British Fertility Society

BFS STUDY WEEK

19-22 June 2017

PGD/PGS e-PROGRAMME

In Association with

ACE
The Association of Clinical Embryologists

This event is paperless
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Millennium Gloucester Hotel, Kensington, London

www.bfsstudyweek.org.uk
@BritFertSoc @UKEmbryologists

FOREWORD

On behalf of the BFS I would like to welcome you all to *Study Week 2017*, which will be the largest one yet. Those of you who have been before will notice many changes. To accommodate our rapid growth, we have moved venue to the very pleasant Millennium Gloucester Hotel. To ensure that you have the latest up to date information and to make the event more 'green' and efficient we have gone 'paperless'.

We are delighted to have two new additional *Study Days* this year (*Fertility Nursing* and *PGD/PGS*) and there have been changes to some of the existing Study Days too, to ensure that you are getting the very best experience. I would like to thank the Speakers for taking time out of their busy schedules to come and teach at the event; as well as the sponsors who generously support our educational program.

I would particularly like to thank the delegates for coming, because you really make the event the success that it is. We hope that you all enjoy it and leave London with knowledge that will aid your personal development and the care of your patients. Please ask the speakers questions, we are here for you.

If you aren't already a BFS member, please consider joining and also, consider enrolling for the highly regarded *BFS Training Modules* that are linked to many of the Study Days. All the relevant details are on our website www.fertility.org.uk.
Feel free to share your opinions on social media @BritFertSoc and @UKEmbryologists and do please complete the feedback form which will be sent to you after the event online, we want to know what you think.

Now, get ready, it's time to be educated!

All the very best wishes,

Kevin McEleny
Chair of Education and Training
British Fertility Society

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PGD/PGS PROGRAMME

CROMWELL ROOM 1

07.45	Registration, welcome refreshments, exhibition
08.50	**Chair's opening welcome** *Yacoub Khalaf*
08.55	**Introduction to genetic diseases, their mode of inheritance and their burden on health and reproduction** *Anne Lampe*
09.15	**Reproductive options available to couples at risk** *Janine Elson*
09.35	**The current status of NIPT and prenatal diagnosis** *Kathy Mann*
09.55	**An introduction to PGD and PGS and expanded carrier screening** *Joyce Harper*
10.15	**PGD counselling and clinical pathway** *Alison Lashwood*
10.35	Refreshments, exhibition and networking *(25 minutes break)*
11.00	**How does the HFEA regulate PGD and PGS?** *Hannah Verdin*
11.30	**Embryology of PGD and PGS** *Alpesh Doshi*
12.00	**PGD and PGS diagnostic technologies** *Dagan Wells*
12.30	Lunch, exhibition and networking
13.30	**Clinical assessment/ preparation of PGD and PGS couples and factors that affect success and clinical results** *Tarek El-Toukhy*
14.00	**MDT interactive session service delivery models** *Jonathan Skull*
14.20	**Case Discussions**
15.00	Refreshments, exhibition and networking
15.30	**DEBATE: This house believes that clinical evidence supports routine use of PGS.** *(Please vote online using Kahoot)* *Chair: Joyce Harper, For - Dagan Wells, Against -Yacoub Khalaf*
16.10	**Open discussion** *Yacoub Khalaf*
16.30	**Overall discussion of the day** *Joyce Harper and Yacoub Khalaf*
17.00	**Close of day and Networking**

PGD/PGS ABSTRACTS AND BIOGRAPHIES

Introduction to genetic diseases, their mode of inheritance and their burden on health and reproduction

Anne Lampe

Key Learning Points:
1. Mode of inheritance affects genetic risk
2. A genetic diagnosis may affect different members of a family unit in different ways

Apart from affecting physical health, genetic disorders can also have a major impact on psychological and social well being of both patients and their families. Using examples from the "Telling Stories Understanding Real Life Genetics" project (http://www.tellingstories.nhs.uk) I will explore how genetic disorders and genetic testing results may affect inter-generational relationships, pose emotional challenges and ethical dilemmas.

