2nd UK Fertility Preservation Conference

14 September 2018
St Anne's College, Oxford

Public Lecture
Fertility on ice: fertility preservation for adults and children
Thursday 13 September 2018
Prof Allan Pacey MBE, University of Sheffield & Dr Suzannah Williams, University of Oxford
The Examination School, Oxford

www.srf-reproduction.org
Welcome Letter

Dear Friends and Colleagues,

It is my pleasure to welcome you to the 2nd UK Fertility Preservation Conference at St. Anne’s College at the University of Oxford. This meeting follows on from the 1st highly successful meeting in Edinburgh in 2017.

Oxford is home to The Future Fertility Trust which provides a comprehensive tissue cryopreservation service for girls and boys alongside a dynamic research programme.

This meeting will provide a diverse and rewarding scientific programme with a focus on recent advances in fertility preservation for girls, boys, women and men, as well as including highly topical aspects of fertility preservation for non-malignant conditions. We have national and international speakers who are experts in their fields and will discuss the latest research and key developments.

I are delighted that you are joining us for the 2nd UK Fertility Preservation Conference. We believe that your involvement will make a significant, positive impact on the future of fertility preservation.

I am grateful to our sponsors for their generous support.

Dr Suzannah A Williams
Conference Chairperson

Local Organising Committee
Professor Anne Goriely (University of Oxford)
Dr Sheila Lane (Children’s Hospital, Oxford)
Dr Rod Mitchell (University of Edinburgh)
Dr Suzannah Williams (University of Oxford)
2nd UK Fertility Preservation Conference

Programme

09:00 - 11:00  Symposium 1
Effect of treatment on childhood and adolescent fertility
Chair: Dr Sheila Lane

09:00 - 09:45  Overview of the need for fertility preservation in children with cancer or HSCT: who are the patients at risk?
Prof Kirsi Jahnukainen

09:45 - 10:30  Susceptibility of primordial follicles to chemotherapy
Dr Karla Hutt, Monash University, Australia

10:30 - 11:00  Androgen and the ovary
Dr Stine Gry Kristensen, Laboratory of Reproductive Biology, Copenhagen, Denmark

11:00 - 11:30  Morning Tea & Coffee Break

11:30 - 13:30  Symposium 2
Dilemmas of Fertility Preservation
Chair: Dr Rod Mitchell

11:30 - 12:00  Fertility Preservation Communication - how to get the best deal for the patient
Dr Ephia Yasmin, University College London Hospitals NHS Foundation Trust, UK

12:00 - 12:30  Beyond fertility recovery: how safe is fatherhood following cancer treatment?
Dr Geoffrey Maher, University of Oxford, UK

12:30 - 13:30  Gender Dysphoria - what fertility services might usefully know
Dr James Barrett, Gender Identity Clinic and Imperial College, London, UK

13:30 - 14:30  Lunch with Poster Session
Programme

14:30 - 15:30  Symposium 3  
Developments in fertility preservation  
Chair: Prof Norah Spears

14:30 - 15:00  Growing human eggs in vitro  
Prof Evelyn Telfer, University of Edinburgh, UK

15:00 - 15:30  Uterus transplantation: results of an international program and update of worldwide results  
Prof Cesar Diaz Garcia, IVI UK

15:30 - 16:00  Afternoon Tea & Coffee Break with Poster Viewing

16:00 - 17:00  Symposium 4  
Fertility preservation for non-cancer diseases  
Chair: Prof Anne Goriely

16:00 - 16:30  Fertile offspring from sterile sex chromosome trisomic mice  
Dr James Turner, The Francis Crick Institute, UK

16:30 - 17:00  Fertility challenges in women with Turner Syndrome  
Prof Melanie Davies, University College London Hospitals, UK

17:00 - 17:05  Close of Meeting  
Dr Suzannah Williams, University of Oxford  
Conference Chair
Overview of the need for fertility preservation in children with cancer of HSCT: who are the parents at risk?
09:00 - 09:45

