focus on REPRODUCTION

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SCIENCE MOVING PEOPLE MOVING SCIENCE

On the fertility journey

- Developments in infertility counselling
- The case for patient centred treatment

- Look ahead to Lisbon
- ESHRE news
- Best of ESHRE & ASRM 2015

// MAY 2015

Cover picture: Getty Images

MAY 2015

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CHAIRMAN'S INTRODUCTION

ESHRE activities have remained brisk during the first months of this year. Several meetings and workshops have been held with many members commendably taking part. The fourth 'Best of ESHRE & ASRM' meeting in New York in early March was a great success. A record number of more than 900 attended, with 300 from Europe. The scientific programme proved both interesting and practical, which has been the purpose of these joint events from the beginning. In the future the Best of meetings will be held every two years, with the next in Europe in 2017.

This is my last Chairman's Introduction to *Focus on Reproduction*. As expected, my term as Chairman of ESHRE has passed quickly. Most of the time has passed in everyday affairs, but many new activities have been initiated. I am particularly pleased that the e-learning project has now begun in earnest, that certification and accreditation programmes have expanded, and that ESHRE has taken part in numerous science policy issues as an active contributor. Several practical changes have been made for the Annual Meeting, perhaps the most visible a paperless congress for Lisbon. Please be prepared for that and read the instructions on the website.

The first ESHRE grant initiated by our Past Chairman Anna Veiga was awarded late last year and will be officially handed to the winner at the Opening Ceremony in Lisbon. However, not all major objectives have been met and the new Executive Committee will have important issues to resolve. The Annual Meeting and *Human Reproduction* journals are the most important source of income for the Society, and competition for funding and in journal publishing will get tougher. This will need special attention and careful planning.

One of the most enjoyable things about my chairmanship has been getting to know so many hard working professionals who put themselves out for the sake of a common good. With that in mind, I would like to thank all members of the the Executive Committee and the officers of our many committees and journals with whom I have worked in the past four years. In particular, I wish to thank Anna Veiga, who leaves the ExCo, and Kersti Lundin, who will take over as Chairman in Lisbon. They have supported me unconditionally and helped in every way. I will continue as Past Chairman for the next two years. Special thanks go to Bruno and his staff at Central Office. I find it hard to imagine a more loyal and effective team.

All the omens suggest that the Annual Meeting in Lisbon will be another huge success. More than 1800 abstracts were submitted, which usually predicts a big attendance. So don't forget to join the get-together on Tuesday evening after the charity run, to meet friends old and new, and enjoy good food, drinks and music - and all at an affordable price! See you there.

Juha Tapanainen
ESHRE Chairman 2013-2015

// MAY 2015

Lisbon abstract submissions climb to yet another record-breaking peak

A total of 230 abstracts of original studies - from a record total of 1800 submissions - have been selected for oral presentation in Lisbon. A further 800 abstracts have been selected for poster presentation.

The total of abstracts submitted marks another record entry and reflects the very high standards now required for selection. As ever, submissions were refereed blind by a selection committee, which included, among others, the co-ordinators of ESHRE's 12 Special Interest Groups. Selection for the oral or poster programme was dependent entirely on the committee's score, and represented for oral presentation an acceptance rate of around 12%.

A total of 360 abstracts were received in the category of embryology, and 317 in reproductive endocrinology, as ever ESHRE's two leading categories as reflected in membership interests. However, considerable interest was evident in andrology (192 submissions), female infertility (171), endometriosis (152), and reproductive genetics (124).

Nationally, the highest number of abstracts came from the UK (135 submissions), followed by Italy (125), Spain (123), China (123), Japan (118), and Turkey (105). The ever-growing presence of China and Japan in the scientific programme of an ESHRE Annual Meeting was described as a welcome development by the ESHRE Chairman, a trend also evident in submissions to the journals. Europe, of course, remains the meeting's most prolific source of abstracts, with around 1000 submitted, but Asia is now responsible for more than 500.

The main scientific programme of this paper-free meeting is now in place and will begin as customary with the Robert G Edwards keynote session featuring

All change for ESHRE's first paper-free Annual Meeting

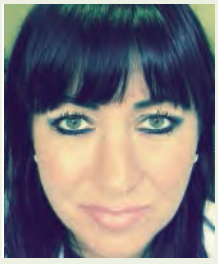
The programme for this year's Annual Meeting will be available in digital format, with the former abstract and programme books now replaced by electronic material. There will be three access options:

- **A PDF of the programme and abstract books (the closest to what regular participants are familiar with).**
- **An itinerary planner to check the programme and presentations, read abstracts and compose an itinerary.**
- **An app for mobile devices with the same functions as the itinerary planner but many additional features to create a personalised congress (QR code below).**

The app will allow note-taking, presentation-rating during the sessions, and posting documents to a virtual library. A continuous notification service will keep participants up to date with congress news, while a listing of congress delegates will allow exchange of messages to other participants.

iPad hire on site will be available for those without a device and choosing the app option.

GENERAL ASSEMBLY TO RATIFY SELECTION OF FIVE NEW ExCo MEMBERS



Basak Balaban is an embryologist and head of the IVF lab at the American Hospital in Istanbul. As a member for Turkey, she joined ESHRE's Committee of National Representatives in 2008. She was Chair of Alpha - Scientists in Reproductive Medicine between 2008 and 2012, and is currently Chair of the Turkish Society of Clinical Embryologists.

Mariëtte Goddijn is a consultant gynecologist at the Centre for Reproductive Medicine of AMC Amsterdam. Her special interest is recurrent miscarriage, for which she is principal invesigator. Mariëtte was Co-ordinator of ESHRE's SIG Early Pregnancy from 2012 to 2014, and led the review committee for ESHRE's latest recurrent miscarriage guidelines.

Borut Kovacic is head of the reproductive biology lab at the University Medical Centre, Maribor, Slovenia, and Associate Professor of Cell Biology at the University of Ljubljana. He has represented Slovenia on ESHRE's Committee of National Representatives and is currently a member of ESHRE's embryology certification committee.

Nick Macklon is Professor of Obstetrics and Gynaecology at the University of Southampton, UK, and Director of the Complete Fertility Centre, Southampton. Nick is a past Co-ordinator of ESHRE's SIG Reproductive Endocrinology, and presently holds Visiting Professorships at the Universities of Adelaide, Australia, and Copenhagen.

Rita Vassena is Scientific Director of the Clinica EUGIN in Barcelona, and chair of its ethical committee for clinical research. She was formerly Senior Researcher at the Centre for Regenerative Medicine of the National Stem Cell Bank, Spain. Rita has been Co-ordinator of ESHRE's SIG Stem Cells since 2013, and has published widely in reproductive science.

Agenda of the General Assembly of Members

To be held on Tuesday 16th June 2015, from 18.00 to 19.00, Room Braga, FIL, Internation Fair Lisbon, Portugal, venue of the 31st Annual Meeting.

1. Minutes of the last meeting (held in Munich and published in *Focus on Reproduction*, September 2014)
2. Matters arising
3. Membership of the Society
4. Society activities
- **Annual meetings - Campus meetings**
- **Studies and data collection - Accreditation and certification**
- **Special Interest Groups and Task Forces**

5. *Human Reproduction* journals
6. Paramedical Group
7. Financial report
8. Ratification of the new Executive Committee
- **Roy Farquharson to be elected as Chairman-elect and retirement of Anna Veiga as immediate Past Chairman**
- **Carlos Calhaz-Jorge (PT), Jacques De Mouzon (FR), Anis Feki (CH), Niels Lambalk (NL) and Cristina Magli (IT) to step down as members having served two two-year terms**
- **Basak Balaban (TK), Mariëtte Goddijn (NL), Borut Kovacic (SI), Nick Macklon (GB) and Rita Vassena (ES) as new members**
- **Petra De Sutter (BE), George Griesinger (DE), Grigoris Grimbizis (GR), Tatjana Motrenko (ME) and Andres Salumets (EE) to serve a second two-year term as members**
- **Cristina Magli (IT) to become an ex officio member as Chair of the SIG & TF Sub-committee**

9. Retirement of the Chairman, Juha Tapanainen (FI), and installation of the new Chairman, Kersti Lundon (SE)
10. Election of the Honorary Members for 2016
11. Any other business **12. Date of the next Annual General Assembly**

the *Human Reproduction* lecture. The subject and lecturer are derived from the paper with the highest number of full-text downloads during the first six months of publication in *Human Reproduction* between January 2013 and June 2014. You can find more details on page 8.

The main programme will comprise a series of invited presentations on topics of current interest and development. Notable among these will be a Tuesday session (planned by the journal *Molecular Human Reproduction*) on the prevention of mitochondrial disease in which Professor Mary Herbert from the

Wellcome Trust Centre for Mitochondrial Research in Newcastle, UK, will review the techniques recently granted legal approval in Britain (see page 15). There will also be much clinical interest in two presentations in a hot-topic session on 'safer and better' IVF - on the promise of an OHSS-free clinic and the potential benefits of a freeze-all embryo policy.

This year will also mark the first exchange session with the Chinese Society for Reproductive Medicine. ESHRE exchange sessions have long been held with the ASRM (since 1993) and Fertility Society of Australia (since 1996), but 2015 will be a first for China. Topics in the programme will be genomic and transcriptome analysis of oocytes and embryos, and PGD by non-invasive haplotype screening.

New figures in the hot seats. At this year's General Assembly the Swedish embryologist Kersti Lundin will take over as ESHRE Chairman, while the UK gynaecologist Roy Farquharson has been selected for ratification as Chairman Elect.

This year's social programme has moved with the times and will be more about the community of ESHRE than mere socialising. Thus, while Sunday evening's opening ceremony and welcome reception will remain as before, the congress party has been reshaped as an ESHRE community evening. This includes the charity run after the main programme on Tuesday and, following the run, a chance for everyone to say hello, for scientists to meet clinicians, juniors to meet their seniors, and of course for everyone to meet friends and colleagues. Registration details are on the ESHRE website.

The General Assembly of Members, as detailed in the box on page 5, will see the introduction of a new Executive Committee for ESHRE and a farewell to those members who have served two two-year terms - Carlos Calhaz-Jorge (a joint organiser of this meeting in Lisbon), Jacques De Mouzon, Anis Feki, and Niels Lambalk. The Italian embryologist Cristina Magli will remain an ex officio member of the ExCo as Chairman of the SIG/Task Force sub-committee.

The Swedish embryologist Kersti Lundin, whose past responsibilities with ESHRE have included development of the certification programme for embryologists and co-ordination of the SIG Embryology, will take over as Chairman of the Society from Juha Tapanainen, and the British gynaecologist Roy Farquharson has been selected for ratification as Chairman Elect. Farquharson, already a member of the Executive Committee with a responsibility for the accreditation of centres for EBCOG sub-specialist training and a past Co-ordinator of the SIG Early Pregnancy, would thus become Chairman of the Society in 2017 - and, as a clinician, would continue the ESHRE tradition of alternating the interests of its chairmen between science and clinical medicine.

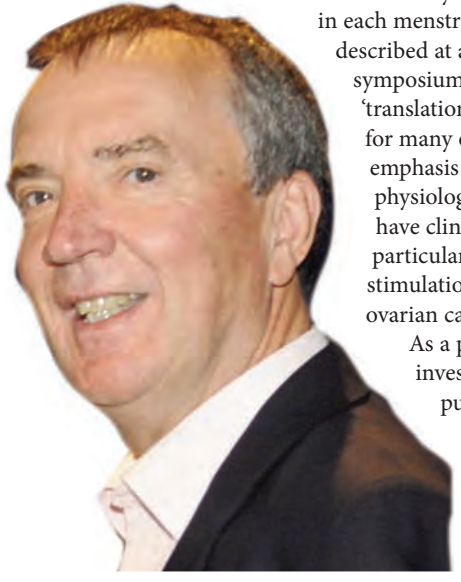
Two stalwarts of ESHRE awarded honorary membership in 2015

Past *MHR* editor Steve Hillier and former ESHRE Chairman Paul Devroey will receive their awards at this year's Opening Ceremony

Steve Hillier, who will receive honorary membership of ESHRE this year, was also honoured by the Queen of England in January with an OBE for services to international higher education. Over the past 15 years, Hillier had established strong academic links between his own University of Edinburgh and overseas institutions, helping develop international centres of excellence with Russia, China, India, Latin America and in Islamic studies. Hillier retired last year from his position as Vice Principal International at the University of Edinburgh but remains active in reproductive science as Emeritus Professor, with a personal chair in reproductive endocrinology.