Dr Anne Lampe is a consultant in Clinical Genetics at the South East of Scotland Clinical Genetic Service in Edinburgh has a special interest in rare syndrome diagnosis and eye genetics. She provides adult and paediatric services for Fife, inclusing prenatal and predictive testing. Anne graduated from medical school at the Albert-Ludwigs-University in Freiburg, Germany and completed a PhD researching the role of collagen V1 in muscular dystrophy at Newcastle University. Anne is a Fellow of the Royal College of Physicians (Edinburgh) and is a member of the British Society for Genetic Medicine, the European Society of Human Genetics, the Clinical Genetics Society and the UK Eye Genetics Group. She is also an authority member of the HFEA.

Reproductive options available to couples at risk

Janine Elson

Key Learning Points:
1. Importance of individualised patient care
2. Genetic and reproductive counselling is key
3. Information giving is key

Those at risk of a genetic condition may be aware of this because of screening tests carried out preconception, following pregnancy loss, after the birth of an affected child or because of their individual or family history. The key to managing such patients is counselling regarding the condition at which they are at risk, and a detailed discussion of the options available to them. This presentation will look at who is at risk, and the reproductive options that should be considered in each scenario.

Janine Elson is currently the Associate Medical Director for the CARE Fertility Group and has been an RCOG accredited subspecialist in Reproductive Medicine, Obstetrics and Gynaecology since 2004, and for the last 12 years has worked as a Consultant in the UK with a particular interest in recurrent implantation failure and miscarriage, all aspects of donation and genetics. She currently leads the Genetics Programmes for the CARE Fertility Group, encompassing Carrier screening, PGD and PGS and NIPT. With a research background in early pregnancy loss, she was responsible for the Genetics chapters of the soon to be released ESHRE Recurrent Pregnancy Guideline.

The current status of NIPT and prenatal diagnosis

Kathy Mann

Key Learning Points:
1. NIPT for trisomies is a screening test; confirmation of high risk results by invasive testing is recommended.
2. Evidence supports the use of NIPT for trisomies 13, 18 and 21; the use of NIPT for sex chromosome aneuploidy and microdeletions is not currently recommended and will result in additional unnecessary non-invasive tests.
3. NIPD results for single gene disorders and fetal sexing are diagnostic and do not require confirmation. NIPD for a growing number of disorders is available from 10 weeks gestation.

Prenatal testing for genetic conditions has undergone a transformation in the UK in recent years; QF-PCR and array CGH technologies have largely replaced FISH and karyotype analysis for the detection of chromosome abnormalities and the long awaited goals of non-invasive prenatal testing and diagnosis (NIPT and NIPD) are finally being realised with an immediate impact on prenatal testing strategies. Whilst there is no doubt that these exciting developments have the potential to improve prenatal testing, understanding of the limitations of these tests is necessary to minimise unhelpful and unexpected results. These technologies and their prenatal application will be reviewed with particular focus on current recommended practice.

Kathy Mann PhD FRCPath, is lead Clinical Scientist for Prenatal & Reproductive Genetics within the Regional Genetics Laboratory, Guy's Hospital, London. With colleagues she developed the first QF-PCR service in the NHS for the rapid detection of prenatal aneuploidy and is widely published in the field of prenatal QF-PCR analysis including co-authorship of the UK QF-PCR Best Practice Guidelines. She sits on the UK NEQAS Specialist Advisory Group for Molecular Rapid Aneuploidy testing which has recently published guidelines for the reporting of NIPT results.