Advances in treatment of childhood, adolescent and young adult cancer have greatly improved the 5-year survival which now exceeds 80%. Unfortunately, nearly all young survivors treated with hematopoietic stem cell transplantation (HSCT) and two thirds of those treated for cancer will experience at least one late effect. The increased risk of gonadotoxicity, which causes profound emotional distress, is a prominent concern among the survivors. It is known to be associated with conditioning therapies for HSCT, very high cumulative doses of alkylating agents and irradiation exposure of the gonads. An impaired spermatogenesis or a decreased oocyte pool results in reduced or lost fertility. Testosterone and estrogen deficiency causes a delayed or arrested puberty in adolescents, and a range of adverse physiological and psychological consequences in adults. The nature of the sexual dysfunction may be physiological, psychosexual, or both. Due to the innate biological differences between ovaries and testes, spermatogenesis in men may recover over time, whereas women are at risk of a premature menopause. This lecture summarizes the present evidence of the treatment associated testicular and ovarian toxicity in cancer survivors and after HSCT.
Dr Karla Hutt
Monash University, Australia

Dr Karla Hutt is head of the Ovarian Biology Laboratory at the Monash University and the Biomedicine Discovery Institute Outstanding Woman in Science Fellow. She obtained her PhD from the Australian National University in 2006, where her studies focussed on the establishment and maintenance of the primordial follicle pool. She then undertook her postdoctoral studies at the University of Kansas Medical Center (USA), where she investigated the impact of environmental toxicants on oocyte and embryo quality. In 2008 she returned to Australia to join the Ovarian Biology Laboratory at Prince Henry’s Institute. She subsequently moved to Monash University and now investigates the role of DNA repair and apoptosis in determining oocyte number and quality, with the aim of i) improving women’s health and fertility during aging and ii) understanding how cancer treatments damage the ovary.

Susceptibility of primordial follicles to chemotherapy
09:45 - 10:30

Standard cytotoxic cancer treatment can damage the oocytes and somatic cells within the ovary, leading to a reduction in the size of the ovarian follicular reserve, which predisposes females to infertility and premature menopause later in life. With improving survival rates for many cancers, there is a growing need to devise new strategies to improve the long-term fertility and health of women post-treatment. With this goal in mind, we are interested in identifying precisely which cells in the ovary are targeted by different chemotherapies and are investigating the cellular mechanisms that regulate follicle loss during cancer treatment. Such studies will facilitate the development of novel and specifically tailored adjuvant therapies to preserve future fertility and prevent premature menopause in girls and women being treated for cancer. Our recent studies have demonstrated that the transcription factor TAp63 and the pro-apoptotic protein PUMA, are essential for follicle loss following exposure to cisplatin and cyclophosphamide. Notably, elimination of TAp63 or PUMA in mice prevents follicle loss after treatment with these agents and fertility is preserved and offspring health is maintained. Furthermore, our data show that cisplatin and cyclophosphamide damage the DNA of primordial follicles oocytes and induce their apoptosis. Thus, effective pharmacologic fertility preservation strategies will likely need to prevent primordial follicle oocyte apoptosis and support the repair of DNA damage.
Androgen and the ovary
10:30 - 11:00

It is well-known that androgens have a physiological role in normal ovarian function. In theca cells, androstenedione and testosterone are produced in response to the LH stimulus and provide the obligatory substrate for estradiol production by maturing antral follicles. However, exposure to excess androgen is associated with ovarian dysfunction which is a major feature of women with polycystic ovary syndrome (PCOS). In polycystic ovaries, the development of antral stage follicles is abnormal, and growth of these follicles is typically arrested at a diameter of 5–8 mm. Abnormalities have also been observed in preantral follicle development, but they are characterized by enhanced rather than impaired activation and growth, and there is evidence that androgens may play a part.

Concerns exist with regard to cryopreservation of ovarian tissue for fertility preservation in transgender people due to the potential effect of a prolonged exposure to supraphysiological doses of testosterone to the ovary. However, it has been shown that primordial follicles are not depleted from the ovarian cortex of trans men receiving gender-affirming hormone treatment, and cortical-residing follicles can resume growth and maturation after xenotransplantation. Moreover, a recent clinical study has shown that the cortical follicle distribution (including primordial and primary follicles) does not shift in ovaries from trans men exposed to supraphysiological doses of testosterone for about a year. Thus, current results are reassuring and might contribute to counselling of trans men, even though the entire effect of testosterone on the ovary remain to be determined.
Ephia Yasmin is clinical lead of the reproductive medicine unit at UCLH. Her sub-specialties are reproductive medicine and surgery and paediatric and adolescent gynaecology. She is chair of policy and practice of the British Fertility Society. She holds an honorary senior clinical lecturer position at UCL. Her current research interest is fertility preservation.

