Wider implications of the findings: Whilst the findings of this study need to be interpreted in the context of surrogacy in the UK, they show that family relationships within the surrogate’s own family are good and that the children are not negatively affected as a result of their mother’s decision to be a surrogate. These results are of importance to counsellors and support groups offering advice to surrogates and intended parents.

Study funding/competing interest(s): The study is funded by the Economic and Social Research Council, UK.

Trial registration number: n/a

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O-081  Significantly reduced ovarian reserve in female offspring of consanguine parents

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Study question: To analyze the impact of consanguinity on the reproductive health of daughters from consanguine parents.

Summary answer: Significantly reduced ovarian reserve is a likely cause of infertility in daughters of consanguine parents. Hence, in societies with a high rate of consanguinity, consanguinity-related premature ovarian failure might be a frequent cause of infertility. Thus, clinical work up requires extensive family anamnesis.

What is known already: Marriage between first grade cousins is common in various regions and populations worldwide, e.g. in the Middle East. In Kuwait, epidemiological studies show consanguinity rates of 50-64.3%. Retrospective epidemiological studies indicate an increased rate of children arising from marriages between first-degree cousins, while in one Swiss study, the daughters of consanguine couples showed reduced fertility. However, to date, no clinical data exists on the reproductive health of women from consanguine marriages.

Study design, size, duration: In this observational study 301 normal cycling patients, aged ≤ 39 years and with a normal karyotype visiting the satellite centre for reproductive medicine of the university of Brussels in the state of Kuwait between January 2010 and November 2011 were included.

Participants/materials, setting, methods: Patients underwent complete history taking, including presence and degree of consanguinity. A transvaginal scan was performed on day 2/3 of the cycle and the antral follicle count (AFC) was determined. To avoid an inter-observer variation, the same investigator did all scans. Moreover, serum LH, FSH, E2, and P were determined.

Main results and the role of chance: The median AFC of 153 non-consanguineous patients was 10.0, while the 148 patients from consanguineous parents displayed a significantly lower median AFC of 7 (p < 0.001). Only 10% of consanguineous patients had a normal AFC (>9) according to their age, in contrast to 55.3% of non-consanguineous women. Consanguineous patients did not exhibit an age-dependent AFC-decline that was expected and observed in non-consanguineous patients, and displayed already around 20 years of age a premenopausal AFC. Detailed analysis of the patient history and risk-factor analysis revealed that significantly more non-consanguineous patients had adnexal surgery than consanguineous patients (p < 0.001), which excludes ovarian surgery as a cause of reduced ovarian reserve in consanguine patients. LH, FSH, E2 and P levels did not vary between the groups.

Limitations, reason for caution: The described population was retrieved from a single center and therefore a selection bias cannot be excluded. Moreover, no AMH values are available in patients with a normal AFC. However, the rate of consanguinity in this study matches published data from Kuwait.

O-082 Can birth hypoxia affect ovarian follicular reserve

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Study question: Is the follicle reserve of the developing mammalian ovary susceptible to the effects of hypoxia at birth?

Summary answer: A brief perinatal exposure of spiny mouse (SpM) foetuses to hypoxia (7.5-8min) resulted in a significant reduction in ovarian volume and depletion of the ovarian follicular reserve at postnatal day (D) 33 compared with controls.

What is known already: Hypoxic-ischemia occurs in about 4 per 1000 live human births and 4-8% of hypoxic infants die at birth. Many of those that survive experience severe health problems from irreversible damage to the brain, kidneys, heart and lungs (Perlman et al. 1989 American Journal of Diseases in Children 143: 617). Despite the possibility that birth hypoxia may also cause lasting damage to the ovary, its effects on the mammalian ovary have not been examined previously.

Study design, size, duration: Controls: pups delivered; C-section 38D gestation (-1 day term). Treated pups: uteri isolated 38D gestation; ~8 minutes in saline; pups resuscitated. Surviving pups placed with foster dams; females killed at 33-35D postnatal age; ovaries removed for histology. Ovarian volume and follicular reserve of postnatal D33-35 SpM (control = 3; treated = 8) were compared.

Participants/materials, setting, methods: A spiny mouse near-term hypoxia model was used in which ~60% of neonates survive hypoxia treatment. Ovaries were fixed (Bouin’s), embedded in glycol methacrylate, serially sectioned (10µ) and stained in H&E. Ovarian volume, total follicle number and mean diameter (primordial, primary, secondary, antral) were estimated stereologically using the optical dissector method.

