FINAL PROGRAMME

LET THERE BE LIFE:
An intimate portrait of the birth of IVF in Manchester
Tuesday 24 July 2018
Manchester Royal Infirmary

EDWARDS, STEPTOE... AND DR KERSHAW:
An SRF symposium to mark the 40th anniversary of IVF
Wednesday 25 July 2018
Manchester Conference Centre

www.srf-reproduction.org

Kindly supported by:
We are delighted that you could join us in Manchester to mark the 40th anniversary of IVF. We have planned two special events with stellar speakers, and we hope you will agree, a wide and interesting range of subjects.

On the evening of 24th July, Professor Roger Gosden, one of the pre-eminent scientists in the field takes the stage to deliver an open lecture entitled “LET THERE BE LIFE: An intimate portrait of the birth of IVF in Manchester’. Professor Gosden is known internationally for his scientific contributions, but in this event he plays the role of an exponent of the early history of human IVF, with special reference to the role of the Greater Manchester region and the northwest in its development. As a biographer of Bob Edwards and an acquaintance of many of the pioneers in the field, he brings a unique perspective and knowledge to his subject.

On the 25th July, we are pleased to bring you a scientific symposium entitled ‘Edwards, Steptoe... and Dr Kershaw: an SRF symposium to mark the 40th anniversary of IVF’. We have an array of speakers of international renown for their expertise and enthusiasm for their chosen fields. Topics will range from basic science at the edge of application, through clinical techniques to ethics and future regulation of this complex and exciting field. Reflecting the diverse and complex nature of the programme, this event is brought to you by the Society of Reproduction and Fertility, with the support of the British Fertility Society, Association of Clinical Embryologists, Association of Biomedical Andrologists and the law firm, Hempsons.

The Greater Manchester area has a long tradition in reproductive medicine, stretching back to Walter Heape in the 19th century and Bob Edwards who grew up and went to school in central Manchester. The symposium venue is within sight of Bob Edwards’ old school. Patrick Steptoe famously practiced in Oldham, and the pioneering IVF work leading to Louise Brown was carried out by Edwards, Jean Purdy and Steptoe at Dr Kershaw’s Cottage Hospital in Royton, the world's first successful IVF clinic. We are delighted to welcome you here for these two events to mark this important milestone in scientific and clinical progress.

With best wishes

Professor John Aplin, Professor Daniel Brison and Dr Raj Mathur
Local Organising Committee
PROGRAMME

Tuesday 24 July 2018 - Manchester Royal Infirmary

18.15 - 19.15 Roger Gosden:
LET THERE BE LIFE: An Intimate Portrait of the Birth of IVF in Manchester

Wednesday 25 July 2018 - Manchester Conference Centre

08:30 - 09:00 Registration, coffee & tea

09:00 – 10:30 IVF, the First 40 Years and the Next 40 Years
Session Chair: John Aplin

09:15 Teresa K. Woodruff: Engineering Reproduction: The 3-D Printed Ovary
10:00 Chris Barratt: Male infertility 40 years of progress and 40 years on

REFRESHMENT BREAK

11:00 – 12:30 Understanding the Human Embryo
Session Chair: Daniel Brison

11:00 Kathy Niakan: Mechanism of lineage specification in human embryos
11:30 Dagan Wells: Mitochondria and embryos
12:00 Michael Summers: 40 Years of IVF Culture Media

LUNCH BREAK

13:30 – 15:00 Implantation: bottleneck or final frontier?
Session Chair: Tom Fleming

13:30 Mostafa Metwally: The Endometrial Scratch
14:00 John Aplin: Implantation and beyond
14:30 Andy Vail: The science of evidence-based practice

REFRESHMENT BREAK

15:30 – 17:30 Future Challenges in Ethics, Regulation Medicine and Science
Session Chair: Raj Mathur

15:30 Jonathan Ives: Should the state fund fertility treatment in the future?
16:00 Margaret Gilmore: The HFEA 40 years on
16:30 Tom Fleming: IVF children come of age. Little embryos and big implications

17:00 Oliver Schmidt: Science and fiction: from micromotors to spermbots
LET THERE BE LIFE:
An intimate portrait of the birth of IVF in Manchester
Tuesday 24 July - Manchester Royal Infirmary
18:15 - 19:15