Fertility Preservation Communication - how to get the best deal for the patient
11:30 - 12:00

The offer and uptake of fertility preservation depends on the collaboration amongst the oncology team, the patient and the reproductive medicine team. The patient pathway from diagnosis to decision making for fertility preservation needs to be efficient and at the same time facilitatory. The clinicians work together to offer the best options to the individual and carry out procedures that are safe and beneficial. For the best outcomes there needs to be clear channels of communication between the oncologists and the reproductive medicine team. Evidence suggests that patients appreciate discussions on effect on fertility and options for preservation early in their diagnosis. The information whilst being clear must also be in a manner that manages expectations. Collaboration ensures that the patient pathway is as smooth as possible. Initial investigations can also be carried out by the referring team to facilitate discussions on fertility preservation. The amount of information provided to the reproductive medicine team, the adherence to established channels of communication, the timing of referral and the provision of reliable means to contact all play a role in being able to optimise the patient's experience and outcome of fertility preservation.
Dr Geoffrey Maher
University of Oxford, UK

Geoffrey Maher is a postdoctoral researcher with an interest in the origins of de novo mutations and their links with male germ cell biology. His research focuses on selfish spermatogonial selection, a process whereby ‘selfish’ disease associated mutations confer a selective advantage to the spermatogonial stem cells in which they arise, leading to clonal expansion and an increased risk of transmission to the next generation. To study this process he uses a variety of sensitive genetic approaches to screen human testes and sperm and has developed methods to visualise the mutant clones directly in normal human testes.

Beyond fertility recovery: how safe is fatherhood after cancer treatment?
12:00 - 12:30

Chemotherapy and radiotherapy can have severe gonadotoxic effects, resulting in temporal or long-term infertility. For cancer survivors whose fertility has recovered, the effect of such treatments on the risk of genetic disease to their future children is a common cause of concern. Although epidemiological data suggest no increased risk of disease in the offspring of cancer survivors, experimental studies have demonstrated that treating mice with chemotherapy or radiotherapy increased the risk of genetic disease in their offspring. In humans, increased rates of aneuploidy in sperm are common but the effects are transient; however, the effects at the DNA base resolution have received little attention. To study the effects of chemotherapy and radiotherapy on levels of disease-associated mutations in human sperm, we utilised a sensitive assay to measure spontaneous mutation levels in the FGFR2 gene (at positions associated with Apert and Crouzon syndromes) in semen samples from 18 cancer patients. We demonstrate that cytotoxic therapy does not increase the levels of such mutations in sperm and in the case of highly sterilising treatments may even reduce the mutational burden, which should reassure patients contemplating reproduction several years after treatment.
Dr James Barrett
Gender Identity Clinic and Imperial College, London

Dr Barrett has worked in this field for a little over 30 years and in the course of that time has assessed around 10,000 patients with gender dysphoria. Aside from having 3 children, he has no particular expertise in fertility treatment as such.

Gender Dysphoria - what fertility services might usefully know
12:30 - 13:30

Gender dysphoria isn’t as uncommon as might be supposed and increasingly large numbers of patients with gender dysphoria are now presenting at fertility preservation services in the course of treatment. This lecture aims to give an idea about the medical and social experiences such patients have had before they present for gamete storage, as well as those they might undergo prior to later presenting seeking assisted fertility.
Professor Evelyn Telfer
University of Edinburgh, UK

Professor Evelyn Telfer holds a personal chair in Reproductive Biology at the University of Edinburgh where she heads a research group in Ovarian development. Her group have developed culture systems to support complete development of human and bovine immature primordial ovarian follicles to the stage where mature oocytes can be obtained. Current work is focusing on characterising germ line and somatic stem cells within the adult human ovary and within a range of mammalian species including cow, elephant and the naked mole rat.

Evelyn is a member of the Edinburgh Fertility Preservation group and has had a long standing collaboration with Profs Richard Anderson and Hamish Wallace. She has published widely in the field and is a regular invited speaker at International conferences. Evelyn is also actively involved in Public engagement.

Growing human eggs in vitro
14:30 - 15:00

Removal and storage of ovarian cortical tissue is currently offered to young female cancer patients undergoing potentially sterilizing chemotherapy and/or radiotherapy. For patients at high risk of re-introduction of malignancy through auto-transplantation, the ultimate aim is to achieve complete oocyte development from this tissue in vitro. The ability to develop human oocytes from the earliest follicular stages through to maturation and fertilisation in vitro would revolutionise fertility preservation practice. This has been achieved in mouse where in vitro grown (IVG) oocytes from primordial follicles have resulted in the production of live offspring.