Hillier was editor-in-chief of *Molecular Human Reproduction* from 2007 to 2013, and saw the journal's impact factor rise to 4.5 during his editoriship. It was also Hillier who rebranded the journal as *MHR*, in a bid to make the title more more memorable and 'more loved'.

Throughout his illustrious career in Edinburgh he enjoyed 22 years of uninterrupted funding from the UK's Medical Research Council, totalling around £4 million. His work, which explains many of the cellular pathways controlling ovulation - and helped explain why women normally ovulate only one egg in each menstrual cycle - was described at a retirement symposium last year as 'translational endocrinology', for many of his findings, with emphasis on steroid hormone physiology, would indeed have clinical application, particularly in ovarian stimulation for IVF and in ovarian cancer.



As a prolific author and investigator, Hillier published the 'medical textbook of the year' in 1996, *Scientific Essentials of Reproductive Medicine*.

Although Paul Devroey, the second recipient of honorary membership in 2015, was ESHRE's tenth chairman, serving from 2005 to 2007, his history with ESHRE stretched back to the very foundation of the Society. He represented Belgium on the first and second Advisory Committees (from 1986 to 1990) and, with André Van Steirteghem, organised ESHRE's second annual meeting in Brussels in 1986 (having served on the organising committee for the first meeting in Bonn in 1985). He was also a member of the second ethics committee formed in 1988. Devroey joined the Executive Committee in 1993, and was treasurer from 1993 to 1995, when he became Co-ordinator of the Special Interest Groups (until 2003).

Paul Devroey qualified in medicine in 1971 at the Dutch-speaking Catholic University of Leuven. In 1989 he was awarded his PhD (on oocyte donation) at the Dutch-speaking Free University of Brussels (VUB), and it was here two years later that he pioneered the technique of intracytoplasmic sperm injection with Van Steirteghem. Following trials in animal models, with ethical approval secured and pre-conditions in place (karyotyping, prenatal diagnosis), the VUB's first ICSI embryo had been transferred in 1991, and the first baby born in January 1992. The event was reported (along with four pregnancies) to the *Lancet* (by Palermo, Joris, Devroey and Van Steirteghem). Data from all subsequent patient series appeared in *Human Reproduction*, which no doubt had a lasting effect on the journal's impact factor.

Paul Devroey retired from his posts as Professor of Reproductive Medicine and Clinical Director of the Centre for Reproductive Medicine at the VUB in 2011. He is a past president of the Belgian Society of Reproductive Medicine, a current member of the editorial board of *Fertility and Sterility*, and a former associate editor of *Human Reproduction Update*. And even in 'retirement' he remains as busy as ever. He is still an active member of ESHRE's Ethics & Law committees, and of its position paper writing groups - which he has always described as some of ESHRE's most important achievements.

He is presently director of medical education of the International Federation of Fertility Societies (IFFS) and has established a leading clinical interest in IVF safety, notably in the promise of an 'OHSS-free clinic'.

Stress affects fertility: epidemiology data presented at opening keynote lecture

● *Human Reproduction* paper with the most full-text downloads in 2013
● First study to find association between biomarkers for stress and fertility

Once again, the Robert Edwards keynote session which opens the Annual Meeting will be among the best attended presentations at any congress ever in reproductive medicine. The session, which includes the *Human Reproduction* keynote lecture, has quickly established a record-breaking tradition of bumper crowds and maximum attendance to get the congress under way. Last year in Munich around 3000 packed the auditorium for Chris Barratt's lecture on calcium-signalling pathways in human sperm hyperactivation, a welcome return to the basic science of reproduction.

This year's *Human Reproduction* lecture is a first in reproductive epidemiology, and will feature preconceptional stress and its association with infertility as reflected in data from the LIFE study, a prospective investigation performed with funding from the US National Institute of Child Health and Human Development.[1]

The report of the study had the highest number of full-text downloads during the first six months of publication of all original articles published in *Human Reproduction* between January 2013 and June 2014.

The lecture will be given in Lisbon by the group's principal investigator, Courtney Lynch from the Ohio State University Wexner Medical Center in Columbus, USA. The paper was downloaded on more than 3300 occasions from the *Human Reproduction* website, far more than any other during the six-months assessment period.

The study, which was performed prospectively at two US sites in Texas and Michigan, began in 2005 with the enrolment of 501 couples trying to conceive and followed-up for up to 12 months and through pregnancy if it occurred. The aim, Lynch told *Focus on Reproduction*, was to clarify the 'controversial' role which stress plays in infertility. 'The causes of infertility have become less relevant in many ways, given that ART is so successful in overcoming many fertility problems,' she said, 'but continuing to explain the factors associated with optimising natural fertility is extremely important.'

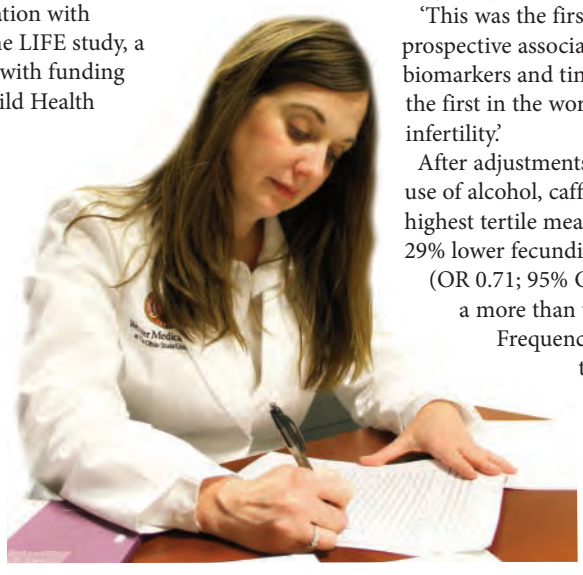
The study itself used data from the LIFE (Longitudinal Investigation of Fertility and the Environment) study in which female subjects provided saliva samples at enrollment and following the first study menses for measurement of cortisol and alpha-amylase, known biomarkers of stress.

Results of the analysis, which were examined in relation to time to pregnancy and covariate data self-recorded in daily journals, showed that higher levels of stress as measured by salivary alpha-amylase (but not cortisol) were associated with a longer time-to-pregnancy and an increased risk of infertility.

'This was the first US study to demonstrate a prospective association between salivary stress biomarkers and time to pregnancy,' says Lynch, 'and the first in the world to observe an association with infertility.'

After adjustments (for female age, race, income, and use of alcohol, caffeine and cigarettes), women in the highest tertile measurement of alpha-amylase had a 29% lower fecundity than women in the lowest tertile (OR 0.71; 95% CI 0.51-1.00), which translated into a more than two-fold increased risk of infertility.

Frequency of sexual intercourse and the timing of ovulation did not differ between high and low stress women, suggesting these were not the mechanisms for the observed association.



Courtney Lynch: 'The first US study to demonstrate a prospective association between salivary stress biomarkers and time to pregnancy.'

1. Lynch CD, Sundaraam R, Maisog JM, et al. Preconception stress increases the risk of infertility: results from a couple-based prospective cohort study—the LIFE study. Hum Reprod 2014; 29: 1067-1075.

More harmony than rivalry, despite an emphasis on transatlantic 'debate'

- More than 900 participants in New York
- Cutting-edge moments in ovarian tissue transplantation and mitochondrial replacement

There was record registration of more than 900 participants for this fourth Best of ESHRE & ASRM meeting, held in New York in March.

Those who attended last year's Best of ESHRE & ASRM in Cortina, Italy, will know that the weather for this increasingly popular meeting is cold with snow. Just like New York in 2015 - though the buildings were a little taller, and there was no skiing on Broadway.

The format of the meeting, like the weather, has also settled into a familiar pattern - of 'cutting-edge' and plenary lectures, and of back-to-back presentations and debates. Because the latter are presented by a distinguished American and European, there is a risk that the format itself encourages a transatlantic rivalry which doesn't really exist, but which may nevertheless be interpreted as representative of the opinion and practice of the two continents.

The potential for such a dichotomy of view was set up in the opening session when Glenn Schattman from Weill Cornell Medical College in New York was pitched against Bart Fauser of Utrecht to debate the contentious proposition that ART results in the USA are 'better' than in Europe. Schattman, drawing his evidence from the database of SART and a few multicentre trials, not surprisingly agreed. Recent trials of urinary and recombinant FSH with fixed protocols, he proposed, had shown better outcomes in the US centres than in the European, as well as more oocytes and better quality embryos. Live birth rate in the US centres of one such trial was 38.2%, while in European centres 27.6%. And the explanation, Schattman suggested, was that 'the quality of care may be different' - in screening and in the lab. 'Every step is better,' he said, and especially in the simple paradigm of the fresh original cycle.

But this, challenged Fauser, is the wrong paradigm. 'This is not a discussion about live birth rates, it's about multiple pregnancies, safety and cost. Glenn,' said Fauser, turning benignly to his opponent, 'you're watching the movie, but unfortunately it's the wrong movie.'

Fauser's approach, putatively representing what goes on in Europe, thus defined 'success' as dependent on live birth, multiplicity, the type of patient treated, complications, cryopreservation, cost and a cumulative outcome from the first started cycle. Fauser's prescription for optimising IVF was that it should be effective as measured by delivery of a healthy baby over a definitive course of time, safe in terms of multiplicity and complications to mother and baby, and cost effective when indicative of broad access to treatment. Such parameters, he proposed, should substitute any reliance on oocyte number, embryo number, implantation rate and pregnancy rate per cycle or transfer as markers of 'success'.

The heart of the matter: Are IVF results better in the USA than in Europe? Bart Fauser, left, and Glenn Schattman,

This, like most others, was nevertheless a back-to-back session in which there was much common ground between the two protagonists, in which entertainment was as much a priority as information. However, the debate which followed - on the ability (if not potential) of PGS to improve live birth rates in IVF - made little concession to transatlantic harmony, and eventually became contentious over patient costs. The debate began with Colorado's William Schoolcraft, whose work has done so much to improve and validate technologies in PGS, proposing that the comprehensive chromosome screening (CCS) of embryos is of genuine benefit in IVF. Yet even he conceded at the outset that screening embryos by FISH for a limited number of chromosomes had been disappointing. 'But that's irrelevant,' he

said, 'that's history.' Now, a 'convergence' of technologies had moved forward such that by 2011 Schoolcraft and colleagues could report that a combination of trophectoderm biopsy, blastocyst vitrification, and single-nucleotide polymorphism (SNP) array technology for CCS does indeed result in high implantation and live birth rates. Such an outcome, Schoolcraft proposed, opened the door not just to better outcomes but also to the practical application of single embryo transfer. With the technology now moving on to next generation sequencing, Schoolcraft noted emerging common features to the various techniques - but notably that blastocyst biopsy 'has many advantages'. He noted a recent systematic review of blastocyst biopsy for CCS (compared with routine IVF) which found the former associated with higher implantation and ongoing pregnancy rates when the same number of embryos is transferred, and improved embryo selection for SET and sharply decreased multiple rates. This finding, said Schoolcraft, is of clinical importance, because the better embryo selection made possible by CCS now makes SET a clinical option for older women. The disadvantage conferred by age seems removed. 'With the development of CCS, blastocyst vitrification and trophectoderm biopsy,' said Schoolcraft, 'older women have the opportunity of elective single-embryo transfer with live birth rates as high as those reported for younger good-prognosis infertility patients.'

In response, the Amsterdam biologist Sjoerd Repping opened his comments with a denial that PGS could ever improve outcomes in IVF. 'Can PGS improve live birth rates?' he asked rhetorically. 'It never will.'

Repping, of course, was a member of the Amsterdam group whose 2007 RCT in the *New England Journal of Medicine* hammered the first nails into the coffin of PGS with FISH. Yet at the time he and his colleagues were severely criticised (on technicalities) by those promoting PGS, particularly in the USA. Now, for Repping if not for Schoolcraft, these lessons of history were a salutary warning not to make the same mistake twice. And for Repping these lessons were underscored by the arguments of evidence-based medicine, ulterior motive, and logic.

Thus, with FISH consigned to history, PGS has entered its second phase with a shift to polar body or blastocyst cell analysis and array CGH. But argued Repping, most of the trials in support of these second-phase technologies are also flawed. For example, the study of Scott et al of 2013 (an RCT of blastocyst biopsy with CCS) was criticised by Repping as only in good prognosis patients, with randomisation on day 5, and with all subjects progressing to transfer.

A debate which became contentious, on the benefits of PGS. Above, William Schoolcraft, and Sjoerd Repping.

What it finally came down to, of course, was the contentious question of recent years of how to introduce new technologies into IVF. Repping unsurprisingly supported the gradual approach in which these 'potentially risky reproductive technologies' remained the subject of research until after preclinical investigation, clinical trials and follow-up studies.