SPEAKER PROFILE

Roger Gosden
Visiting Scholar at the College of William & Mary; Virginia Writer, Publisher & Naturalist

After his PhD and fellowship with Robert Edwards in Cambridge, he joined the physiology faculty at Edinburgh University in 1976. He moved to a chair at Leeds University in 1994 and afterwards to North America, appointed to McGill University, the Howard and Georgeanna Jones Professor of Reproductive Medicine at EVMS, and Weill Cornell Medical College in NYC, where he joined Lucinda Veeck Gosden on the faculty, the embryologist for America’s first IVF baby. His research focused on oocyte development and fertility preservation. He now works fulltime as an author, biographer and publisher, and volunteer in conservation research and education.

LECTURE ABSTRACT

Forty years after the birth of Louise Brown, it is hard to remember the scandalous origins of IVF technology. Controversy raged from the authenticity of claims to the reproductive safety and ethics of conceiving babies in vitro. The Manchester gentleman-scientist Walter Heape demonstrated embryo transfer in 1890, but seventy years passed until MC Chang, a Cambridge-trained biologist in Massachusetts, presented proof that animal eggs fertilized in vitro are healthy. Robert Edwards dreamed of adapting this technology for treating infertility. A Mancunian born in Yorkshire, his efforts in London and Cambridge were frustrated until he met the Oldham gynaecologist Patrick Steptoe. Steptoe was ridiculed for developing laparoscopy and Edwards derided for research on human embryos; they were matched as mavericks and both were determined to succeed. Their experimental IVF programme was based on a shoestring budget in the Oldham & District General Hospital and then at Dr. Kershaw’s cottage hospital. It was valiantly supported by nurse volunteers, junior doctors, Edwards’ assistant Jean Purdy, and the health authority, but least known are the patient volunteers who could only have timid hopes that IVF could help them. When the final breakthrough came in 1978 after a decade of struggle and controversy, the NHS turned down a request for a nationwide service and Edwards and Steptoe had to open a private clinic. A few years later IVF was standard practice, and well over six million babies worldwide vindicate the pioneers’ endeavour.
EDWARDS, STEPTOE... AND DR KERSHAW:
An SRF symposium to mark the 40th anniversary of IVF

SPEAKER PROFILE

Professor Teresa K. Woodruff
Thomas J. Watkins Professor of Obstetrics and Gynecology
Dean of The Graduate School
Northwestern University, USA

Teresa K. Woodruff Ph.D. is the Dean and Associate Provost for Graduate Education in The Graduate School at Northwestern University. She is also the Thomas J. Watkins Professor of Obstetrics & Gynecology, the Vice Chair for Research and the Chief of the Division of Reproductive Science in Medicine in the Department of Obstetrics and Gynecology, Feinberg School of Medicine. She is Professor of Molecular Biosciences in the Weinberg College of Arts and Sciences, and Professor of Biomedical Engineering in the McCormick School of Engineering. She is the Director of the Center for Reproductive Science (CRS), Founder and Director of the Women’s Health Research Institute (WHRI), and Director of the Oncofertility Consortium. She is an internationally recognized expert in ovarian biology and, in 2006, coined the term “oncofertility” to describe the merging of two fields: oncology and fertility. In 2018, she was inducted into the National Academy of Inventors for the creation of this field along with her other patents in the fields of reproductive biology and bioengineering.

LECTURE ABSTRACT:
Engineering Reproduction: The 3-D Printed Ovary
09:15 - 10:00

In 2017, teams in the Woodruff, Laronda, and Shah Labs at Feinberg School of Medicine, Northwestern University, developed an ovarian bioprosthesis using 3-D printed scaffolds made of gelatin, a biological hydrogel made from broken-down collagen. In pre-clinical trials using mice, these prosthetic ovaries are able to house immature eggs, ovulate, and birth healthy pups. Ultimately, the objective for these prosthetics is to restore fertility and hormone production in women and children who have undergone cancer treatment or otherwise lost ovarian function to disease. This technique may also inform other soft tissue engineering in regenerative medicine.
Professor Chris Barratt  
Professor Head of Systems Medicine, University of Dundee, UK

Professor Barratt is Head of the Reproductive Medicine Group at the University of Dundee as well as a clinical scientist (Hon) with NHS Tayside. He graduated with an Honours degree in Zoology and then completed a Post Graduate Certificate in Education (University of Wales, Swansea). His PhD, also in Zoology, was under the supervision of Jack Cohen (sperm selection fame) at the University of Birmingham. His formative post-doctoral studies and IVF experience was gained at the University of Sheffield [with Ian Cooke] where they specialized in natural cycle IVF.

