to morula pre-embryo	– (4)	– (4)	– (4)	+ (4)	+ (4)	+ (4)
Blastocyst	– (4)	+ (4)	– (4)	+ (4)	+ (4)	+ (4)
Granulosa luteal cells	+ (2)	+ (2)	+ (2)	+ (2)	+ (2)	+ (2)
Endometrial stromal cells	– (10)	+ (10)	– (10)	+ (10)	+ (10)	+ (10)
Progesterone-treated endometrial stromal cells	– (2)	+ (2)	– (2)	+ (2)	+ (2)	+ (2)

Conclusions: Transcripts of inhibin/activin subunits were detected in granulosa luteal cells. Inhibin/activin subunits were not found in preimplantation embryos, but activin A mRNA was found at the blastocyst stage. Only activin A transcripts were detected in endometrial stromal cells treated with or without progesterone. Activin receptors (types I and II) were detected in all embryos and cells studied. This may suggest that activin, not inhibin, plays an important role in early embryo development. We postulate that embryo–endometrium interactions may occur via activin produced by endometrial stromal cells and preimplantation embryo receptors.

14.15–14.30

O-114. The presence of pregnancy-specific β1-glycoprotein in serum before embryo transfer is associated with lower endometrial thickness and poor pregnancy prognosis in IVF

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Introduction: To develop an HCG-independent early pregnancy test to be used in IVF cycles under luteal support with HCG, we developed a highly sensitive microplate enzyme immunoassay method for pregnancy-specific β1-glycoprotein (SP1), a monomeric glycoprotein of syncytiotrophoblastic origin. We observed that, even in the presence of such exogenous support, HCG was superior to SP1. However, we also observed, in selected patients only, the presence of small amounts of serum SP1 around the time of oocyte retrieval (OPU) and embryo transfer, which seemed to be associated with a bad pregnancy prognosis. The aim of this study was

to test this hypothesis and to investigate the role of such 'ectopic' SP1.

Materials and methods: A total of 97 consecutive cycles of conventional IVF, without male infertility and with uncomplicated embryo transfer, distributed among 75 women, were studied. The 'long' protocol of agonist down-regulation and ovarian stimulation with menopausal gonadotrophins was used. Serum was obtained on at least two occasions between days OPU–3 and OPU+2 (i.e. day of embryo transfer). SP1 was determined with a sensitivity of 0.05 ng/ml. On day OPU–2 endometrial thickness was measured by ultrasound and serum steroid hormone concentrations determined. Pregnancy was diagnosed by HCG on day ET+15–17, and confirmed by ultrasound 2–3 weeks thereafter.

Results: The cycles were divided into group A (no detectable serum SP1 at any time between OPU–3 and embryo transfer) and group B (presenting at least one SP1 reading >0.1 ng/ml). Amongst the 72 cycles not leading to pregnancy, 27 (38%) fell into group B; in the 25 pregnancy cycles only two were classified as group B (8%). In all, 22 unsuccessful women underwent a second attempt: of 12 group A patients, six (50%) became pregnant, while no pregnancy was achieved in the remaining 10 group B patients. Moreover, nine of these 10 women presented a repeat group B pattern, while one was group A (no SP1). All six previously group A, second-attempt non-pregnant women were a repeat group A. Endometrial thickness was negatively correlated with SP1 before embryo transfer ($P = 0.0115$). However, no difference in day OPU–2 endometrial thickness was observed between group A non-pregnant and subsequently pregnant patients.

Conclusion: The occurrence of serum SP1 concentrations on or before the day of embryo transfer >0.1 ng/ml and in combination with a slightly reduced endometrial thickness is associated with a poor IVF pregnancy prognosis not only in the current but also in subsequent treatment cycles. Further studies will focus on the identification of factors responsible for SP1 secretion by an as yet unknown source and, because patients tend to remain in either group A or B, on treatment lines for changing group B patients to group A, thus obtaining a better prognosis in subsequent attempts.

14.30–14.45

O-115. Cytokines in peri-implantation endometrium of recurrent miscarriage and normal women

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Introduction: Normal pregnancy is an immunological paradox because the embryo, a semi-allograft, manages to evade rejection by the maternal immune system during its intrauterine life. In contrast, recurrent miscarriage (RM) patients experience rejection (miscarriage) in early pregnancy. The maternal allograft immune response comprises a T helper 1 (TH_1) cell-mediated cytotoxic rejection immunity and a TH_2-mediated B cell humoral immunity. Cytokines are of pivotal importance in the mediation of TH_1 and TH_2 immunity. Normal pregnancy is associated with a cytokine-induced modulation of predominant TH_2 immunity, whereas idiopathic RM may involve an increased systemic TH_1 but a decreased TH_2 immunity. To evaluate further the hypothesis of cytokines and TH_1 and TH_2 immunity in human reproduction, we studied the pattern of cytokine expression in the peri-implantation endometrium of RM patients and compared it with that in normal, fertile women.

Materials and methods: A total of 11 RM patients (having three or more consecutive first trimester miscarriages) and 10 fertile women with previously successful pregnancies were recruited to the study. Endometrial pipelle sample collection was timed to the mid-cycle ovulatory LH surge using serum or urine LH monitoring. All samples were collected during the peri-implantation period LH+7–LH+10 and stored in liquid nitrogen until analysed. The samples were processed by reverse transcriptase-PCR after messenger ribonucleic acid extraction to identify the presence of the TH_1 cytokines IL-2 and interferon-γ (IFN-γ), and the TH_2 cytokine IL-6.

Results: The TH_1 cytokine IL-2 was expressed in 10 out of 11 of the RM patients compared with one out of 10 of the controls ($P = 0.001$), whereas IFN-γ is expressed in eight out of 11 of the RM patients compared with two out of 10 of the controls ($P = 0.047$). The TH_2 cytokine IL-6 is expressed in two out of 11 of the RM patients compared with eight out of 10 of the controls ($P = 0.017$).

Conclusion: To our knowledge, this is the first study to demonstrate a predominant TH_1 and a lack of TH_2 immune response in the peri-implantation endometrium of RM patients compared with normal fertile women. We hypothesize that successful implantation and maintenance of a normal pregnancy are dependent on the type of maternal immunity present in peri-implantation endometrium, derangements of which may result in RM. A predominantly TH_1 and a lack of TH_2 immunity may result in pregnancy rejection, whereas the converse may be conducive to maintaining pregnancy. In future, attempts at cytokine-induced immunomodulation may be used to treat RM, as have been tried successfully in animals. In addition, cytokine-induced immunomodulation may improve implantation rates in assisted conception treatments and has potential as a reversible immune contraceptive.

14.45–15.00

O-116. Antiprogestin action in primate endometrium: are glandular and stromal effects mediated by the progesterone receptor?

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Introduction: Besides being an antiprogestin, mifepristone (RU 486) was recently shown to antagonize oestrogen-