There was potential for similar confrontation in a debate in which time-lapse imaging was proposed as 'superior to classical morphology' for embryo selection. In this case, however, the proponent of the new technology was European and his evidence derived from a European RCT. Giovanni Coticchio from Monza, Italy, first proposed that time-lapse imaging can detect aberrations in the embryo which morphology cannot do - notably 'reverse cleavage' and multinucleation. However, his strongest evidence came from the 'long awaited' RCT of Rubio and colleagues at IVI in Spain, finally published in *Fertility and Sterility* in November last year. Results from this study, which included 843 patients whose embryo development was assessed by morphology or a time-lapse monitoring system, showed a higher ongoing pregnancy rate in the time-lapse group (51% vs 41% per treated cycle), with lower pregnancy loss and higher implantation rates. However, as Coticchio himself asked, were the better results achieved by time-lapse imaging itself, or by the better culture and observation conditions?

This question was at the heart of his opponent's presentation, but Catherine Racowski from Harvard Medical School was unable to find an answer in the available evidence - including the IVI trial. 'I believe we are still in the development/calibration phase,' she said, noting that the majority of studies are retrospective (though not Rubio et al) and heterogeneous in their design. However, her greatest criticisms came in the design of the IVI trial in which, she said, 30 of the patients randomised to morphology were placed on request in the time-lapse group. Moreover, she added, the study had a high risk of bias for selection, attrition, selective reporting and performance – particularly in that different incubators were used for the two groups. No study, sais Racowski, has yet reported increased live birth rate as its endpoint.

There was similarly little contention in a back-to-back session on the treatment of unexplained infertility. Owen Davies from Weill Cornell Medical College in New York favoured the 'expedited' approach, even if recognising that the slow approach proposed by Roy Homburg was associated with lower risk of OHSS. A quick recourse to IVF would, however, reduce the risk of multiples and provide a better opportunity of embryo selection

Cutting-edge lectures on mitochondrial replacement from Mary Herbert and on robotically assisted ovarian tissue transplantation from Kutluk Oktay.

and SET (while stimulation with a GnRH antagonist would rescue the OHSS threat). Davies's principal argument lay in results of the 2010 FASTT trial in which an accelerated protocol (three IUI cycles and immediate IVF) was compared with a standard protocol of clomiphene- and later FSH-stimulated IUI followed by IVF. The accelerated protocol was associated with a higher pregnancy rate (31% vs 98% and 7.6%), lower time to pregnancy, lower cost, and comparable multiple rates.

Roy Homburg was more equivocal in designating the place of IVF in unexplained infertility, noting that around one-third of couples will conceive within three years without treatment (and 30% within a year). Treatment outcome, however, would depend upon prognosis, which is mainly determined by female age and duration of infertility. Recent studies (see page 15, for example) had found no difference in live birth rates between IVF and IUI, and there seemed no rationale for a 2012 NICE recommendation from the UK advising expectant treatment for up to two years and then IVF. A more definitive answer to this still cloudy question may emerge from a RCT now in progress with Homburg's own group - 280 couples randomised to three cycles stimulated IUI or one cycle IVF.

And yet again, in debating the best treatment for women with diminished ovarian reserve, both speakers - Frank Broekmans from Utrecht and Marcelle Cedars from San Francisco - were in considerable agreement. This time that no single stimulation protocol for IVF would suit all cases, and that increasing FSH doses have little effect. Indeed, said Broekmans, 'it's all about female age . . . the cohort, not the FSH dose' (or the many adjuvant treatments proposed).

Kutluk Oktay, formerly of Europe and now of New York Medical College, reported that some 40 babies had so far been born following ovarian tissue transplantation. Although not a new procedure, he described it as 'still evolving' as a means of fertility preservation, particularly in view of new tissue harvesting and cryopreservation techniques. Oktay described two strategies to improve ovarian transplant revascularisation: the use of agents (such as S1P) to accelerate the process, and enhanced surgical techniques, notably robotically assisted. The latter was illustrated by remarkable footage of the robot procedure in action - and an announcement by Oktay that the technique had already produced its first pregnancy. 'Now,' said Oktay, 'we have the chance to do a more delicate job.'

Roy Homburg, left, found no need to rush to IVF in unexplained infertility, while Catherine Racowski still considered time-lapse imaging in a developmental phase.

MENOPAUSE THERAPY 'COMES FULL CIRCLE'

Fertility specialists have little opportunity to meet the menopause (unless premature), but a presentation by former ASRM President Roger Lobo brought home to this meeting the scale of the scandal brought about by the Women's Health Initiative (WHI) trial. This was an RCT testing two menopausal hormone therapies (estrogen alone and estrogen + progestogen) against placebo. The trial, which cost an eye-watering $260 million at 2012 rates, was stopped early because of an increased risk of breast cancer (and cardiovascular disease) when reported in 2002. The effect was devastating, with most guidelines abandoning hormone therapy - and women to their symptoms. Since then, said Lobo, many studies have found the WHI methodology flawed and its results inapplicable - and even a secondary analysis by the WHI itself found that women who began therapy within the first ten years following menopause actually reduced their risk of coronary heart disease. With so many WHI conclusions reversed or constructively dismantled over the past ten years, only now, said Lobo, is menopause therapy for symptoms 'coming full circle' and returning to where it was before that first catastrophic WHI report.

Another lecture at the cutting-edge of research came from Mary Herbert from the Newcastle, UK, centre now likely to be the first in the world to begin clinical trials in mitochondrial donation and replacement. Following approvals in both houses of the UK parliament, Herbert said that the regulations are likely to be in place before the year's end, with clinical licence applications shortly following. She explained that mutations in mitochondrial DNA affect energy production and thereby have serious consequences for those organs which require a lot of energy (such as the heart or brain). Prevalence of mitochondrial disease is thought to be around one in 5000, with debilitating and fatal consequences. In cases of high mutation load - in which other procedures such as PGD are not indicated - two nuclear DNA transfer techniques have been investigated in Newcastle, meiotic spindle transfer and pronuclear transfer. In each, said Herbert, there are two principal considerations: the onward development of the embryo and the reduction in mutation load sufficient to prevent disease. Both principles have been met in mouse models, and now, following public consultation and with legal constraints removed, the work can progress to human zygotes. More details can be found on page 17.

● This year's 'Best of' programme, spread over three days in New York, attracted a record 900+ participants. The steering committee for the meeting announced that the annual schedule will now be extended to every two years, with the next event planned for Europe in 2017.

Simon Brown
Focus on Reprodcution

ESHRE's data collection poised for online upgrade

New online systems for EIM and PGD Consortiums ready for Lisbon launch

ESHRE's two registries, the European IVF Monitoring (EIM) Consortium and PGD Consortium, are to introduce online data collection this year. Both registries, which started data collection in 1997, began with paper forms sent to ESHRE's Central Office for analysis. But now that cumbersome system will come to an end.

The EIM Consortium has been in contact with several companies familiar with data collection for national registries. And one of them, Dynamic Solutions, a Spanish company, was asked to develop the EIM database. This was completed in 2014 and now the online version of the database is set for introduction. The database will not only be more user friendly for participating countries, but will also cut the time needed to analyse the data and compile the 24 tables, which will all be generated automatically.

The database itself is now almost ready and the Steering Committee is completing final checks for the tables. Hopes are that the new database can be introduced in Lisbon - meaning that the next data collection, for 2013, can be performed completely online.

The PGD Consortium was also in need of a new database and participated in the EIM discussions and developments. Dynamic Solutions was considered the most suitable for the PGD database, which needed a complete make-over. In the past the Consortium had collected data first using Excel and later File Maker Pro with four different modules (referral, cycle, pregnancy and baby). Thus, the PGD Steering Committee had to rethink its complete database before any new development could start. However, Dynamic Solutions has now delivered a first draft to the Steering Committee, and it is hoped that by the Annual Meeting in Lisbon the database could be ready for its 60+ member centres to start providing data prospectively.

For both data collections, a speedier process of analysing and reporting could give more time for more detailed and specific reports from the huge amount of data collected.

Veerle Goossens
ESHRE Science Manager

PhD for ESHRE's Science Manager

ESHRE's Science Manager Veerle Goossens has been awarded her PhD from the Vrije Universiteit Brussels (VUB). Her thesis - *Preimplantation genetic diagnosis: from bench to data collection* - was partly based on her work for the ESHRE PGD Consortium in addressing the importance of large-scale in-depth multicentric data collection. Veerle's promoter was Professor Karen Sermon at the VUB, with co-promoters Professors Joep Geraedts and Sjoerd Repping from the Netherlands.

Venues for 2017 and 2018 agreed

Following Helsinki in 2016, the venues for the Annual Meetings of 2017 and 2018 have now been confirmed by ESHRE's Executive Committee. The 2017 event will take place in Geneva, Switzerland, at the Centre International de Conference Genève (CCIG), a modern convention centre located above the city and not far from the Palais des Nations of the WHO. This will be the second time that an ESHRE Annual Meeting has been held in Switzerland - after Lausanne in 2001.

In 2018 ESHRE will return to Barcelona, the fourth time an Annual Meeting has been held in Spain (Barcelona 1988, Madrid 2003, Barcelona 2008). Even though the city is no stranger to ESHRE, the venue - the Centre de Convencions Internacional de Barcelona (CCIB) - will be a new departure. The centre, with capacity for more than 15,000 participants, is located in the Diagonal Mar district overlooking the Mediterranean.

ESHRE guideline on psychosocial care good to go

● Second ESHRE guideline developed according to established protocol

A second ESHRE guideline developed according to the Society's thorough protocol has now been completed. The guideline, *Routine psychosocial care in infertility and medically assisted reproduction – A guide for fertility staff*, was developed by a group chaired by Sofia Gameiro, Deputy Co-ordinator of the SIG Psychology & Counselling, and including psychologists, a gynaecologist, a midwife with a special interest in infertility, a patient representative, and the ESHRE research specialist.

The guideline offers evidence-based best practice advice to all fertility clinic staff on how to incorporate psychosocial care into routine fertility care. Psychosocial care is defined as *care that enables couples, their families, and their health care providers to optimise infertility care and manage the psychological and social implications of infertility and its treatment*.

By combining the best available evidence, from literature searches and quality assessment, expert opinion and patient input, 120 recommendations have been formulated answering 12 key questions. All recommendations have been derived from consensus within the development group and were submitted to an extensive transparent review by relevant stakeholders.

The guideline provides information in two sections. In the first, information is given on the preferences of patients about the psychosocial care they receive at clinics and how this care is associated with their well-being. In the second section, the psychosocial needs which patients experience before, during and after treatment, and how staff can detect and address these needs, are described.

Needs are defined as *behavioural (lifestyle, exercise, nutrition and compliance), relational (with partner, family, friends and larger network), emotional (anxiety, depression, quality of life, well-being) and cognitive (treatment concerns and knowledge)*.

The guideline describes patient needs, risk factors for specific psychosocial needs, and tools to detect them, and lists evidence-based psychosocial interventions which can be delivered by members of staff without specialist training and which don't require the active intervention of mental health professionals.

In addition to the recommendations, four main conclusions have been drawn.

- Patients have clear preferences about the care they receive. Fertility staff should be informed about these preferences and consider implementing them.
- Fertility staff should be informed about the specific needs patients experience at different treatment stages and tailor their psychosocial care accordingly.
- Some patients are more vulnerable to the demands of treatment and need additional psychosocial care or specialised mental-health services (infertility counselling or psychotherapy). Fertility staff should know the risk factors for increased psychosocial needs.
- The most effective way to start implementing psychosocial care is by providing preparatory information, which is expected to be simple and feasible to implement, and more effective in addressing many patient needs (compared with other reviewed interventions).

All recommendations can be found in the full guideline which is now available at the guideline section of the ESHRE website. A public version of the guideline is in development, and a paper with the main messages will soon be published in *Human Reproduction*.

Nathalie Vermeulen
ESHRE Research Specialist

Extraordinary AGM extends Society objectives

An extraordinary General Assembly of ESHRE members was held in Brussels on 27 March to extend the statutory aims of the Society as set out in the by-laws.

The extension - that 'The Society can also acquire participations in whatever form, in all existing or future legal entities and companies, under the condition that these legal entities and companies have a closed/limited character and this happens within the framework of realizing the statutory goal of the society' - would effectively give the Society the authority, as allowed by the articles of association, to acquire participation in organisations considered commercial.