From 1997-2005 he was the Scientific Director of the ART Centre at the Birmingham Women’s Hospital.

In 2002 he was awarded Young Andrologist of the Year (American Andrology Society) for outstanding contributions to the discipline.

He is a regularly invited speaker at national and international scientific conferences/workshops. He was a member of the WHO Male Fertility Semen Analysis Taskforce (for both the 4th and 5th editions) and is now director of the new WHO (2012-2016) Male Fertility Expert Working Group which is devising a new system for the diagnosis and treatment of the infertile male. He was a member of the Human Fertilisation and Embryology Authority for 6 years.

Professor Barratt has very recently appointed to editorial board of WHO for development of new Semen Analysis manual (6th edition).

He has been on the Editorial Board of Human Reproduction, Human Fertility, Biology of Reproduction, Human Reproduction Update and Journal of Andrology.

In 2014 Professor Barratt presented the Professor Sir Robert Edwards keynote lecture at ESHRE. This presentation was based on the highest downloaded paper in Human Reproduction for 2013. Currently, he is Editor-in-Chief of Molecular Human Reproduction (Impact factor 5 year 3.9).

His life’s ambition is to see - live - Wales comprehensively beat the All Blacks.

LECTURE ABSTRACT:
Male infertility 40 years of progress and 40 years on
10:00 - 10:30

ICSI aside, there has been very little progress in the diagnosis or treatment of male infertility since 1980. However, very recent advances in our knowledge base using techniques such as proteomics, electrophysiology are likely to change the landscape dramatically. Whist in vitro generation and manipulation of germ cells will be very important in the near future the real game changers will be at home diagnosis and treatment of the male so that in vivo conception is the norm again. This complemented with an array of new male contraceptives will mark the future.
Kathy Niakan obtained a B.Sc. in Cell and Molecular Biology and from University of Washington, a PhD at University of California, Los Angeles and undertook postdoctoral training with Kevin Eggan at Harvard University. She was a Centre for Trophoblast Research Next Generation Research Fellow at University of Cambridge. She started her lab at the Francis Crick Institute in May 2013 to understand the mechanisms of lineage specification in human embryos.

LECTURE ABSTRACT:
Mechanism of lineage specification in human embryos
11:00 - 11:30

The central question we are addressing is what are the molecular mechanisms that regulate early cell fate choices and how do pluripotent cells become distinct in their fate and function from extra-embryonic cells during human development? We are defining the genetic hierarchy and the influence of extracellular signalling acting during early human development, and the extent to which these mechanisms are conserved between humans and mice. The molecular basis of these early cell lineage decisions is of fundamental biological importance and has significant clinical implications for infertility, miscarriage, developmental disorders and therapeutic stem cell applications.
Mitochondria are small structures found inside virtually all the cells of the body. They have a variety of functions essential for cellular life, but their best known, and perhaps most important, role is in the generation of energy. For this reason mitochondria are considered as the powerhouses of cells. Unlike other organelles within animal cells, mitochondria contain their own DNA (mtDNA). The mtDNA carries important genetic information for the maintenance of correct cellular function, especially energy production. Not surprisingly, mitochondria and mtDNA are vital for the proper functioning of gametes and for successful embryo development. Recent findings suggest an association between alterations in mitochondria and their genome, female reproductive ageing and the generation of chromosome abnormalities detected in embryos. Chromosome abnormalities are extremely common in human preimplantation embryos and are the principal cause of embryo implantation failure and miscarriage. Importantly, a direct relationship has been described between mtDNA quantity in embryo cells and the potential to form a viable pregnancy. It is therefore possible that the assessment of mtDNA quantity could represent a novel way of identifying the embryos produced during IVF treatments that have greatest likelihood of producing healthy pregnancies. Methods that reveal the embryos with the greatest potential to produce a child may help to improve the efficiency of IVF treatments, meaning fewer embryo transfers are necessary to achieve a live birth. It is also important to note that mutations in the mitochondrial DNA can lead to serious conditions in children and adults, which are untreatable and frequently fatal. The use of assisted reproductive technologies has provided a unique opportunity to access human eggs and embryos and potentially to intervene to ‘cure’ mitochondrial disease by replacing defective organelles.
Lecture Abstract: 40 Years of IVF Culture Media