Main results and the role of chance: The number of primordial (3178 ± 288 [mean ± SE]) and primordial plus primary follicles (3762 ± 401) in the control ovaries was significantly greater than in the ovaries from the hypoxia group (2177 ± 334 and 2502 ± 271 respectively, p < 0.05; One-way ANOVA, Tukey post-hoc). The mean diameter of primordial follicles was significantly smaller in the treated group compared to controls (20.09 ± 0.45 vs 22.03 ± 0.15, p < 0.05). The volume of the ovary was also significantly reduced in the treated group (0.70 ± 0.21 vs 1.06 ± 0.09, p < 0.02). The mean ovarian volume was positively correlated with mean diameter of primordial (R² = 0.708) and secondary plus antral follicles (R² = 0.9487). A pilot study that compared the maturation potential of oocytes from the follicles of control and treated ovaries from postnatal D33-35 SpM showed no significant difference in survival or maturation rates in vitro.

Limitations, reason for caution: This study was limited to observations in the spiny mouse. Group sizes were uneven and, while differences are significant, a larger group of controls is required to extend these data. Caution is needed in applying these findings to similar situations of birth hypoxia in other mammalian species, in particular humans.

Wider implications of the findings: This is the first evidence that birth hypoxia causes detrimental changes to ovarian structure and depletion of the follicular reserve in an adult female mammal exposed to hypoxia at birth. The results confirm our hypothesis that like other important organs of the body the ovary is also affected by perinatal hypoxia. The spiny mouse is a proven model for near-term hypoxia and our results suggest the possibility that hypoxia may also affect the human ovary.

Study funding/competing interest(s): This study was funded from in-house budgets and the authors have no conflicting or competing interests to declare.

Trial registration number: N/A
**O-083** Comparative study about ART outcome in patients with Turner’s syndrome or partial X monosomy using own oocytes with preimplantational genetic screening or ovum donation

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**Study question:** Is there a difference among the reproductive outcome of preimplantational genetic diagnosis (PGD) in patients with mosaic Turner’s syndrome (MTS) using own oocytes, compared to mosaic and pure Turner syndrome (PTS) using ovum donation (OD)?

**Summary answer:** A remarkable trend to have lower live-birth rates are found in PGD-PTS, compared with any OD patient with TS, either MTS or PTS. Moreover, being mosaic or pure TS also seem to condition reproductive results. This trend is confirmed in implantation rates as well.

**What is known already:** PGD can be offered in the infertility treatment of MTS, enabling the selection of euploid embryos. To improve the number of euploid embryos available, thus enhancing reproductive results, OD is an interesting alternative, although other features of the patients including endometrial receptivity, can complicate implantation, pregnancy maintenance or obstetric outcome.

Scarce information is available in the literature regarding TS, mainly in the form of case reports, and short series of patients.

**Study design, size, duration:** Retrospective cohorts study from January 2000 until January 2011, scrutinizing >200000 medical charts from 14 infertility clinics in Spain, searching for pure or mosaic TS, confirmed by the karyotype.

**Participants/materials, setting, methods:** University-affiliated private infertility centre. 30 PGD-PTS patients, on which 77 controlled ovarian hyperstimulation cycles (COH) were performed, and embryo transfers (ET) performed in 37. As well, 22 women belonged to the OD-PTS group, with 79 COH cycles and 17 ET, and 9 OD-PTS women with 39 COH cycles and 27 ETs.

**Main results and the role of chance:** Mean age, body mass index, and height were 37.6y(36.5-37.8) vs. 34.3y(30.0-37.7), 23.7kg/m2(22.7-24.6) vs. 23.7kg/m2(21.7-26.1) and 1.53m(1.50-1.57) vs. 1.64m(1.61-1.66) for MTS and PTS respectively, without significant differences found, except for height.

The mean number of oocytes retrieved/received, for PGS-PTS, OD-PTS and OD-PTS respectively were 11.6(9.5-13.8), 13.4(11.6-15.2) and 11.6(9.2-14.0), embryos transferred 1.86(1.66-2.06), 1.83(1.71-1.94) and 1.52(1.32-1.72), implantation rate per ET 10.4%(3.11-17.8), 26.2%(16.8-35.6) and 14.6%(3.8-25.5), not reaching statistical significance, but showing considerable differences.