This would extend the aims of the Society defined in the original by-laws as to 'promote the study and treatment of reproductive biology and medicine'. This was explained in the original by-laws as 'to promote improvements in the field of medical practice by organising training, education and advanced medical training activities, by setting up and keeping up databases and by applying methods that promote the safety and quality of clinical and laboratory procedures'.

The motion, which was carried unanimously (118 votes to zero) by the March extraordinary General Assembly, will thus now extend (and not replace) the Society's objectives in accordance with the text.

In explaining the background to the meeting and the extension of the Society's objectives, ESHRE Chairman Juha Tapanainen said that the question of aims and objectives arose over discussions about a fourth ESHRE journal. It has long been a matter of concern to ESHRE's ExCo that, with an ever decreasing acceptance rate for *Human Reproduction*, more and more manuscripts submitted to the journal are being rejected. While *Human Reproduction Update* provides an appropriate title for reviews in reproductive medicine, and *MHR* for basic science, ESHRE has no alternative accommodation for original articles. The acquisition of a fourth title would provide that facility, but may require the purchase of a commercially run journal. The by-law extension will now allow negotiation in such circumstances, although Tapanainen added that no such negotiations are presently taking place.

EU Court of Justice concedes that cells derived by parthenogenesis can not be defined as 'human embryos'

In response to a request for clarification, the European Court of Justice has ruled that stem cells, cell lines and tissues derived from the parthenogenetic activation of oocytes - parthenotes - cannot develop into human beings and are thus outside the meaning of 'human embryo' as defined by the Biotech Directive of 1998.[1]

However, in its judgment in the case of Greenpeace vs Oliver Brüstle in 2011, the Court had ruled that the concept of a 'human embryo' as defined by the Biotech Directive did include human ova whose division and further development had been stimulated by parthenogenesis. Such cells, the Brüstle judgement had implied, are comparable to embryos created by fertilisation and thus capable of development into a human being.[2]

Now, however, that judgement has been challenged and the Court asked if the concept of 'human embryo' as interpreted in the Brüstle case is indeed limited to organisms capable of beginning the process of development which leads to a human being.

And in response the High Court of Justice has now recognised that, according to current scientific knowledge, parthenotes are not capable of developing into a human being and are thus not sufficient to be regarded as a 'human embryo'.

Behind this latest challenge and subsequent judgement lies the Biotech Directive of 1998 which, while promoting scientific innovation through the patent system, also ruled that the human body was not patentable. Thus, the use of human embryos for industrial or commercial purposes was specifically listed as 'contrary to ordre public or morality' and were not patentable. This latest ruling now appears to revise those former restrictions and, in redefining the meaning of 'human embryo', to indicate that human parthenotes are indeed amenable to patent.

The implications in stem cell research are likely to be considerable, opening the door to work on cell lines derived from parthenogenetically-activated oocytes, which previously had appeared as proscribed as cell lines derived from human embryos.

Rita Vassena, Scientific Director of the Clinica EUGIN in Barcelona and Co-ordinator of ESHRE's SIG Stem Cells, explains that parthenotes have been used in research for the derivation of pluripotent stem cells for regenerative medicine.

'Parthenogenetic stem cell lines do have some immunological advantage over embryonic stem cells,' she says, 'because of their monoparental origin. However, their relevance to clinical practice is still much debated, because of defects in the expression of imprinted genes.

'Nevertheless, parthenogenetic stem cell lines can be a very useful tool in basic research, and this ruling will be useful in countries where research on human embryos is forbidden. The new ruling makes it clear that human parthenotes do not have any potential for term development and should not, therefore, be considered as embryos.'


Court of Justice of the European Union
PRESS RELEASE No 181/14
Luxembourg, 18 December 2014

Judgment in Case C-364/13
International Stem Cell Corporation v Comptroller General of Patents, Designs and Trade Marks

Press and Information

An organism which is incapable of developing into a human being does not constitute a human embryo within the meaning of the Biotech Directive

Accordingly, uses of such an organism for industrial or commercial purposes may, as a rule, be patented

The Directive on the legal protection of biotechnological inventions[1] provides that uses of human embryos for industrial or commercial purposes are considered unpatentable.

In its judgment in *Brüstle* of 18 October 2011,[2] the Court held that the concept of a 'human embryo' in

1. See press release 181/14. http://curia.europa.eu/jcms/upload/docs/application/pdf/2014-12/cp140181en.pdf
2. See press release 112/11. http://curia.europa.eu/jcms/upload/docs/application/pdf/2011-10/cp110112en.pdf

Artificial human primordial germ cells created from induced pluripotent stem cells

Scientists from Israel and UK have reported the creation of human primordial germ cells, described as the precursors of sperm and eggs, from iPS cells in a procedure first applied in mice.[1] Now, they describe development of a 'robust approach' to the specification of human PGC-like cells, whose earliest marker and 'key regulator' is the transcription factor gene SOX17.

The first reports of artificial primordial germ cells created from iPS cells came in 2012 when biologists from Kyoto University developed a procedure in mice.[2] Although these cells could not develop beyond this precursor stage in the dish, the Japanese researchers found that they would mature into functional oocyte and sperm cells if introduced to the testes and ovaries. The Kyoto group, including iPS pioneers Shinya Yamanaka and Mitinori Saitou, reviewed these advances in *Fertility and Sterility* in 2012 and proposed strategies to develop in vitro disease models of infertility using human embryonic and iPS cells.[3]

Now, the latest human artificial cells have been described as similar to human precursor germ cells - as the earlier cells were to mice.

Reports suggest that, while developments in Japan are likely to continue functionality experiments in mice, there are no plans as yet to test function potential in humans and take the technology to the clinic. Many jurisdictions - the USA, for example - would require a change of regulation for any federal funding.

1. Irie N, Weinberger L, Tang WWC, et al. SOX17 Is a critical specifier of human primordial germ cell fate. Cell 2015; 160: 253-268.
2. Hayashi K, Ogushi S, Kurimoto K, et al. Offspring from oocytes derived from in vitro primordial germ cell-like cells in mice. Science 2012; 338: 971-975.
3. Hayashi Y, Saitou M, Yamanaka S. Germline development from human pluripotent stem cells toward disease modeling of infertility. Fertil Steril 2012; 97: 1250-1259.

Bisphenol A: 'no health risk' in male reproduction

- European Food Safety Authority re-evaluation
- Studies continue to show association with sperm quality

Despite fears (and alarm) to the contrary, the European Food Safety Authority has concluded that bisphenol A, a chemical used in the manufacture of food packaging materials and can coatings, poses no health risk to consumers of any age group.

The conclusion, delivered in January, comes after a re-evaluation of bisphenol A by the EFSA amid concerns that it may have endocrine-disrupting effects on the reproductive and other systems. However, current exposures from diet or other sources, says the EFSA, are 'considerably under the safe level'.

Although new data and refined testing methodologies have led the EFSA to reduce the bisphenol A safety level from 50 µg/kg per kg body weight per day to 4 µg/kg, the highest estimates for dietary exposure and for exposure from other sources (for example, through the skin from thermal cash register paper) are three to five times lower than the new tolerable daily intake.

In the USA the FDA banned bisphenol A from baby bottles in 2012 but presently maintains that levels currently used in food packaging are safe.

However, just months before the EFSA delivered its verdict, specialists from the University of Copenhagen reported detectable urinary levels of bisphenol A in 98% of 308 young men examined.[1] Men with concentrations above the lowest quartile had higher concentrations of serum testosterone, LH, estradiol, and free testosterone than those in the lowest quartile. Men in the highest quartile also had significantly lower percentage progressive motile spermatozoa than men in the lowest quartile (–6.7 percentage points). However, bisphenol A was not associated with other semen parameters. Nevertheless, the investigators concluded that, while the effects of bisphenol A in male reproduction are 'generally related to its estrogenic effect', an effect on the hypothalamic–pituitary–gonadal hormone feedback system may be a further mode of action.

A more recent US study in mice is the first to suggest that even low exposures to bisphenol A early in life (or other estrogen contaminants) can alter the stem cells responsible for producing sperm later in life.[2] Exposure, said the principal investigator, 'is not simply affecting sperm being produced now, but impacting the stem cell population, and that will affect sperm produced throughout the lifetime'.

It was such fears - built on a huge catalogue of studies on the toxic effects of bisphenol A - which no doubt prompted the French authorities in January (just weeks before the EFSA announcement) to ban the use of bisphenol A in food packaging. Ségolène Royal, recently appointed environment minister, denounced bisphenol A as a danger to human health.

Declining sperm counts have been a subject of concern and conjecture since the early 1990s, when the same University of Copenhagen group as cited above reported 'a genuine decline in semen quality over the past 50 years'.

1. Lassen TH, Frederiksen H, Jensen TK, et al. Urinary bisphenol A levels in young men: Association with reproductive hormones and semen quality. Environ Health Perspect 2014; 122: 478–484.
2. Vrooman LA, Oatley JM, Griswold JE, et al. Estrogenic exposure alters the spermatogonial stem cells in the developing testis, permanently reducing crossover levels in the adult. PLoS Genet 2015; 11: e1004949. doi: 10.1371/journal.

IVF no better than stimulated IUI in unexplained and mild male infertility

A substantial randomised trial in the Netherlands has found that IVF with single embryo transfer and modified natural cycle IVF were each non-inferior to stimulated IUI in terms of a healthy live birth and low multiple pregnancy rates, in couples with unexplained infertility or mild male factor.[1]

The investigators - from 17 centres in the Netherlands - note that stimulated IUI is still first-line treatment in cases of unexplained or mild male factor infertility with a poor chance of natural conception - but that there are concerns about increased rates of multiple pregnancy with IUI. This three-arm trial was designed to test the two increasingly popular IVF procedures against stimulated IUI.

More than 600 women were randomised to the three arms and results showed comparable live birth rates in all three (43-52%), with low rates of multiple pregnancy (5-7%).

Commenting on the results, the investigators propose that, in the absence of a marked difference in pregnancy outcomes, 'the more invasive' IVF with SET and modified cycle IVF 'may not be desirable alternatives' to stimulated IUI.

'In view of these results,' they add, 'there seems no reason to abandon intrauterine insemination with controlled ovarian hyperstimulation as a first line treatment of couples with unexplained or mild male subfertility.'

1. Bensdorp A, Tjon-Kon-Fat RI, Bossuyt PMM, et al. Prevention of multiple pregnancies in couples with unexplained or mild male subfertility: randomised controlled trial of in vitro fertilisation with single embryo transfer or in vitro fertilisation in modified natural cycle compared with intrauterine insemination with controlled ovarian hyperstimulation. BMJ 2015; 350:g7771 doi: 10.1136/bmj.g7771.

SET mainly explains 'significant improvements' in ART baby health over the past 20 years

Findings from the world's largest study of ART baby health over time

The last two decades have seen a steady improvement in the health of children born after ART, with fewer preterm and still births, low birth weights, and perinatal deaths.

These encouraging findings come from the CoNARTaS study, the largest study to date to investigate the health of ART babies over time; data from more than 92,000 children in Denmark, Finland, Norway and Sweden were analysed for this population study, which was published in *Human Reproduction* earlier this year.[1]

Dr Anna-Karina Henningsen, from the Rigshospitalet in Copenhagen, and her Nordic colleagues analysed the outcomes of 62,379 singleton and 29,758 twin births between 1988 and 2007 in the four Nordic countries. They compared them with control groups of 362,215 spontaneously conceived singletons and 122,763 spontaneously conceived twins born in the same countries in the same period.

There was a 'remarkable' decline in the risk of being born preterm and very preterm among the singletons conceived after ART. The proportion of ART singletons born with a low and very low birthweight also decreased, while the stillbirth and infant death rates declined among both ART singletons and twins.

'These data show,' said Dr Henningsen, 'that if there is a national policy to transfer only one embryo per cycle during assisted reproduction, this not only lowers the rates of multiple pregnancies, but also has an important effect on the health of the single baby.'

Dr Henningsen added that other factors had also contributed to the improvement in the health of ART babies over the past 20 years - which included technical skills in the laboratory, clinical skills of the doctors, and milder ovarian stimulation.

She concluded: 'These findings show convincingly that, while there has been a considerable increase in assisted reproduction cycles over the past 20 years, this has been accompanied by a significant improvement in health outcomes for these babies, particularly for singleton babies. The most important reason is the dramatic decline in multiple births due to policies of choosing to transfer only one embryo at a time.'

The study was partly funded by ESHRE, going back to 2007 when Anders Nyboe Andersen and Karl Nygren, pioneers of ESHRE's EIM Consortium, sought funding to create an ART database from the four Nordic countries to monitor safety. This led to the CoNARTaS (Committee on Nordic ART and Safety) collaboration, which was initially funded in part by ESHRE and largely driven by Dr Henningsen and Anja Pinborg. The collaboration is now being funded by various sources - including NordForsk (Norwegian Public Funding Institution) - and has published several papers.