12:00 - 12:30

Whitten (1956) using modified Krebs-Ringer bicarbonate as the physiologic saline added glucose, penicillin, streptomycin and egg white confirmed good development of eight-cell mouse embryos into blastocysts. Later, he replaced egg with bovine serum albumin. McLaren and Biggers (1958) showed that mouse blastocysts produced by Whitten's technique developed into normal adults following transfer to surrogate females. These studies paved the way for the experimental manipulation of the mammalian preimplantation embryo in vitro. On July 25th, 1978 at 11:47 pm a baby girl, Louise Brown, was delivered by primary Caesarean section at Oldham General Hospital to a woman without functional fallopian tubes following the fertilisation in vitro of an ovum from the patient by her husband's sperm and replacement of the resultant embryo into her uterus. Thus, a new treatment was introduced for an intractable cause of infertility first described by Burns (1809) nearly two centuries earlier. Edwards and co-workers (1981) summarized the media used for culture of early human embryos including use of heat-inactivated human serum. Since then several strategies have been introduced for the culture of human preimplantation embryos: firstly, use of chemically-defined media; and secondly, methods to increase the yield of blastocysts. Preimplantation embryos placed in a chemically-defined medium are exposed to stress since inevitably any medium provides only a partial representation of the natural environment. To survive an embryo must adapt using innate physiological mechanisms the long term consequences of which are not known at this time. The commercialisation of media and secrecy surrounding the composition of media used for the manipulation of human gametes and embryos are issues that are not yet resolved.
Despite the great advances in the field of IVF, success rates over the years have only modestly increased. This has led to many attempts over the decades to explore innovative approaches to improve the chance of a pregnancy. Many such approaches have been dismissed due to lack of evidence and only a few have shown promise. Controlled endometrial trauma is one such technique that is currently under investigation. The potential benefits of endometrial trauma to improve the receptivity of the endometrium, has long been recognised from animal studies, and recently this technique has been suggested to be beneficial in women undergoing IVF treatment and having had several unsuccessful attempts. The use of controlled endometrial trauma (the endometrial scratch) was consequently rapidly adopted into clinical practice, and in many cases in groups of women where the evidence simply did not exist or was very poor. In this presentation, we will review the historical background to the use of endometrial scratch to improve pregnancy rates, the currently available evidence, clinical uses as well as current and future research.
I started as a chemistry undergraduate, became interested in cell adhesion as a postdoc and have been for some years researching implantation and placental development.

The lab’s focus is mainly on human, though we keep an eye on comparative aspects of implantation biology. We have developed in vitro and ex vivo methods for the study of embryo-epithelial interactions, the trophectoderm-trophoblast transition and trophoblast invasion. We’ve become interested in the cascade of challenges presented to the embryo as successive waves of trophoblast attach to and locally displace the epithelium, invade the decidualising stroma and access maternal blood vessels. We hypothesise that there are selection pressures at all three of these distinct stages of early pregnancy – the enterprise may falter at any one of them.

LECTURE ABSTRACT: Implantation and beyond

From the first contact with the endometrial surface, concurrent programmes are initiated for embryonic morphogenesis and placental development. The inner cell mass self-organises to generate spatially discrete epiblast and primitive endoderm compartments, and an amniotic cavity. Meanwhile, maternal cells trigger differentiation in trophoblast, beneath which there develops a supporting layer of extraembryonic mesoderm, leading to yolk sac and placental development and establishment of the crucial vascular link to the embryonic heart. Successive interactions with endometrial tissue layers - epithelium, decidualising stroma and vasculature – impose progressive hurdles for the embryo to surmount. Stepped programmes of gene expression in trophoblast invoke biological responses underlying a highly sensitive negotiation that can either progress or fail at a multiplicity of early time points. Trophoblast lineage allocation is sensitive to environmental factors including osmotic stress and carbon supply, and a poorly supportive uterine cavity may advance the differentiation of invasive (hCG+) lineages; aneuploid mosaic embryos may thus sustain the corpus luteum long enough to allow time for recovery by selective expansion of euploid cells. In this light we face new challenges in selecting embryos for replacement.