Pregnancy rates tended to be higher (p = 0.25) in OD-PTS 38.3%(95 CI (24.4-52.2) vs. PGS-PTS 24.3%(95CI(10.5-38.1) and OD-PTS 22.2% 95 CI (6.5-37.9), while miscarriage rates remained statistically comparable, although with a noticeable higher rate when using own oocytes, being OD-PTS 27.7% 95 CI (7.0-48.4) vs. PGS-PTS 66.6%(95CI(35.8-97.4) and OD-PTS 33.3% 95 CI (7.0-71.0) respectively, resulting in live-birth rates of OD-PTS 27.7% 95 CI (14.9-40.5), almost three times those observed for PGS-PTS (8.1% 95 CI (0-16.9)) and almost doubling those on OD-PTS (14.8%(95CI(1.4-28.2).

**Limitations, reason for caution:** Although this is, to our knowledge, the biggest series ever reported in assisted reproduction techniques in TS, the limitation of the study is the low number of patients included. Subsequently, this must be taken into account, and the conclusions reached taken carefully until a larger body of evidence is available.

Wider implications of the findings: On TS patients, given the low success of PGD using their own oocytes, after extensive information being provided by the practitioner, oocyte donation should be recommended, since it seems, based on the available information, the best reproductive option in female who are missing one of the X chromosomes, with or without mosaicisms present, being also this feature relevant for the reproductive results.

**Study funding/competing interest(s):** None

**Trial registration number:** Not applicable

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**O-084** Caffeine intake does not affect female ovarian reserve. Analysis of a cohort of 1963 consecutive blood samples evaluating ovarian hormonal status

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**Study question:** The objective of the study was to investigate, in a population of women addressed for an ovarian reserve (OR) determination whether caffeine intake through coffee consumption has a deleterious effect on this reserve, taking in account main confounding factors.

**Summary answer:** Despite a wide cohort and the use of multivariate models, the present study did not find any relationship between caffeine consumption and ovarian reserve markers. Caffeine intake does not appear deleterious for ovarian reserve, even in case of high consumption.

**What is known already:** Epidemiologic studies evaluating the role of caffeine on fertility show inconsistent results (Wilcox A, Lancet 1988, Hakhim RB, Fertil Steril 1998). In a recent cohort study of 3628 women planning a pregnancy, in Denmark (Hatch EE, Epidemiology, 2012), there was a weak association between caffeine intake and fertility, different according to beverage type, and possibly explained by confounders. However, no study was published on the potential relationship with ovarian reserve.

**Study design, size, duration:** A transversal epidemiological study was performed on 1958 women 18-45 years recruited from August 1st to December 31st 2012 in a single private laboratory involved in assisted reproductive technology, with OR testing between cycle day 1 and Day 5. All women are questioned on their current caffeine consumption.

**Participants/materials, setting, methods:** AMH was measured using AMH/ MIS enzyme-linked immunosorbent assay kit (Beckman Coulter), FSH and E2 by Chemiluminiscent Microparticle (Abbott). Coffee consumption (Yes/No), and the number of cups/day were recorded. Main confounders were considered: age, BMI, cycle day and previous cycle duration. Women with current hormonal treatment were discarded (n = 59).

**Main results and the role of chance:** Women were aged 36.0 ± 4.9 years, 60.6% were coffee consumers (2.4 ± 1.5 cups / day, 23.1% ≥ 1 cups). With increasing age, AMH strongly decreased (r = -0.40, p < 0.001), and FSH increased (r = 0.21, p < 0.001). The previous cycle duration was correlated to AMH (r = 0.22, p < 0.001), and slightly to FSH (r = -0.07, p = 0.01). Globally, caffeine consumers had not a decreased AMH (3.7 ± 3.7 vs. 3.9 ± 4.0 pg/ml), or increased FSH (8.7 ± 5.7 vs. 8.6 ± 6.9 UI/l) and the percentage of low OR (AMH < 1.5pg/ml) was not increased (31.1% vs. 29.0%, p = 0.32). The results were similar when entering women’s age and other confounders in the models and when considering the number of cups. In the multilogistic model, only age was related to low OR assessed by AMH.

**Limitations, reason for caution:** The study concerned 79.9% of potential patients (18-45 years, no treatment, measurement Day 1-5). Potential bias cannot totally be ruled out (incomplete participation, infertile women). Moreover, only the current exposition was measured. However, the large number, the consideration of major confounders (age, BMI, cycle day, previous cycle duration) re-inforce the results.