A new study track is currently under way, adding a further 50,000 infants born after 2007 to the dataset.

1. Henningsen AA, Gissler M, Skjaerven R, et al. Trends in perinatal health after assisted reproduction: a Nordic study from the CoNARTaS group. Hum Reprod 2015; doi:10.1093/humrep/deu345.

German court gives DI children the right to know their donor's identity

Germany's Federal Court of Justice shocked many clinics in January by declaring that children conceived by 'anonymous' sperm donation have the right to know the identity of their biological father, whatever the age of the child. The Court ruled that a minimum age was not necessary for disclosing donor identity and that the rights of the child were greater than those of the donor.

Thus far, sperm donation in Germany had been anonymous, although the donor clinic had a responsibility to ask and retain identifying information from the donor. Those identities could only be disclosed with permission of the donor. But now, Germany joins a growing number of EU countries - such as Finland, Sweden and UK - in only allowing non-anonymous sperm donation. (Oocyte donation remains outlawed in Germany.)

The new decision came after two sisters, 12 and 17 years old, appealed to the Federal Court of Justice after a Karlsruhe clinic refused to provide their father's identity. The girls' legal parents had already signed a document saying they accepted the anonymity of the donor.

However, as the children grew older, the parents, acting as the girls' legal representatives, changed their views and appealed to the state court in Hannover for disclosure permission. The court rejected the appeal, after which the girls took their case to the Federal Court of Justice.

The federal judges did attach conditions, notably that all parents requesting donor identity must be able to prove that the child has requested the information, and that possible effects on the private life of the donor must be taken into account.

According to press reports, the number of people in Germany fathered by sperm donations is estimated to be around 100,000. Up to 5000 children are said to be conceived annually with donor sperm.

Legislation for mitochondrial donation approved in UK

- Move follows public consultation
- Questions over ethics of gene modification

Legislation to allow clinical trials of mitochondrial donation in couples known to be at high risk of passing on mitochondrial diseases to their children have been approved in the UK. The move follows votes in the UK's lower and upper Parliaments (the House of Commons and House of Lords) and means that the first trials could begin towards the end of this year. The trials are likely to be at the Wellcome Trust Centre for Mitochondrial Research at Newcastle University, under the direction of Professor Doug Turnbull, which would need to apply for a research license from the HFEA, the UK's regulatory authority. Professor Mary Herbert from the Newcastle group will review the techniques of mitochondrial donation and replacement during the main programme of ESHRE's Annual Meeting in Lisbon.

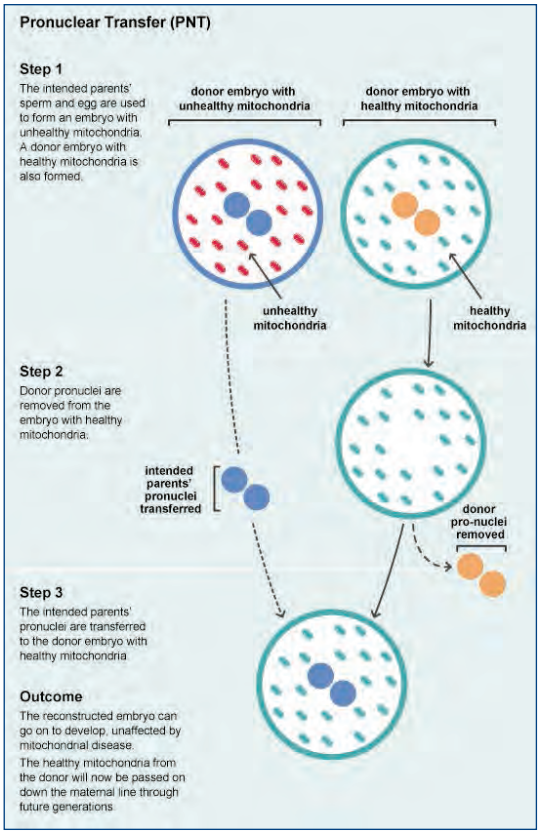
The possibilities of preventing the transmission of mitochondrial diseases (which are said to affect around 2500 women in Britain) was previously the subject of a favourable public consultation by the HFEA.

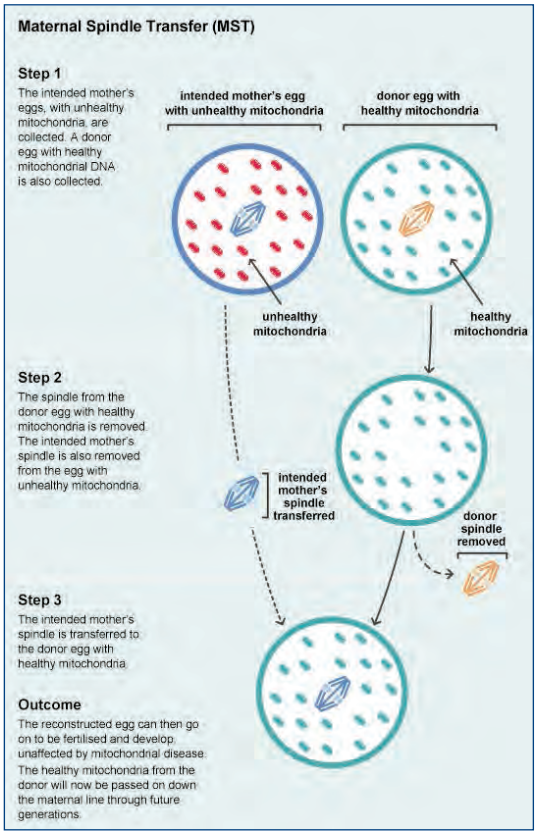
Two techniques have been explored so far: nuclear transfer from the intended parents' affected zygote to an enucleated donor zygote with healthy mitochondria; and maternal meiotic spindle transfer in which the meiotic spindle from the mother's affected oocyte is transferred to a healthy donor oocyte (whose spindle has been removed) before fertilisation with the partner's sperm. Speaking at the 'Best Of' meeting in New York in March, Professor Herbert said that her group had concentrated on pronuclear transfer. Both techniques, however, involve genetically modifying a human oocyte, which has not been permitted in any treatment in the UK.

The controversial issue, however, as demonstrated in the consultations and Parliamentary debates, is not the technique, but the ethics of gene modification - and the inevitably that in each of these techniques the healthy reconstructed zygote will contain the donor's mitochondria as well as the intended parents' own DNA. It was for this reason that the ever inventive British press dubbed the technique 'three-parent IVF' and rightly raised the question of future genetic inheritance in these families - even though the proportion of donor mitochondrial DNA in these embryos would be very small (around 0.2% of the total genetic material).

While ESHRE has made no formal statement on mitochondrial donation (or any contribution to the consultations), Anna Veiga, ESHRE's former Chairman, said: 'The minor contribution from the donor's mitochondria to the genetic constitution is not expected to cause any unexpected adverse outcome in the offspring. In my opinion, no major ethical concern arises in such cases, considering that oocyte donation is a frequently used alternative in affected couples. As in any other ART procedure, couples must receive complete and detailed information.'

Members of both Houses were subject to intense lobbying before the votes. Protests came from the Church of England and, in a letter to *The Times* newspaper, from 55 Italian MPs.





HFEA

Two techniques have been proposed: pronuclear transfer and meiotic spindle transfer.

ICSI use still growing in USA in new CDC review

Preliminary data reported in Munich last year from ESHRE's EIM Consortium suggested that the preference for ICSI over IVF is at last declining. Yet no such patterns seem yet to be evident in the USA.

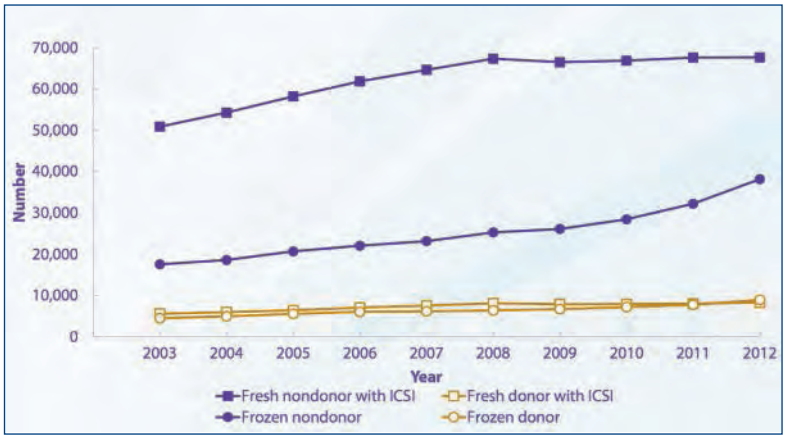
An analysis of all US ART data submitted to the CDC shows that ICSI use increased from 36.4% in 1996 to 76.2% in 2012, with the largest relative increase among cycles without male factor infertility.[1] Compared with conventional IVF, ICSI use was not associated with any improved outcomes post-fertilisation in the absence of a male factor infertility diagnosis.

The retrospective study was performed by the CDC's National Assisted Reproductive Technology Surveillance System (NASS), a data reporting system for the federally mandated collection of all ART cycles performed in the USA, and reviewed more than 1.3 million fresh cycles from 1996. High ICSI use proved no surprise in male factor cycles, but its use reached a prevalence rate of 67% in non-male factor treatments.

In these non-male factor cycles outcome analysis showed that ICSI was associated with a lower multiple birth rate than conventional IVF (30.9% vs 34.2%), lower implantation rate (23.0% vs 25.2%), and lower live birth rate (36.5% vs 39.2%).

Markus Kupka, presenting preliminary EIM data for 2011 last year in Munich, reported a similar overall rate of ICSI use in Europe of around 67%, but with little change over the past three years. There was, however, huge variability in the trends, with low utility countries - such as Denmark and Sweden - using ICSI in 40-50% of cycles, and high utility countries - such as Poland, Montenegro, Greece, Spain and Switzerland - in more than 80% of cycles.

Commenting on the NASS report, Kupka said: 'It would be interesting to see the US data presented state by state. This would no doubt demonstrate that the state differences are similar in variability to those of European countries.'



Latest CDC data on the numbers of ICSI procedures performed in the USA according to type of ART cycle, 2003–2012

The CDC report on ICSI was the second sub-analysis from the NASS, after an earlier review of ART safety data between 2000 and 2011.[2] This study, said to be 'the first, to our knowledge, to quantify US ART-associated patient risks', found OHSS the most common adverse event, at a rate of 153 per 10,000 autologous cycles, with no other significant trends detected.

1. Boulet SL, Mehta A, Kissin DM, et al. Trends in use of and reproductive outcomes associated with intracytoplasmic sperm injection. JAMA 2015; 313: 255-263.
2. Kawwass JF, Kissin DM, Kulkarni AD, et al. Safety of assisted reproductive technology in the United States, 2000-2011. JAMA 2015; 313: 88-90.

UK study aims to track the lifetime development of 80,000 babies

A study to track the growth, development, health and well-being of over 80,000 babies and their parents has been announced in Britain. The Life Study, say the organisers, will provide information on the lives of a new generation of babies growing up with global warming and a whole new range of non-communicable diseases.[1]

The UK study thus hopes to succeed where other similar longitudinal birth cohort studies have failed, notably the National Children's Study in the USA which aimed to follow 100,000 children from birth to age 21 but was cancelled in December last year before launch, and 15 years and $1.2 billion later.[2]

According to *Nature*, studies in Norway and Denmark are also following more than 100,000 children, and the UK itself has already had a series of smaller birth cohorts, the first of which started in 1946. But the Life Study aims to set itself apart by collecting detailed information on pregnancy and the first year of the children's lives, a period that is considered crucial in shaping later development.

The Life Study, which will be hosted by University College London and run by Professor Carol Dezateux, will invite women and their partners to take part during pregnancy or soon after birth, and they and their new baby will be seen at specially commissioned Life Study centres on three occasions during pregnancy and the first year of the baby's life, or in their own homes during the baby's first year.

1. http://www.lifestudy.ac.uk/homepage.
2. http://www.nature.com/news/nih-ends-longitudinal-children-s-study-1.16556.

Richard Sharpe, Deputy Editor of Human Reproduction, talks about the journal's status and ambitions - and his own research in male reproduction.