Calls for permission to be extended to maintain embryos in vitro beyond the 14 day limit should be considered in the context of what might be achieved: is better basic understanding an acceptable goal in its own right? Is there an expectation that treatments will improve, or a need to reconsider how implantation should be defined in the context of ART and explained to patients?
SPEAKER PROFILE

Professor Andy Vail
Professor of Clinical Biostatistics, University of Manchester, UK

Andy leads the Centre for Biostatistics at the University of Manchester and directs the Greater Manchester office of the NIHR Research Design Service.

He has been producing and editing systematic reviews of ART interventions since the early 1990’s, when he worked closely with gynaecologists in Leeds. He is a founding member of Cochrane’s statistical methods working group and a long-standing Editor of the Cochrane Gynaecology and Fertility Group.

Andy has published numerous papers encouraging critical consideration of design and reporting of randomised trials. Recent work includes reviews undertaken for the HFEA to inform their patient information materials.

LECTURE ABSTRACT: The Science of evidence-based practice
14:30 - 15:00

Gynaecology has come a long way since Archie Cochrane famously awarded his own discipline the wooden spoon for being the least evidence-based of all medical specialties. Decision-makers need high quality evidence. This presentation will describe and explain the criteria for individual studies of any intervention strategy, laboratory or clinical, to be considered ‘high quality’. It will similarly describe criteria for assessment of the totality of evidence concerning that strategy. Examples will be drawn from work for the Cochrane Gynaecology and Fertility Group and from reviews undertaken to inform the HFEA traffic light system for ‘treatment add ons’.

The complex stages of assisted reproduction cycles lead to complex data. There are several potential pitfalls in trial design that have complicated and even precluded interpretation of published results over the last 40 years. This presentation will describe some of the better-recognised issues such as misuse of cross-over designs. It will also highlight some issues that persist in the published research literature. These include unit of analysis errors, improper subgroups and reporting bias. Efforts are ongoing to circumvent historical poor practice and facilitate better practice moving forwards.
LECTURE ABSTRACT:

Should the state fund fertility treatment in the future?

15:00 - 15:30

In recent years, Clinical Commissioning Groups across the UK have begun to decommission fertility services provided on the NHS in an attempt to cut costs. This has been widely reported in the UK media, and has been met with strong resistance. Cutting fertility services has also been criticised by ‘NICE’, the UK’s National Institute for Health Care Excellence, with Gillian Leng, Director of Health and Social Care at NICE, being quoted in The Guardian as saying that infertility can have a “devastating effect on people’s lives, causing depression, severe distress and the break-up of relationships”, and that it was “unacceptable that parts of England are choosing to ignore Nice guidelines”. The case against cuts is summarised well by one service user who, speaking to Fertility Fairness, said “Infertility is not a choice, treatment is not a luxury, and allocating treatment based on postcode is discriminatory. It astonishes me that following the NICE guideline is not compulsory”.

In this paper I explore arguments for and against the de-prioritisation of IVF. I argue that IVF is good and permissible in its own right, and push the argument that the best reason to fund it is provided by the ‘argument from suffering’. I then explore a significant problem with the implications of this argument, and argue that it follows that both funding and deprioritising ART is justified. I conclude by attempting to show that, given this, the question ceases to be a prime facie moral one, and becomes a question of preference.
LECTURE ABSTRACT: The HFEA 40 Years On
16:00 - 16:30