An introduction to PGD and PGS and expanded carrier screening

Joyce Harper

Key Learning Points:
1. The methods used in PGD and PGS
2. The need for evidence based medicine
3. How expanded carrier screening may be brought into the ART arena

For almost 30 years we have been able to perform genetic tests on preimplantation embryos. This has taken two forms: preimplantation genetic diagnosis (PGD) for couples at risk of transmitting specific genetic or chromosomal abnormalities and preimplantation genetic screening (PGS) as an adjunct to IVF treatment to try and improve IVF outcome. The biopsy can be performed on polar bodies, blastomeres or trophectoderm cells. Various techniques are used to analyse the cells including arrays and sequencing.

For decades specific preconception carrier tests have been applied to certain populations at risk of a particular genetic disease, so that couples can make informed decisions about their reproductive options. With advances in genetic testing it is possible to offer expanded preconception carrier screening to any couple before they start their family. A number of companies offer these tests, analyzing hundreds of recessive conditions.

Joyce Harper is Professor of Human Genetics and Embryology at University College London in the Institute for Women's Health where she is head of the Reproductive Health Department, Principal Investigator of the Embryology, IVF and Reproductive Genetics Group, Director of Education and Director of two MSc programmes - Prenatal Genetics and Fetal Medicine and Reproductive Science and Women's Health. She has been working in the fields of IVF and reproductive genetics since 1987 and written over 170 scientific papers and published two textbooks. Her research includes preimplantation genetic diagnosis, factors affecting preimplantation development, comparison of in vivo and in vitro development, differences in culture media, embryo selection methods, sperm DNA damage and social and ethical issues surrounding IVF and reproductive genetics including gamete donation and surrogacy.

PGD counselling and clinical pathway

Alison Lashwood

Key Learning points:
1.Understanding of what clinical and molecular requirements are required to enable couples to access a reliable and clinically appropriate PGD service.
2.Understanding of the complexities of PGD and how the. patient pathway is managed to accommodate the diversity of referrals which includes PGD with HLA or fertility preservation.
3.Appreciation of the ethical, practical and psychosocial aspects involved in delivering a PGD service which supports patients, staff and meets requirements of HFEA

The Centre for PGD at Guys Hospital has 20 years experience of delivering a service. We hf;1ve completed over 2500 cycles and delivered over 800 babies. The dynamism of Genetics & Reproductive Medicine technology demands constant re-evaluation of the service and what can be delivered to patients to meet changing needs and expansion of what can be offered. This requires a flexible approach to management of patient expectations whilst balancing HFEA requirements with increasing diversity and clinical demand. We have developed a pathway to PGD treatment which involves a genetics and reproductive medicine multidisciplinary team approach. This includes a robust referrals triage system, weekly joint clinical meeting and shared care of the patient pathway from referral to post embryo transfer.

Alison Lashwood is Consultant Genetic Counsellor and Clinical Lead (Genetics) for the PGD service at Guy's Hospital. She set up the PGD service with Professor Peter Braude which started in 1997 and helped develop the unique Genetics and Assisted Reproduction integrated team that represents .the PGD service at Guy's today. She has worked in a strategic and clinical role since and has helped build the PGD service into one of the leading PGD units in Europe. She has contributed to ESH RE PGD guidelines and contributed to a number of chapters in PGD book publications.

How does the HFEA regulate PGD and PGS?

Hannah Verdin

Key Learning Points:
1. What the law says about PGD and PGS
2. The regulatory pathway for PGD from patient consultation to embryo transfer
3. The HFEA's position on PGS

The Human Fertilisation and Embryology Authority (HFEA) is responsible for regulating embryo testing in the UK. The HFEA needs to approve any new genetic conditions to be tested using PGD; at the moment nearly 400 conditions have been approved.

This presentation will outline the legislation underpinning this regulation, the licensing and approval pathways and guidelines relating to the use of PGD and PGS. It will also explore the HFEA's policy position and patient information on PGS.

Hannah Verdin is the Head of Regulatory Policy at the Human Fertilisation and Embryology Authority, leading on policy development, scientific reviews and public consultations relating to topics such as sperm, egg and embryo donation, embryo testing, multiple births, mitochondrial donation and consent. Her work focuses on ensuring that the HFEA's policy framework is effective in delivering high quality care for patients and engenders high quality research and responsible innovation in clinics.