In pursuit of the evidence in the journal and the lab

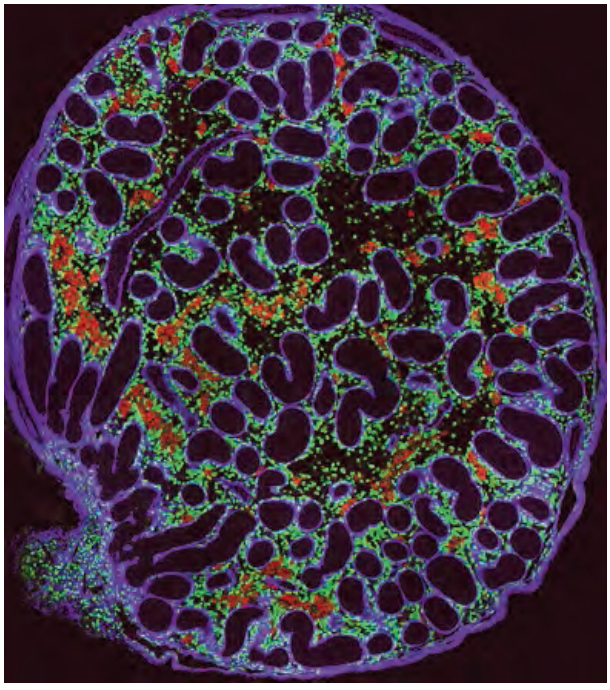
'In the areas the journal covers there are a lot of developments which are not evidence-based.'

oR: You've been Deputy Editor of *Human Reproduction* since 2012. What does the job involve?
RS: Mainly dealing with problem manuscripts and unsolicited manuscripts, case reports, opinions . . . and deciding which of these non-routine manuscripts should be sent out for review. The two Deputy Editors deal with all these papers, plus any appeals by authors and other problems . . . fraud, plagiarism. In these cases, I and the other Deputy Editor and Editor-in-Chief discuss the best course of action.

These are the problems with editing a journal, but overall, how do you see *Human Reproduction* right now? It seems to be a steady, well respected publication.
There's a wish by the Editor-in-Chief - with which I agree - to improve its impact, to try and be more selective in the manuscripts published. This means that we're trying to remove a lot of the more routine papers from the huge number we receive, so that we can focus on material which is likely to be highly cited - and which may help raise the profile of the journal and research in reproduction.

How do you form an impression of what is likely to be well cited? And are citations your only motivation?
I'd say that citability is our primary motivation. We can't publish everything. That's the bottom line, so we have to decide what our main goal is. And our goal is to be the top journal in reproductive medicine and science, one which only publishes excellent papers and sets the standard throughout the world. And how do we go about that? It's by simply selecting the best papers and by weeding out the rest. There's often nothing wrong with them scientifically - they can go through the peer review process and be perfectly OK, but they are often what I might describe as just another brick in the wall - as opposed to a completely new wall. Ideally, of course, we don't want to go through the whole review process and then say no. So we need to ensure that the Associate Editors and everyone else making decisions can triage these manuscripts, to identify them at the submission stage and say, we don't think this one will make it.

Some have said that *Human Reproduction* puts too great an emphasis on randomised trials and high-grade evidence.



Edinburgh has become one of the world's leading centres for understanding the fetal programming of adult disease. In the male, disorders manifest at birth such as hypospadias and cryptorchidism, or in young adulthood such as low sperm counts, testicular germ cell cancer and reduced testosterone levels, are common and/or increasing in incidence. Sharpe has consistently argued that lifestyle and/or environmental factors must be responsible for this increase. The aim of his research is to establish the pathways that govern normal testis development and function (pictured left) in fetal life which are vulnerable to disruption.

Well, that's a policy I would subscribe to. In the areas the journal covers there's a lot of activity, a lot of developments, which are not evidence-based. Just people trying things out, often on patients. There are various ways in which people can say that that's OK, but for most of us it is scientifically indefensible. We need solid evidence, and we should always try to make decisions based on evidence.

So citability and the strength of evidence is a far greater consideration than a talking point over coffee?
Of course. We're not gong for sensation in *Human Reproduction*, unless that sensation is underpinned by real, strong evidence.

So with that in mind how do you see the next few years of the journal? More of the same? Do you think growth in terms of impact factor has got as far as it can go?
It depends. We've set out a game plan where we want to improve the impact factor and improve the overall quality of the journal. And we need a five-year plan to do that. It's only when you get to the end of that five years that you'll know how successful you have been, and whether or not you need to rethink. What we anticipate will happen is that, as we decline more and more routine manuscripts, authors will recognise this and not submit them. This could mean that we will have fewer manuscripts submitted. But if as planned the impact factor continues to go up, it might also mean that we get more and more manuscripts, as authors increasingly hope to get their work published in a high impact factor journal.

'It's only in the last 20 years that we've learnt that the early fetal period is by far the most important for determining your overall reproductive health.'

Would increased frequency of *Human Reproduction* help absorb those extra manuscripts?
Rejected manuscripts are an ongoing matter of discussion. Certainly, if we put a manuscript through the review process and it comes out as OK but just not quite good enough to be published in *HR*, then what do we do with it? Could we divert these borderline papers to another journal? But that's the only consideration under discussion. The idea of publishing more frequently hasn't come up.

You're here working in Edinburgh, where there's a huge tradition in the science of reproduction.
I came her 35 years ago to join what was then the reproductive biology unit. My interest was in a certain aspect of male reproductive function, and that interest has really expanded since then. It's changed shape a little, but it's become much more embracing of male reproductive disorders - their origins and their causes. Now the focus is very much the prenatal origin of reproductive disorders. And I think that was largely triggered by the falling sperm counts issue in the early 1990s. This led us to the realisation that the important determinants of sperm counts - indeed all aspects of male reproductive function - are set up early in fetal life. And that poses a huge problem for human studies - because we can't directly study it. We can't intervene. So a lot of this work has had to focus on developing and validating animal models, to give us the information that we could then take into the human.

So after 35 years how much further down the road are you? What more do we know about these conditions?
What we didn't know back then was the influence of different periods of life. So if you have a male reproductive disorder, does it arise in puberty, or in adulthood, or does it have earlier origins. It's only in the last 20 years that we've learnt that the early fetal period is by far the most important for determining your overall reproductive health. That's because there is a critical period - the masculinisation programming window - in which you have to have enough androgen exposure to programme the later development of your reproductive system.

So given the importance of this early phase, how important are the effects of lifestyle and environment? Hasn't there been a suspicion that environmental effects have a role in testicular cancer and hypospadias?

Sperm counts and fertility in men: a rocky road ahead

Science & Society Series on Sex and Science

Richard M. Sharpe

We all exist because of our parent's fertility; yet in the grand scheme of evolution, fertility is a crucial selection factor that has determined the ...ure of our own and many other spe... ...imal stand... ...ans have r... societies the consequences of which are unknown. Equally important, there will be fewer taxpayers to provide governments with the necessary finances for running their countries. ...his 'brave ... ...nario is an ... abstinence is variable, whereas Sertoli cell number is fixed early in development [3].

Sperm are produced continuously in the testes after puberty, with each sperm taking ... ...ately 10 weeks to ... ...facture—

Since the early 1990s and the first reports of a 'genuine' decline in sperm concentrations over the previous 50 years, Sharpe's research has focused on the determinants of reproductive disorders in men.

It's true that the changing incidence of testicular germ cell cancer has been dramatic in Western countries. It's certainly nothing to do with altered diagnosis or living longer, because it's a disease of young men. And it's a disease which has its origins in fetal life but is manifest in young adulthood. So it has become in many respects an archetypal male reproductive disorder.

So what's the consensus explanation for the dramatic rise in incidence?
That's the $64,000 question. Clearly, it is something to do with our environment and lifestyle. It's not genetic, because the incidence rose so rapidly. But what? The critical period seems to be 8-12 weeks gestation, so there's potential for the mother's diet, lifestyle, chemical exposures and occupation to get to the fetus and exert an effect.

So is this mechanism only acting through the mother?
Yes, but we've yet to understand the epigenetic effects. This will be the next big issue. There's certainly growing evidence in male reproductive health for exposures that can induce epigenetic effects - the diet your grandfather had is one good example.

Do you think that's likely to emerge with greater strength as a hypothesis?
I think so. There's already evidence in humans, and certainly in animal studies, that this can happen, but we've no idea of the scale of such effects in humans.

But getting back to the basics of this, you do believe that there has been a genuine decline in sperm concentrations?
I think that where we have good evidence within a country - where we have measures determined by similar methodology today and 50 years ago - yes, I think sperm counts have fallen. But whether that's true in every country, we just dont have enough evidence.

You have described human fertility as on 'a rocky road' to the future. Do you see an overall decline in fertility?
I think that's almost beyond debate. But we shouldn't be too worried about the past, we should be focused on young men now. We know that average sperm counts in young men today, at least across Northern Europe, are at a level at which they begin to impact a couple's fertility. They're at a level that will affect the time it takes to get your partner pregnant- it will take longer than if you had a sperm count which was twice as high. And it's in that context that you then have to factor in the fact that women are postponing their first children to 30 and beyond, at which point they too are on a downward fertility decline. If you put that change together with a man with a low sperm count, there's only one conclusion to be drawn, and that's increasing fertility problems.

Does it matter?
Yes, of course. It matters to the couples, and to populations across Europe. All EU countries are below population replacement level for births. There's no magic solution. IVF is not the answer, because IVF outcomes also get worse with female age.

Is it any coincidence that your work - research and editing a journal in reproduction - is taking place in Edinburgh. There's a huge tradition here, going back to Robert Edwards, even Dolly the sheep.
Edinburgh has always been one of the top centres in the world in reproduction. But Edinburgh is also one of the leading centres for understanding fetal programming of adult disease. You could say that the most important determinants of health happen in the womb - most important because once they've happened, there's very little you can do to change it. It may be possible, but we certainly don't know how to do it now. And that's a big challenge for us in Edinburgh.

PROUST QUESTIONNAIRE*

- **Which trait do you dislike in others?**
Any mix of selfishness, arrogance and disregard for others

- **And in yourself?**
Do you want a list? I am too unemotional

- **What is your greatest fear?**
There are a few, but the greatest would be to become physically (or mentally) incapacitated

- **Who do you most admire?**
My wife – for putting up with me and my work

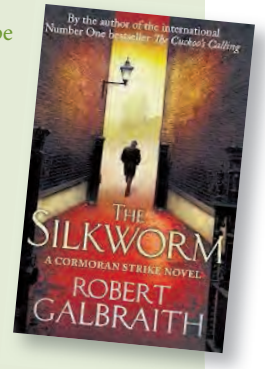
- **What do you consider your greatest achievement?**
Helping my wife bring up four kids

- **If not Scotland, where would you most like to live?**
Any part of the West Country of England, where I'm originally from

- **A talent you would most like to have?**
To be a great thriller writer who can create real believable people simply out of words

- **What is your favorite occupation?**
Research scientist! Or as I describe it to schoolchildren, an explorer

- **And your favorite writer?**
Michael Connelly. I love crime fiction as an escape



- **What was the last book you read?**
The Silkworm by JK Rowling under her alias Robert Galbraith. Another brilliant storyteller.

- **And the last vacation?**
The Canary Islands – in November

- **Your greatest extravagance?**
I don't really do anything extravagant, although two years ago I did spend nearly £30,000 on a decent car!