**Wider implications of the findings:** This study is one of the first on the impact of caffeine intake on OR assessed by the currently best marker, AMH. It brings a piece in the debate, showing that, if caffeine impacts female reproduction, it apparently not goes through an action on ovarian reserve. Caffeine consumption is probably underestimated in this study since it does not take into account other sources (soda, tea etc...), which may deserve to enlarge our questionnaire.

**Study funding/competing interest(s):** This study was performed in a single lab without external funding. There was for any of the authors

**Trial registration number:** Not applicable

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**O-085** Association of urinary phthalate (UrP) metabolite concentrations with ovarian response and early in-vitro fertilization (IVF) outcomes

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Study question: In women undergoing in-vitro fertilization (IVF), is there an association between UrP and ovarian response, oocyte yield, embryonic development and/or implantation failure (IF)?

Summary answer: Increased UrP were associated with decreased yield of retrieved and mature oocytes and increased odds for implantation failure.

What is known already: In experimental studies, some phthalate (P) metabolites alter endocrine signaling pathways in the rodent ovary. Limited occupational studies link phthalate exposure with adverse reproductive outcomes. Despite widespread human exposure to phthalates, little is known about the effects of low-level, daily exposures to phthalates on ovarian function and hence on women’s reproductive health.

Study design, size, duration: Prospective cohort; 231 women (18-45 years old) undergoing 325 fresh IVF cycles at the Massachusetts General Hospital Fertility Center in Boston, MA, USA. Between 11/2004 and 03/2012, 598 urine samples were collected either at the early/mid-follicular phase and/or at oocyte retrieval.


Outcome measures: Serum peak estradiol, number of retrieved, mature, and fertilized oocytes, embryonic cleavage and implantation failure.

Main results and the role of chance: Most UrP were detected in >95% of urine samples. The odds for IF increased with increasing quartiles of i) sum-DEHP metabolites (Odds Ratios (ORs) for quartiles Q2, Q3, and Q4 vs Q1: 1.41, 1.76, 2.05, respectively, \( p\)-trend = 0.031), and ii) MBP (ORs: 1.96, 2.02, 1.85, respectively, \( p\)-trend = 0.087). There was a 4.17% (Q2), 6.19% (Q3), and 11.4% (Q4) decrease in the number of retrieved oocytes with increasing MEHP quartiles (as compared to Q1, \( p\)-trend = 0.052), and a similar 9.09%, 9.46%, 10.2% decrease with increasing quartiles of sum-DEHP metabolites (\( p\)-trend = 0.074). There was a decrease in the number of mature oocytes with increasing MEHP quartiles (range: 3.03%-14.8%, \( p\)-trend = 0.016), and sum-DEHP metabolites (range: 11.9%-14.4%, \( p\)-trend = 0.018). There were no associations of UrP with peak estradiol, rates of fertilization or embryonic cleavage.

Limitations, reason for caution: UrP were measured in urine samples collected during the IVF cycle and reflect only short-term exposure. Measured urinary concentrations might not accurately represent long-term exposure and its contribution during the IVF cycle and reflect only short-term exposure. Measured urinary concentrations might not accurately represent long-term exposure and its contribution during the IVF cycle and reflect only short-term exposure. Measured urinary concentrations might not accurately represent long-term exposure and its contribution during the IVF cycle and reflect only short-term exposure. Measured urinary concentrations might not accurately represent long-term exposure and its contribution during the IVF cycle and reflect only short-term exposure.

Wider implications of the findings: MEHP and sum-DEHP metabolites were associated with lower oocyte yield and the latter was also associated with increased odds of implantation failure in IVF. Our data support the hypothesis that exposure to specific phthalates might lead to adverse female reproductive outcomes.

邀访嘉宾

O-087 Defining the PCOS by biochemistry - pitfalls and practice
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Polycystic ovary syndrome (PCOS) is a common disorder which has considerable phenotypic variability and this has led to controversy over its exact definition and diagnosis. The main diagnostic definitions used over the past two decades have been very vague. They are clear about the duration of the menstrual cycle and what ultrasound appearance represents the features of polycystic ovaries. However, the published definitions all use synonymous expressions embracing the concept of clinical and laboratory hyperandrogenism as a diagnostic criterion. How can these words be converted into measurables that can be used for patient management?

The scoring systems for acne and hirsutism are clear and observers can be trained to use them reproducibly but what is normal or abnormal since all women will have some body hair and the occasional menstrual aeciform spot? The laboratory definition of hyperandrogenism is equally poorly defined – which and how frequently should serum androgens be measured? what are normal values? This ambiguity is likely to lead to misdiagnosis. It may be that