Embryology of PGD and PGS

Alpesh Doshi

Key Learning Points:

1. Embryo biopsy
2. Embryology of pgd and pgs
3. Blastocyst biopsy

The presentation will focus on all aspects of embryo biopsy and will discuss the advantages and disadvantages of performing biopsy at polar body, cleavage stage and blastocyst stage. Details on how to optimise the laboratory to obtain good development of embryos will also be discussed. The future of cell sampling and a focus on non invasive methodologies of obtaining embryonic DNA will also be discussed. The candidates will be able to see many videos on how the biopsy procedure is carried out at all the stages of preimplantation embryonic development.

Alpesh Doshi completed his postgraduate studies in Human Reproductive Biology at Imperial College in 1997, then obtained his training in clinical embryology at the Churchill Clinic in London. Alpesh Joined The Centre of Reproductive and Genetic Health (formerly the Assisted Conception Unit at UCLH) in 1999, a clinic that has consistently achieved one of the highest live birth rates in the UK. He is currently the Head of Embryology and also an honorary consultant at the UCLH NHS trust. Alpesh is an HFEA licenced ICSI and Embryo Biopsy practitioner. In 2004 he became recognised by the Health professions Council as a state registered clinical embryologist and in 2008 he was in the first group of to qualify with ESHRE as a European Senior Clinical Embryologist. In 2009 Alpesh was accepted for Diplomate Membership of the Royal College of Pathologists. In addition he is an executive committee member of Alpha – Scientists in Reproductive Medicine and the Association of Clinical Embryologists (UK). He has authored several papers in peer review journals and has contributed book chapters in 5 International Embryology publications edited by renowned scientists in the field. He has been an invited speaker in several International and National workshops and Conferences and has organised embryo biopsy hands on workshops in India, Turkey and Africa.

PGD and PGS diagnostic technologies

Dagan Wells

Key Learning Points:

1) At the end of this lecture attendees will be able to describe the karyomapping method used for PGD of single gene disorders
2) Attendees will learn the technical basis of current PGS methods such as array-CGH, quantitative PCR and next generation sequencing
3) After the lecture participants will be able to describe the benefits and drawbacks of the different PGS methods

The technologies used for the genetic analysis of the human preimplantation embryo have shown remarkable evolution over the last two decades. Methods for obtaining genetic material for testing have undergone a pronounced shift, away from removal of a single blastomere at the cleavage stage to a near total dominance of trophectoderm biopsy. The diagnosis and transfer of embryos within the same cycle, always a logistical as well as a technical challenge, has largely been replaced by strategies involving the cryopreservation of embryos post-biopsy and transfer in a subsequent cycle. While embryological advances have been significant, the changes in molecular genetic approaches to PGD and PGS have been even more dramatic. The diagnosis of inherited single gene disorders has moved from highly customised and time consuming methods (e.g. multiplex PCR) to more generic approaches such as karyomapping. Not only has this dramatically shortened the amount of work-up and patient waiting time required prior to initiating a PGD treatment cycle, but the method has conveyed a range of additional benefits, including the detection of some forms of chromosome abnormality common in human embryos. The use of preimplantation genetic screening in an effort to improve IVF outcomes by avoiding the transfer of aneuploid embryos has also experienced huge changes. Indeed, in the space of just seven years four different methodologies have been introduced only to be rapidly overtaken by the next wave of technology. Most recently, next generation sequencing techniques have supplanted microarray-based strategies as the methods of choice for aneuploidy detection, providing significant lower costs and enhanced detection of challenging diagnostic issues such as chromosomal mosaicism. The rapid period of change that PGD and PGS methods have been through does not yet appear to be at an end and it is highly likely that the coming years will continue to witness radical technological advances applied in this field.