* A personal questionnaire celebrated and originally made popular by the French writer Marcel Proust

ART regulation and reimbursement in Europe

Country	How regulated	ET limit?	Allowed?					State funding?	Public clinics
			PGD	PGS	Embryo freezing	Gamete donation	Surrogacy		
Austria	Legislation	Yes[1]	Yes	Not yet	Yes	Yes, non-anonymous	No	Yes	8
Belgium	Legislation	Yes[2]	Yes	Yes	Yes	Yes, anonymous and non	Yes	Yes	34 in total
Bulgaria	Legisaltion	Yes[3]	Yes	Yes	Yes	Yes, anonymous	No	Yes	3
Croatia	Legisaltion	Yes[4]	Yes	Yes	Yes	Yes, non-anonymous	No	Yes	7
Cyprus	Legislation + guidelines	Yes	Yes	Yes	Yes	Yes, anonymous and non	Yes	Yes	0
Estonia	Legislation	Yes[5]	Yes	Yes	Yes	Yes, anonymous[5]	No	Yes	3
Finland	Legislation	No	Yes	Yes	Yes	Yes, non-anonymous	No	Yes	10
France	Legislation + guidelines	Yes[7]	No	No	Yes	Yes, anonymous	No	Yes	50
Georgia	None							No	0
Germany	Legislation + guidelines	Yes[8]	Yes	Yes[8]	Yes[8]	Non-anonymous sperm only	No	Yes	30
Greece	Legislation + guidelines	Yes[9]	Yes	Yes	Yes	Yes, anonymous	Yes	Yes[9]	9
Hungary	Legisaltion + guidelines	Yes[10]	Yes	No	Yes	Yes, anonymous	No	Yes	3
Ireland	Guidelines	No	Yes[11]					No[11]	0
Italy	Legislation + guidelines	No	Yes	Yes	Yes	Yes, anonymous	No	Yes	63
Lithuania	No specific ART regulation	Yes[13]	No	No[13]	Yes	No	No	No	0
Macedonia	Legislation	Yes[14]	Yes	Yes	Yes	Yes, anonymous and non	Yes	Yes	1
Netherlands	Legisaltion + guidelines	Yes[15]	Yes[15]	Yes	Yes	Yes, non-anonymous	Yes	Yes	13
Norway	Legislation	No	Yes	No	Yes	Non-anonymous sperm only	No	Yes	6
Poland	Guidelines[16]	Yes[16]	Yes	Yes	Yes	Yes, anonymous		Yes	4
Portugal	Legislation	Yes[17]	Yes	Yes	Yes	Yes, anonymous	No	Yes	11
Romania	Legislation + guidelines[18]	No	Yes	Yes	Yes	Yes, anonymous and non	Yes	No[18]	2
Serbia	Legislation	Yes[19]	Yes	Yes	Yes	Yes, anonymous	No	Yes	5
Slovakia	Legislation	No	Yes	Yes	Yes	Yes, anonymous	No	Yes	1
Slovenia	Legislation + guidelines	Yes[20]	Yes	Yes	Yes	Yes, anonymous	No	Yes	3
Spain	Legislation + guidelines	Yes[21]	Yes	Yes	Yes	Yes, anonymous	No	Yes	41
Sweden	Legislation + guidelines	Yes[22]	Yes	No[22]	Yes	Yes, non-anonymous	No	Yes[22]	6
Switzerland	Legislation + guidelines	Yes[23]	No	No	No	Sperm only	No	No	7
Turkey	Legislation + guidelines	Yes[24]	Yes	Yes	Yes	No	No	Yes	25
UK	Legislation + guidelines	Yes[25]	Yes	Yes	Yes	Yes, non-anonymous[25]	Yes	Yes	78 in total

The most common questions received from journalists by ESHRE's communications manager relate to regulations in different European countries. It was to provide Christine Bauquis with a reference of up-to-date information that we asked members of ESHRE's Committee of National Representatives to summarise their local arrangements.

The result - in answers to a simple questionnaire - was completed by almost all country representatives and now provides a unique snapshot of how ART is organised and run throughout Europe.

ESHRE itself has conducted such surveys before, but not with the same blanket coverage, nor in such detail, and we are very grateful to the CNR for their co-operation. A summary of the results is presented in table form below. In all cases we have had to summarise the information provided by each country into note form (for reasons of space), so we hope our interpretation is accurate and a fair reflection of

Private clinics	Cycles/yr	% reimbursed . . . with eligibility criteria?	Are the following reimbursed?						
			Medication	FET	IUI	Cryo	PGS	Time-lapse	Blastocyst culture
23	~8000	~80%, age, indication, no. cycles	Y	N	N	Y	N	N	Y
	~21,000	~90%, female age, max 6 cycles	Y	Y	Y	Y	Y (but not biopsy)	N	Y
32	~8500	~35%, resident, female age, indication	Y	N	N	Y	N	N	N
5	~5000	~80%, female age (42 yrs)	Y	Y	Y	Y	N	N	Y
5	~2000	~50%, female age (40 yrs)	Y	Y	N	N	N	N	N
2	~1900	~90%, health insurance, F age (41 yrs)	Y	Y	N	Y	N	N	Y
14	~10,000	~90%, indication, female age	Y	Y	Y	N	N[6]	N	Y
50	~60,000	100%, female age (45 yrs)	Y	Y	Y	Y	N	N	N
15	~1000	0%							
100	~55,000	~65%, F age (25-40 yrs), married	Y (50%)	N	Y (50%)	N	N	N	N
43		~90%, married, state insured, max 3 cycles	Y	N	Y	N	N	N	N
9	~7000	~85%, female age (45 yrs), indication	Y	Y	Y	Y	N	N	N
7	~2000	0%	Y in part	N	N	N	N	N	N
95[12]	~56.000	~65%, female age, previous attempts	Y	Y	Y	N	N	N	N
5	~700	0%							
9	~2000	~50%, indication	Y	N	N	N	N	N	Y
0	~17,000	~80%, ETs, female age, previous cycles	Y	Y	Y	Y	N	N	N
5	~6300	~70%, 3 cycles max, only public centres	Y	Y	Y	Y		Y	Y
37	~15,000	~70%, indication, duration infertility, age	Y	Y	Y	Y	N	N	Y
16	~5000	~50%, heterosexual couples, F age (40 yrs)	Y	Y	Y	Y	N	N	Y
20	~2000	~30%, residency, insured, F age (40 yrs), BMI	N	N	N	N	N	N	N
12	~4000	~30%, F age (40 yrs), BMI, FSH[19]	Y	Y	Y	N	N	N	Y
8	2150	~80%	Y	N	N	N	N	N	N
0	~4000	~90%, indication	Y	Y	Y	Y	Y	Y	Y
197	~80,000[21]	~25%, F age, children	Y	Y	Y	Y	Y	Y	Y
10	12,500	~60%, F age (40 yrs), no previous children	Y	Y	Y	Y	N	Y	Y
22	~5600	0%	N	N	Y	N	N	N	N
135	~35,000	~20%, indication, F age (40 yrs), insurance	Y	Y	Y	Y	N	N	Y
	~65,000	~40%, indication, F age (39 yrs)	Y	Y	Y	Y	N	N	Y

Continued from previous page

each country's situation. Details related to embryo transfer and reimbursement eligibility have been added as footnotes.

What does the snapshot tell us? First, there is increasing evidence of homogeneity among countries. Many of the regulatory anomalies evident ten years ago have been removed, to be replaced by legislation and regulation more in line with a common theme. This is especially evident in the case of Austria, from where CNR members Thomas Ebner and Ludwig Wildt reported that new legislation introduced in February this year has now set a limit on the number of embryos for transfer and allowed PGD and (non-anonymous) egg donation.

Similarly, as a paper by Benagiano et al recently confirmed, the draconian restrictions imposed by Italy's Law 40 of 2004 have now all but been dismantled. The proscribed treatments - involving gamete and embryo donation, PGD, embryo cryopreservation, and the transfer of more than three embryos - have now been largely reintroduced following legal challenges in the Italian courts. It is also clear that many of the countries of eastern Europe have finally introduced legislation where formerly there was none. Poland, for example, which has long agonised over ART in both its public and political arenas, is now finally preparing legislation, having introduced reimbursement just two years ago.

Other trends are similarly evident. Notably, IVF is now largely provided by a mix of private and public clinics in most countries of Europe. Only in a few countries (notably, Belgium, Estonia, Greece, Finland, France, Slovenia and the Netherlands) are all (or almost all) patients generously and without exception fully reimbursed by state schemes. But even though many countries do not meet these same standards, almost all countries do now provide some state funding to their citizens. However, while most countries seem happy to cover the costs of medication, cryopreservation and frozen transfers in their reimbursement schemes, none has so far extended their generosity to PGS or time-laspe microscopy.

Notes to the table

1. Austria. Since February 2015. one embryo/blastocyst to be transferred; a decision to transfer two must be documented (female age, embryo quality, previous failed cycles). Reimbursement is set at 70% of a fixed price for IVF or ICS (treatment + medication). Four cycles (fresh and/or frozen) are funded.
2. Belgium. Number of embryos for transfer:
<36 yrs: 1st transfer max one embryo; 2nd transfer one or two embryos; 3rd transfer max two embryos
36-39 yrs: 1st transfer max two embryos; 2nd transfer max two embryos; 3rd transfer max three embryos
40-42 yrs: 1st-3rd transfer unlimited
3. Bulgaria. Number of embryos for transfer:
<38 yrs: three cleavage stage embryos, two blastocysts; two embryos with assisted hatching; four embryos after cryopreservation
>38 years, and/or more than two unsuccessful attempts: four cleavage stage embryos; three blastocysts; three embryos with assisted hatching; four embryos after cryopreservation
4. Croatia. ≤38 years two embryos; >38 years three embryos
5. Estonia. Up to three embryos, and up to 50 yrs of age. Non-anonymous in egg donor cases unless the donor is a relative of the recipient
6. Finland. PGD reimbursed only for genetic transmitted diseases
7. France. Two embryos max - any more must be documented. No restrictions according to age.
8. Germany. A general restriction to three embryos according to the Embryo Protection Law; however, professional guidelines recommend two up to the age of 38 (and three after). PGD only allowed with ethical approval. PGS only permitted on polar bodies. Embryo freezing only allowed in emergency (PN freezing allowed without restriction).
9. Greece. Two embryos up to age 38 (three after three failed cycles). The couple can apply for reimbursement of 300 euro after every cycle.
10. Hungary. The law allows a maximum of four embryos transferred but the professional guidelines breaks it down according to age groups: <35 1-2; 35-40 1-3; >40 max 4.
11. Ireland. No more than three embryos at any age by self-regulation. No legislation to ban any procedures, though law in preparation to make gamete donation non-anonymous. Medication costs only are covered after 144 euro.
12. Italy. There are also 21 private clinics providing state services.
13. Lithuania. There is no specific law regulating infertility treatment, although some aspects are regulated in other legislation - for example, legislation in 1999 ruled that no more than three embryos could be transferred in women under 45.
14. Macedonia. Two embryos if first IVF attempt or patient younger than 35 yrs. Max three embryos if has had more than two IVF failures or is older than 35 yrs.
15. Netherlands. Single embryo transfer in the first two cycles of IVF/ICSI in women under the age of 38. Only one centre (Maastricht) is permitted to perform PGD, but only in the framework of a scientific study.
16. Poland. Legislation is now being prepared by the Polish government. SET recommended in young women; <35 yrs maximum two embryos transferred.
17. Portugal. Only infertile heterosexual couples are allowed ART (including IUI). No single women or lesbian couples. Public health service limits the number of cycles (with embryo transfer) to three per couple and women below 40 years. No limits in the private sector.
18. Romania. EU Directives incorporated in national legislation. No specific ART law, but is regulated in health legislation. No set limit on number of embryos transferred, but the majority of transfers are with 1 or 2 embryos. Romania had an ART reimbursement programme for 18 month (01.06.2011-31.12.2012), which hopes to restart this year.
19. Serbia. Three embryos maximum, regardless of age. No reimbursement for azoospermia.
20. Slovenia. Maximum three (by law) but practically only two (by professional guidelines), including insurance/professional guidelines for only one good quality embryo in first two cycles in patients under 36 yrs.
21 Spain. Three maximum. Own eggs 40,000 cycles per year; donor eggs 15,000; frozen embryo replacement 20,000; PGD 4000.
22. Sweden. 'As a rule, only one embryo should be transferred. If the risk for a twin pregnancy is considered small, two embryos may be transferred.' No reference to age. PGS only performed in a research setting with ethical approval and informed consent. Three pick-ups reimbursed - until live birth. Public centres may only treat patients eligible for reimbursement.
23 Switzerland. Three at any age.
24. Turkey. One for women under 35, and max two for women over 35 and with at least two implantation failures.
25. UK. 40 yrs and under: one or two embryos (SET preferred); 40 or over: max three embryos (unless with donor eggs). Donor information held by regulator until offspring reaches 18.

'The guidance of clinical decisions by patient values is the crucial pillar of patient-centredness.'

Patient-centredness

Confessions of a convert

Putting patients themselves at the heart of their fertility treatment is a mark of quality care. Patient-centredness, argues Jan Kremer, is about guidance through the clinical process by the values of patients themselves.

'I fear the inevitable day on which I will become a patient.' With these words the celebrated paediatrician Don Berwick opened the 2009 International Forum on Quality and Safety in Berlin.[1] Berwick was not expressing concern about the errors and lack of reliability in healthcare; he could stand guard against them alongside the fine skills and good hearts of his caregivers. No, what he feared was to be a patient for other reasons. He was afraid of losing his dignity, his influence and his individuality. 'I fear to be no longer myself,' he said.

A paradigm shift

Berwick does not stand alone. As head of the Nijmegen IVF team, I sensed this very same feeling for the first time in 2001. We had organised a focus group for infertile couples and were keen to hear their opinion of the care we provided.[2] At the time we thought we did it quite well, offering a high quality service. However, our patients had thought differently.