For many years we have been developing systems that support growth and development of oocytes from human ovarian cortex. We have now developed a multi-step culture system that supports the development of some human oocytes from immature follicles through to meiotic maturation demonstrated by the formation of polar bodies and a Metaphase II spindle. This presentation will give an update on the feasibility of recapitulating many of the steps involved in human oogenesis under in vitro conditions using tissue from a range of patient groups and consider the steps that will be required to determine whether IVG could be used in a clinical setting.
Professor Cesar Diaz Garcia
IVI, UK

Cesar Diaz-Garcia, MD, PhD, MPH, is a gynaecologist and associate professor in Obstetrics and Gynecology at the University of Valencia where he coordinated of the Fertility Preservation Unit at La Fe University Hospital. His scientific background is completed with a stay as visiting researcher at the Sahlgrenska Hospital-University of Gothenburg where he was part of the team performing the first successful uterus transplantation.

His scientific career has been devoted to the field of fertility preservation, with special interest on ovarian cortex transplantation, uterus transplantation and poor response in IVF. Currently, he is the medical director at IVIRMA-London. Dr Diaz-Garcia was a former Associate Editor of Human Reproduction.

Uterus transplantation: results of an international program and update of worldwide result
15:00 - 15:30

Allogeneic uterus transplantation to treat absolute uterine factor infertility has become a feasible option. A description of the surgical technique and an overview of the basic science that led to the first uterus transplantation series will be presented. The results of the human trials conducted by the Swedish team will be presented together with an overview of all the cases done so far by different teams around the world.
Dr James Turner  
The Francis Crick Institute, UK

James Turner is a Senior Group Leader at the Francis Crick Institute, and before that was a junior group leader at the MRC National Institute for Medical Research. He studies the epigenetics, evolution and cell biology of the sex chromosomes in order to understand how they influence human disease. His lab discovered meiotic silencing, as well as Rsx, the Xist-like non-coding RNA that mediates X-chromosome inactivation in metatherian mammals. He demonstrated that the X chromosome plays a specialised function in spermatogenesis and that reprogramming corrects trisomy in Klinefelter and Down syndrome patient cells. He is a Wain Medal recipient and ERC Consolidator Awardee.

Fertile offspring from sterile sex chromosome trisomic mice  
16:00 - 16:30

Having the correct number of chromosomes is vital for normal development and health. Sex chromosome trisomy affects 0.1% of the human population and is associated with infertility. I will discuss our finding that during reprogramming to induced pluripotent stem cells (iPSCs), fibroblasts from sterile trisomic XXY and XYY mice lose the extra sex chromosome through a phenomenon we term trisomy-biased chromosome loss (TCL). Resulting euploid XY iPSCs can be differentiated into the male germ cell lineage and functional sperm that can be used in intracytoplasmic sperm injection to produce chromosomally normal, fertile offspring. TCL also applies to other chromosomes, generating euploid iPSCs from cells of a Down syndrome mouse model. It can also create euploid iPSCs from human trisomic patient fibroblasts. I will discuss the implications of our findings to overcoming infertility and other trisomic phenotypes.
Melanie Davies is the Chair and founder of the British Fertility Society special interest group, Fertility Preservation UK. She works as a consultant gynaecologist at University College London Hospitals, currently Person Responsible for licensed fertility services. She has a longstanding interest in oncofertility, supports the largest UK sperm storage facility (>4000 oncology patients referred), and developed specialist services for women, both urgent referrals for egg & embryo freezing and also cancer survivorship, seeing >1500 patients in the 'late effects' service for fertility, POI, or gynaecology. UCLH has the largest dedicated clinic for women with Turner syndrome and Melanie has particular interests in adolescent care and TS pregnancy.

Fertility challenges in women with Turner Syndrome
16:30 - 17:00

Only 1 in 10 girls with Turner syndrome experience spontaneous periods and thus the potential for fertility, and most of those young women develop secondary amenorrhoea before they have the opportunity to have children. However these figures may be an underestimate, as we do not know how many fertile women are living with undiagnosed Turner mosaicism. A small number of young Turner women have undergone fertility preservation by freezing eggs.

As the pathophysiology in Turner syndrome involves loss of oocytes in prenatal or early life, attempts to preserve fertility and endocrine function have been made by storing ovarian tissue. However this raises ethical concerns, as surgery is undertaken before the child or young girl can consent to an invasive procedure which is not directly therapeutic. As yet, there are no reports of regrafting in this patient group.