Dagan Wells has been actively involved in preimplantation genetic diagnosis (PGD) and the study of human gametes and embryos for 25 years. He spent several years at University College London, where he accomplished the first comprehensive chromosome analysis of cells from human embryos. He spent several years in the USA, joining the faculty of Yale University and working with Reprogenetics, one of the world's largest providers of PGD services. He is now an Associate Professor at the University of Oxford, based at the Nuffield Department of Obstetrics and Gynaecology and until recently was Director of Reprogenetics-UK, a laboratory offering state-of-the-art diagnostic services to IVF clinics. Dagan's work has led to the publication of over 150 peer-review publications and in the last decade has been shortlisted for eighteen major conference prizes (ASRM and ESHRE).

Clinical assessment/ preparation of PGD and PGS couples and factors that affect success and clinical results

Tarek El-Toukhy

Key Learning Points:

1. Understand the clinical assessment needed for PGD couples
2. Review the preparatory steps required before starting a PGD cycle
3. Explore the factors influencing the outcome of PGD cycle

Pre-implantation Genetic Diagnosis (PGD) was developed in the late 1980s as an alternative to prenatal diagnosis for couples at substantial risk of conceiving a pregnancy affected by a known genetic disorder. It enables IVF clinics to select embryos for implantation so that at-risk families can avoid passing on genetic disease to their children and to subsequent generations. Over the past decade the use of PGD has increased as its indications have expanded and changed, both with demand and improvement in molecular diagnostic techniques. The talk will cover clinical assessment and preparatory steps required before starting a PGD cycle, emphasize the difference between PGD and pre-implantation genetic screening (PGS), and explore the factors influencing the outcome of PGD cycle. Clinical results will also be presented.

Tarek El-Toukhy qualified in 1991. He completed a Masters degree and an MD degree in Gynaecology. He completed the RCOG accredited subspecialty training in Reproductive Medicine and Surgery at Guy's and St. Thomas' Hospital NHS Foundation Trust, where he was appointed as a consultant in Reproductive Medicine and Surgery and Pre-implantation Genetic Diagnosis (PGD). His special interests are PGD, recurrent implantation failure, hysteroscopic surgery and prevention of OHSS. He is a scientific editor for the British Journal of Obstetrics and Gynaecology

MDT interactive session service delivery models

Jonathan Skull

Key Learning Points:

1. Satellite PGD services allow patients to receive the majority of their treatment closer to home making the whole procedure more convenient and less stressful.
2. Various models for running a satellite PGD service will be discussed.
3. Good links with local genetic services and communication with the main PGD centre are essential for a successful programme Importance of good communication.

Jessop Fertility started working with Guy's as a Satellite PGD centre in 2008 and the demand for the service has increased significantly. Patients are initially referred to the service after initial assessment by the local Genetics team, where their suitability for PGD is assessed and relevant samples sent for work up. A full fertility assessment is undertaken concurrently in the fertility clinic to ensure that IVF+PGD is appropriate for the couple. Patients are then seen in a Joint PGD clinic to plan their treatment. All IVF monitoring is conducted locally with patients only having to travel to the PGD centre for the egg collection and subsequent frozen transfer. Alternative satellite PGD models where patients could undertake a local embryo biopsy with genetic testing performed at another centre will also be discussed. For satellite programmes to be successful there has to be excellent communication between all relevant disciplines.

Jonathan Skull qualified from Bristol University and undertook postgraduate training in Sheffield and London. He was the Senior IVF Co-ordinator at the Hammersmith before returning to Sheffield in 1998, first as a Lecturer and then as Consultant. He was instrumental in establishing the Assisted Conception Unit at the Jessop Wing, where he has been the Clinical Head of the unit since it opened in 2001. He is also the lead clinician for the PGD satellite service. His other interests include Minimal Access surgery as well as active involvement with postgraduate training in Reproductive Medicine.