human embryonic stem cell line. However, tests of pluripotency, as well as the expression of some other markers commonly used to identify hES cells (SSEA-4, SSEA-3, TRA-1-60, TRA-1-91), should be further performed in order to fully characterize the putative hES cell line. The results of these tests, some of which are ongoing, will also be presented.

This report of our first ES cell line is important because we are convinced that the derivation of more ES cell lines is a requirement for the further development of this promising field.

POSTER SESSION
Contraception

P-441 A transitory effect of etonogestrel implant on platelet aggregation in healthy women
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Introduction: Several studies have suggested that the risk of venous thromboembolism (VTE) is attributable to the estrogen component of a contraceptive in a dose-dependent manner. Recent epidemiological studies have suggested that the risk of VTE was higher with contraceptives containing third-generation progestagens (desogestrel, gestodene) while compared with second-generation progestagens (levonorgestrel). These unexpected findings have been the subject of many debates with no definitive explanation and the question of differences in hemostatic properties of each progestagen has been raised. Although progestagens are not associated with marked changes in hemostatic variables, there are few studies on the effects of these drugs, especially third-generation progestagens, on the hemostatic system. The objective of the present study was to evaluate the acute effect of a long-term contraceptive implant of etonogestrel on platelet aggregation in healthy women.

Materials and methods: Twenty-two healthy volunteer women were enrolled in this prospective longitudinal study, to use a subdermal contraceptive implant of etonogestrel (the biologically active metabolite of desogestrel). Platelet aggregation was measured in all users at baseline and after 1, 3, and 6 months of treatment. Platelet aggregation was induced with 5 μg/ml adrenalin and 1 μg/ml collagen in two separate assays. Statistical analysis included the paired t test to compare differences between each period of treatment from baseline.

Results: Statistically significant 20% and 16% reductions of platelet aggregation were noted before the start of the ring-free period. Endometrial biopsies were taken at baseline, and at cycles 13 (month 3) and 26 (month 24). The baseline biopsy was taken during the mid-luteal phase, and the cycle 13 and 26 biopsies were taken approximately seven days before starting the ring-free period.

Conclusions: Tubal ligation has been blamed for causing luteal phase defect as a result of affected ovarian circulation. In our study, the rate of ovulation was even improved after the procedure and ovarian reserve was not negatively affected. Bipolar electrocoagulation of the fallopian tubes did not alter the ovarian reserve and function.

P-443 NuvaRing does not affect endometrial histology
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Introduction: Various changes in the vaginal endometrium, including atrophy and hyperplasia, have been associated with the use of hormonal contraceptives. NuvaRing is a monthly combined contraceptive ring that delivers contraceptive hormones by the vaginal route. The aim of this study was to assess the long-term effects of NuvaRing on endometrial histology.

Materials and methods: This was a two-year, open-label study that intended to recruit 135 healthy women, 18–35 years old. Subjects received 26 cycles of treatment, comprising 3 weeks of ring use followed by a 1-week ring-free period. Endometrial biopsies were taken at baseline, and at cycles 13 (month 12) and 26 (month 24). The baseline biopsy was taken during the mid-luteal phase, and the cycle 13 and 26 biopsies were taken approximately seven days before the start of the ring-free period.

Results: One hundred women provided sufficient biopsy material at baseline to allow evaluation of endometrial safety. The number of women who provided sufficient biopsic material at cycle 13 was 79, and at cycle 26 it was 38. After 13 cycles of ring use, normal endometrial biopsy results were obtained in all subjects except two. In the first subject, the biopsy showed proliferative activity without evidence of hyperplasia. A repeat biopsy in this subject showed the endometrium to be normal. The second subject showed suspected implantation of trophoblast cells. A pregnancy test showed that the second subject was not pregnant. After 26 cycles of ring treatment, normal biopsy results were obtained for all subjects. No pregnancies occurred during treatment.

Conclusions: These results show that NuvaRing provides long-term contraceptive protection without affecting endometrial histology. These results add to the growing body of evidence which shows that NuvaRing is an effective and well tolerated form of contraception.
P-444  NuvaRing suppresses ovarian function
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Introduction: NuvaRing, a monthly contraceptive vaginal ring that releases etonogestrel (ENG) 120 µg and ethinylestradiol (EE) 15 µg per day, has been shown to suppress ovarian function.1 This study compares the effects of the vaginal ring on ovarian function with those of an oral contraceptive (OC) containing 150 µg levonorgestrel (LNG) and 30 µg EE.

Material and methods: This was an open-label, randomized study. Subjects who ovulated on or before day 21 (+1 day) of a screening cycle were randomized to 2 cycles of 28 days of treatment with either the ring or the OC. Based on the manufacturers’ instructions, OC use began on the first day of menstruation and ring use on the fifth day (to avoid inserting the ring during menstruation). Ovarian function was assessed by transvaginal ultrasound scanning and measurement of circulating levels of progesterone, 17β-estradiol (E2), follicle stimulating hormone (FSH) and luteinizing hormone (LH). Measurements were taken on the day after the first ring was inserted or the first pill was taken, thereafter on every third day until day 20, then on every third day from day 24 until day 48, and also on days 52 and 55. For ring-users, rings remained in place for 21 days, followed by a 7-day ring-free period, and for OC users, pills were taken once daily for 21 days, followed by a 7-day pill-free period.