Women with Turner syndrome have particular risks in pregnancy. The chance of fatal aortic dissection has been estimated at 2%. Hypertension, gestational diabetes, thyroid dysfunction, urinary tract infection, preterm delivery and Caesarean section are all more likely to occur. This has dissuaded some women and their doctors from using assisted reproductive techniques. Spontaneous pregnancies appear less likely to be complicated. The chromosomal quality of oocytes, and the heritability of Turner syndrome, have also been disincentives to egg freezing. However, in recent European series the majority of children conceived naturally have been healthy, and the single report of genetic diagnosis on harvested oocytes was reassuring.
Effects of dietary supplementation of olive oil on fresh and post-thaw semen quality parameters of Teddy male goats

Nazir Ahmad, University of Agriculture, Faisalabad, Pakistan

Does in vitro environment of cultured human cryopreserved ovarian tissue affect follicle development and health?

Briet Bjarkadottir, University of Oxford, UK

Isolation and in vitro development of cells expressing NANOG and/or DDX4 obtained from ovaries of gender reassignment patients

Yvonne Clarkson, University of Edinburgh, UK

Morphological and molecular assessment of cryopreserved bovine ovarian tissue

Paula Cornally, University College Dublin, UK

Dynamic culture of human ovarian tissue greatly enhances follicle progression to the secondary stage

Maddalena Di Nardo, University of Naples, Italy

Pro-invasive effects of 1,25 dihydroxyvitamin D3 on placental trophoblast cells are associated with lack of CYP24a1

Ankana Ganguly, University of Birmingham, UK

Does a Postcode Lottery for IVF funding exist in England?: A Dataset Analysis looking at IVF policy and activity in the years 2012 - 2014

Susan Gorman, St George's, University of London, UK

Ethylene Glycol is a good alternative for the cryopreservation of immature testicular tissue

Patricia Grasa Molina, University of Oxford, UK

Alginate encapsulation of immature testicular cells supports the proliferation of spermatogonial stem cells

Patricia Grasa Molina, University of Oxford, UK
P.10  The use of vascular endothelial growth factor tissue culture to enhance vascularisation of cryopreserved ovarian tissue  
Hayley Jackson, UCL Institute for Women’s Health, London, UK

P.11  Clinical outcome of fertility preservation in breast cancer patients  
Bomee Kim, Imperial College London School of Medicine, UK

P.12  Investigating mechanisms underlying the expression and functional activity of the oocyte activation factor PLCζ  
Alice MacNeill, University of Oxford, UK

P.13  Primordial follicle activation following phosphatase and tensin homologue deleted on chromosome-10 (PTEN) inhibition increased DNA damage of bovine ovarian follicles in vitro  
Mila Maidarti, Centre for Reproductive Health, University of Edinburgh, UK

P.14  IVF for women with medical comorbidities – role of a multidisciplinary team and use of a checklist  
Mariano Mascarenhas, Leeds Fertility, UK

P.15  Effects of Cisplatin and Granulocyte-Colony Stimulating Factor on Immature Human Testis  
Gabriele Matilionyte, Centre for Reproductive Health, University of Edinburgh, UK

P.16  In vitro potential of follicles/oocytes obtained from gender reassignment patients  
Marie McLaughlin, University of Edinburgh, UK

P.17  In vitro generated testis cords: a model for exploration of human testis development  
Mina Mancheva, Centre for Reproductive Medicine and Andrology, University Hospital of Münster, Germany

P.18  Analysis of follicle development in vitro within reaggregated ovaries  
Eleni Papadopoulou, Nuffield Department of Women’s and Reproductive Health, University of Oxford, UK
P.19  Do patients with cancer respond differently to Controlled Ovarian Hyperstimulation (COH) compared with matched healthy controls?
*Benjamin Redshaw, Imperial College London School of Medicine, UK*

P.20  An interpretative phenomenological analysis study into the experience of teenagers and young adults offered ovarian tissue cryopreservation following a cancer diagnosis
*Rebekah Tennyson, Oxford University Hospitals NHS Trust, Oxford, UK*

P.21  The effect of Paclitaxel exposure on the immature human testis.
*Melissa Durgahshree Tharmalingam*

P.22  The effect of freeze-delay on ovarian tissue stored for fertility preservation
*Mila Zemyarska, University of Oxford, UK*

P.23  Prepubertal testicular tissue cryopreservation for fertility preservation – do we procure the intended amount?
*Sheila Lane, Oxford University Hospital*

P.24  Can fertility preservation treatment for children and young adults be delivered safely and effectively via a hub-and-spoke care model in the UK?
*Molly Gilmartin*
2nd UK Fertility Preservation Conference