Margaret Gilmore recalls how as a young journalist she covered the birth of Louise Brown, finally catching up with her in person this year, 40 years and 6 million babies later. Now the Deputy Chair of the HFEA she reflects on how far the sector has progressed, and on the challenges and barriers which had to be crossed before the birth of the HFEA - and its growth into a world class regulator. She discusses the huge advances in scientific research and medicine, and the challenges that come with new technologies such as the developments in embryo testing and egg freezing. The UK fertility sector remains at the forefront of scientific and clinical progress in the field - the UK was the first country in the world to licence groundbreaking mitochondrial donation techniques and this year the HFEA licenced the first Mitochondrial Transfer applications. Mrs Gilmore looks at the HFEA’s vision for the future and talks of the continued need for regulation to ensure patients get the best, safe and ethical treatments, so that patients have access to honest information which will allow them to make the choices that are right for them. She examines the challenges of managing both success rates and the expectations of patients, and the importance of working in partnership so a wider range of people get access to a broader range of treatments.
LECTURE ABSTRACT:
IVF children come of age. Little embryos and big implications
16:30 - 17:00

The success of IVF is recognised worldwide with several millions of children born over the last 40 years. One important aspect of early embryo development of current interest both in the field of ART as well as naturally conceived children is the concept of ‘developmental programming’, also known as DOHaD (Developmental Origins of Health and Disease). The pioneering epidemiological studies of Professor David Barker demonstrated cardiometabolic disease risk in adulthood may derive from adverse growth and development in utero, mediated mainly through poor maternal nutrition. More recently, the peri-conceptional period broadly covering gamete maturation and early embryo development, has been shown to be a sensitive window when adverse programming may occur in response to environmental conditions. These conditions include mainly nutritional quality in vivo but also ART-related treatments in vitro, exemplified in human and animal datasets. Our own work in mouse models show transient embryo culture conditions can modulate the developmental programme and associate with increased cardiometabolic disease risk in adults. One future direction for ART is the recognition and understanding of mechanisms contributing to developmental programming and from this to enhance the safety of assisted conception practice. Funding: BBSRC, MRC, NICHD, EU (especially EpiHealth network).
SPEAKER PROFILE

Professor Dr Oliver G. Schmidt  
Institute Director and University Professor, Leibniz IFW Dresden, Germany

Prof. Dr. Oliver G. Schmidt is the Director of the Institute for Integrative Nanosciences at the Leibniz IFW Dresden, Germany. His interests bridge across several disciplines, ranging from nanomaterials and nanoelectronics to microfluidics, microrobotics and biomedical applications. He has received several awards: the Otto-Hahn Medal from the Max-Planck-Society in 2000, the Philip-Morris Research Award in 2002, the Carus-Medal from the German Academy of Natural Scientists Leopoldina in 2005, and the International Dresden Barkhausen Award in 2013. Most recently, he was awarded the Gottfried Wilhelm Leibniz-Prize 2018 of the German Research Foundation. The Leibniz-Prize is Germany’s most important research award and recognizes his outstanding work in the investigation, manufacturing and innovative application of functional nanostructures.

LECTURE ABSTRACT:
Science and fiction: from micromotors to spermbots  
17:00 - 17:30

What used to be science fiction has now turned into a well-founded scientific treat. Micromotors have recently made major leaps forward in treating medical diseases both in-vivo and in-vitro. And this applies to all known categories of micromotors, which are either propelled by chemical fuels, physical actuation or biological cells/organisms. Naturally, they are explored by different communities bridging from physics, chemistry and materials science to microsystem engineering, biology and medicine. Until recently, the field of micromotors was predominantly concerned with understanding basic operation principles and rudimentary response to environmental cues. However, the Holy Grail has always been to find unique medical applications as this would translate our basic understanding of micromotors into application driven research and development. So the time is right to have a closer look on what the current opportunities and challenges in this emergent field of research and development could be – with a particular focus on sperm driven micromotors for reproductive technologies and gynecological therapies.

This talk will cover a wide spectrum of activities from many groups. However, the focus will still lie on work carried out in our group over the last years.
FUTURE SRF EVENTS

2nd UK Fertility Preservation Conference
14 September 2018
St Anne's College,
Oxford

Preceded by
PUBLIC LECTURE on Thursday,
13 September 2018

Fertility Conference 2019
3-5 January 2019
ICC Birmingham

For more information on future SRF events, visit
www.srf-reproduction.org