Results: Of the 40 randomized subjects, 21 received the ring and 19 received the OC. In the first treatment cycle, the mean maximum follicular diameter (maxFD) was higher with the ring (11.81 mm [95% CI 10.07, 13.85]) than the OC (8.95 mm [95% CI 7.55, 10.61], ratio 1.32), and was related to the difference in starting procedures. In the second cycle, the mean maxFD was comparable for the ring (12.68 [95% CI 10.81, 14.87]) and the OC (11.38 [95% CI 9.60, 13.48], ratio 1.11). Ovulation did not occur in any subject with either treatment. Serum hormone concentrations of LH, FSH and P were suppressed in both treatment groups. Concentrations of E2 showed a similar response pattern to MaxFD. Both treatments were well tolerated and produced similar incidences of adverse events.

Conclusions: Suppression of ovarian function with NuvaRing was effective and comparable to an OC containing 150 µg levonorgestrel and 30 µg ethinylestradiol. Ovarian activity was higher with NuvaRing in the first cycle due to different starting procedures, but not in the second cycle.


P-445  Effects of modern oral contraceptive on carbohydrate, lipid metabolism and hemostasis system in women with type 1 diabetes
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Introduction: At present in Russia a single tactic of contraception choice in diabetic women is absent.

Material and methods: A total of 60 women with Type 1 diabetes were included in this study: 20 women received combined oral contraceptives (COCs) consist of 20 mg ethinylestradiol (EE) and 150 mg desogestrel (DGS); 20 women received COCs consist of 30 mg EE and 150 mg DGS; 20 women received COCs consist of 30 mg EE and 300 mg norgestrel (NGS); 20 women received only progesterin pill with 500 mg lignestrenol. Evaluation (indices of carbohydrate, lipid metabolism and hemostasis system) was performed before and after 3 and 6 months.

Results: The contents of lipids in blood among diabetic women, factor VII, activity of antithrombine III and platelet functions correlate with HbA1c level. The increase of platelet functions occurs with HbA1c level more that 7%, with the one more that 8% hyperlipidemia occurs for sure more often increase of HbA1c level (9% and higher) associated with hypercoagulability (decrease of factor VII, activity of antithrombine III).

COCs containing 20 mg EE and DSG, as for containing only progesterin pill has not occurred the negative influence to the lipid metabolism. The use of COCs containing 30 mg EE has been accompanied by the reduction of total cholesterol, cholesterol LDL levels and by the increase of cholesterol HDL level.

Conclusions: The long duration and/or unsatisfactory compensation of diabetes, presence of hyperlipidemia may have their own place in the realization of venous thrombosis. COCs containing 20 mg EE/DSG and only progestagen pill lead to the less expressed increase of platelet functions that of COCs containing 30 mg EE and NGS. The use of COCs and only progestagen pill has not occurred clinically significant influence to the indices of plasma link and fibrinolitical system of blood plasma.

P-446  Activin A and Inhibin A: correlation of pregnancy outcome in recurrent miscarriage
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Introduction: Recurrent miscarriage is a common problem and despite extensive research, little is known about its pathophysiology. Recent studies show that a high concentration of Inhibin A and Activin A are present in maternal serum in early pregnancy. These proteins may play a part in fetomaternal communication required to establish and maintain pregnancy. Hence the measurements of Inhibin A and Activin A in maternal serum in early pregnancy may provide further possibilities in early diagnosis, prognostication and monitoring diseases of pregnancy.

Material and methods: The study was conducted at The Sheffield Teaching Hospitals NHS Trust and Department of Reproductive Medicine, University of Sheffield.

38 women with history of recurrent miscarriage coming to the clinic after spontaneous conception were recruited for the study. We collected serum samples at two weekly intervals in the first trimester. The serum was then analysed for Inhibin A and Activin A by ELISA (Oxford Bio-Innovation). Serum Beta HCG levels were also measured. Levels of these proteins were then analysed in terms of pregnancy outcome that is, whether pregnancy continued beyond 24 weeks or whether it miscarried. The levels were also correlated with cause of miscarriage and any treatment given.

Results: Mean age group for patients included in the study was 32.5 years and this was similar in the group that further miscarried or that which continued beyond 24 weeks. Both Inhibin A and Activin A concentrations rose in the first trimester of pregnancy. This rise was higher in pregnancies that continued beyond 24 weeks. Inhibin-A levels were significantly higher at first and second visit in the group where pregnancies continued beyond 24 weeks (p=0.001 and p=0.004 respectively, Mann Whitney U test). Activin levels were also higher at both visits in this group, however this difference achieved significance (p=0.008) only at the second visit (7-8 weeks gestation). Of the 38 women included in the study, 21 had no explanation for recurrent miscarriage while others had diagnoses including antiphospholipid antibody syndrome, uterine malformation or luteal phase defects. These diagnoses were equally divided in the two groups of pregnancy outcome.

Conclusions: Inhibin A and Activin A levels are significantly higher in viable pregnancies in women with history of recurrent miscarriages compared to those that are destined to miscarry. Inhibin A and Activin A may be used to establish an early prognosis for pregnancy outcome in patients with history of recurrent miscarriage. Such prognostication may help allay fears and anxiety in women with history of recurrent miscarriages. Further work in larger series is required to see whether the serum concentrations are different in women with different causes of recurrent miscarriage and whether these concentrations are affected by therapeutic intervention.

POSTER SESSION
Early pregnancy: basic research

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