Although they appreciated the quality of our medical care, they felt we did not succeed in delivering the sort of care which showed respect for their individuality. They experienced fragmentation, disrupted continuity, and a lack of influence. Some of them told us that they felt like passive objects, simply to be repaired by us, and not as active human beings with a rich and important context, who could participate in the process. They challenged us with the observation that we as professionals did not make use of this latent power of patients. On the contrary, we raised barriers for their participation, such as waiting-lists for consultations or a denial of their wish to share medical records.

This meeting caused a real paradigm shift in how we did IVF. We came to realise that our work should not be about what doctors do, but about what patients expect. Not about us, but about our patients. So we decided to take action, and began with a digital IVF clinic. This was a website for patients with online access to their medical records, a chat-box, and a forum for quick questions to the team.[3] Within a few months 80% of our patients had produced a profile and were active on the website. Popular sections were the results of fertilisation, the pictures of embryos, and questions to the team. Inspired by the huge success of this venture, we embarked on a series of other patient-centred initiatives which we tried to combine with research (see box on next page).

Patient-centredness

What is the background to the development of patient-centredness? Quality of care? Patient satisfaction? Or

Examples of patient-centred initiatives

Preventing emotional problems
Infertility and its treatment can be associated with emotional problems which are important for patients. We developed a screening test to predict anxiety and depression after IVF.[4] Subsequently, we have designed and tested an online cognitive behavioural therapy to prevent these problems in women at risk (submitted).

Guideline development
Clinical guidelines are tools for professionals to improve infertility care and to decrease practice variation. Doctors mostly write them, although patients are increasingly involved. We developed an innovative method for patient participation in guideline development. This online wiki was used by patients and resulted in a set of patient recommendations that are now part of the Dutch guideline for infertility.[5]

Guideline implementation
We know that writing guidelines does not imply their automatic use in daily practice. That would not be good from the patient perspective. So we asked patients to help in the correct use of guidelines. They were encouraged to give direct feedback to their doctors, based on summaries of the guidelines in lay language.[6]

Shared decision making
One of the important decisions in IVF concerns the number of embryos to transfer. The common belief is that patients choose two instead of one more often than doctors. We found it important that the personal context of the patient was taken into account and developed a decision aid. We asked patients to make the decision after having read and discussed this leaflet. A randomised trial showed that patients actually made the one embryo decision more often than their doctors, contrary to expectations.[7]

Measuring and improving patient-centredness
We want to understand and improve the quality of care through the eyes of our patients. First, we developed a questionnaire based on the eight Picker principles of patient-centred care.[8] Second, in wishing to improve patient-centredness we showed that feedback alone was not enough. Thus, we developed a multifaceted intervention with a leading role for patients, which showed positive effects in a cluster-randomised trial.[9]

Personal health record
If our aim is to respect and respond to patient values and needs, data storage from the perspective of the doctor in a medical record seems a strange choice. That's why we developed a personal record which is owned by the patient (www.mijnzorgnet.nl). We tested this platform in IVF patients and showed promising improvements in care.[10]

is the concept too soft for doctors, and better left to nurses or social workers? Reasons enough to consult the literature and see what's known.

The Institute of Medicine (IOM) defines patient-centredness as 'Being respectful and responsive to the individual patient's preferences, needs and values, while ensuring that the patient's values guide all clinical decisions.'[11] The IOM recognised the importance of patient-centredness, explaining that it is one of the six dimensions of quality of care.

1. Safety
2. Effectiveness
3. Efficiency
4. Timeliness
5. Equity of access
6. Patient-centredness

So quality of care is more than just medical effectiveness, which in our field is so often reduced to pregnancy rate. Indeed, the recognition of patient-centredness as a dimension of quality of care is especially important, because patient-centredness is not the route to the point, but the point itself. We can develop outcome indicators for it, we can measure it, and we can improve it.

So the IOM definition is important but it remains vague to many of us and demands further clarity. And here the principles of the Picker Institute (www.pickereurope.org) may be helpful. They distinguish eight dimensions of patient-centredness:

1. Access to care (eg, waiting times, reimbursement)
2. Respect for patient values, preferences, needs (eg, shared decision making)
3. Coordination and integration of care (eg, collaboration between specialists)
4. Information, communication and education (eg, websites, patient leaflets)
5. Physical comfort (eg, pain relief during ovum pick-up)
6. Emotional support and alleviation of fear and anxiety (eg, social work)
7. Involvement of family and friends (eg, involvement of the partner)
8. Transition and continuity of care (eg, one doctor)

Reading this subdivision of care, one is aware that patient-centredness is much more than just being nice to patients. It is about guidance through the clinical process by the values of patients themselves. This is so much more than patient satisfaction, which is a very subjective concept, but about real experiences which can be measured objectively.[8]

One could ask: Why is patient-centredness the 'good' thing to do? What is the moral nature of patient-centredness? Duggan tried to answer and distinguished three schools of thought: that the basis of the activity is 'good' (deontological school); that the activity itself is 'good' (virtue school); or the consequence of the activity is 'good' (teleological school).[12] It's true that in our present circumstances we focus probably too much on the consequences of patient-centredness (eg, saving money, improving medical outcome) and too little on the fundamentals (eg, seeing patients as people) or virtues (eg, having meaningful and nice work). For example,

many people asked me whether our digital IVF clinic actually saved money or improved outcome (consequences) - and only a few people asked whether it was fun to take part (virtue).

The next step

In the early years we focused our patient-centred activities at the level of patient groups, which was in line with the then dominant principle of standardisation. However, because the guidance of clinical decisions by patient values is the crucial pillar of patient-centredness, we now realise more and more that that those values actually differ from one person to the next and depend on the social, psychological, physical and spiritual context of each individual patient. So, opting for patient-centred care also means opting for a more personalised way of working, which may well be the next fundamental step in evidence-based medicine. You can call it person-based medicine if you wish, but I am sure that this trend will have a big impact on our work the next decade.

So, it is time for action. It's time to improve our IVF services to patients in a way which respects their preferences, needs and values. Hopefully, this will bring us to a situation where they are no longer afraid to be patients. As Don Berwick also said: 'We should not behave with patients as hosts in our system, but as guests in their lives.'

JAN KREMER: 'WE PROBABLY FOCUS TOO MUCH ON THE CONSEQUENCES OF PATIENT-CENTREDNESS (eg, SAVING MONEY, IMPROVING MEDICAL OUTCOME) AND TOO LITTLE ON THE FUNDAMENTALS (eg, SEEING PATIENTS AS PEOPLE) OR VIRTUES.'

Professor Jan A. M. Kremer is a gynaecologist at Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. He was formerly Professor of Reproductive Medicine and is currently Professor in patient-centered innovation.

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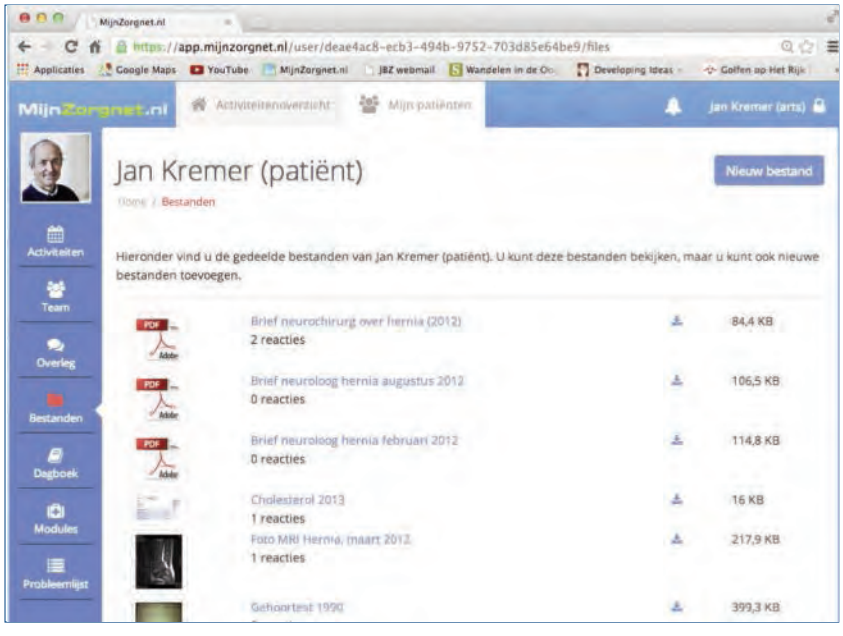

Patient notes, medical records are now online and accessible by patients themselves.

The routine option: what the future holds for fertility counselling

Uschi Van den Broeck and Petra Thorn, present and past co-ordinators of ESHRE's SIG Psychology & Counselling, on the challenges now facing counsellors as clinics move towards greater patient-centred care.

In recent years the importance of infertility counselling has been increasingly recognised in many countries. This is not only reflected in the number of professional books on infertility counselling, but also in the development of guidelines by infertility counselling organisations,[1] not least by latest guidelines on *Routine psychosocial care in infertility and medically assisted reproduction – A guide for fertility staff*, from ESHRE's SIG Psychology & Counselling. Here, we will provide a short overview of the issues and challenges that remain to be tackled in the near future. These include the ongoing endeavour to make counselling a routine option for couples seeking fertility treatment, the challenges for legislative and societal development with respect to anonymity and openness in third-party reproduction, and the need for basic and advanced training for psychosocial professionals.

Routine infertility counselling and/or counselling for specific psychosocial issues?

Currently there is no consensus among professionals regarding the provision of routine infertility counselling for all patients starting or having ART. In a number of countries, clinics do have a mental health professional (such as a psychologist, social worker or psychiatrist) on staff with specific expertise in the psychological aspects of (in)fertility. They provide support in a number of predefined indications. Historically, this has focused on support for patients who experience high levels of stress as a result of their infertility and/or its treatment, which may have a

negative impact on various aspects of their lives and partner relationship. More recently, counselling organisations are moving towards international consensus for counsellors to meet with couples considering third-party conception. In addition, counsellors are ideally placed to provide supervision to medical team members.

As the field of reproductive medicine has evolved, various specific issues have arisen. These include couples presenting with HIV, the need for fertility preservation prior to oncological treatment, the desire for social freezing, sexual issues and dysfunctions, cross-cultural questions and cross-border reproductive services, transgender individuals seeking treatment, preconceptional care and lifestyle challenges. Many of these bring about very specific, and often unexplored, psychological and societal challenges.

In addition, various ethical and legal challenges remain to be tackled. Infertility counsellors will thus have to develop their responsibilities to provide specialised psychosocial care for patients dealing with these complex issues, while at the same time providing expertise and education for their (para)medical team members in these evolving psychological developments and their implications.

Petra Thorn, top, and Uschi Van den Broeck: 'It thus seems clear that infertility counselling must be better integrated into medical treatment.'

Routine psychosocial care by all fertility clinic staff

Recent years have also witnessed an important move towards greater focus on patient-centred care.[2] It thus seems clear that infertility counselling must be better integrated into medical treatment and that closer collaboration between medical and mental health professionals is vital. A current example of such collaboration is the new ESHRE guideline on routine psychosocial care in infertility just published (see page 13). These are the first such evidence-based guidelines within the infertility field. They offer best practice advice to all fertility clinic staff (doctors, nurses, midwives, counsellors, social workers, psychologists, embryologists, and administrative personnel) on how to incorporate psychosocial care into routine infertility care.

Future challenges in third party conception

Third-party conception has been increasingly recognised as a legitimate and positive family building option. This is not only reflected in changing legislation (such as in Austria where oocyte donation as well as donor insemination for lesbian couples has now been legalised), but also in high court decisions which recognise this option, granting children the right to access their biological origins (as in Germany). At least in Europe, this shift seems to be more towards pre-treatment counselling and psycho-education than in screening for all parties involved in third-party conception.

These changes will have an impact on counselling in several ways: closer collaboration between the medical and the psychosocial fields will result in more intending parents seeking counselling prior to medical treatment; more options for third party conception will result in a higher uptake; greater social acceptance of this family-building treatmemt will result in a higher disclosure rate; and - very likely - more parents with older children will seek support for disclosing the nature of the conception to their child. For many counsellors, these will present new or extended dimensions to their work and they may benefit from training.

Towards European training and education

The need for specialist training has been recognised by several European infertility counselling organisations. For the last three years, the German Society for Fertility Counselling (www.bkid.de) has been conducting many training courses for psychosocial professionals for both general infertility counselling and for advanced counselling (such as in third-party conception). The British Infertility Counselling Association (www.bica.net) is offering foundation courses to develop specialist knowledge and skills as well as study days on specific issues. In addition, the International Infertility Counselling Organisation (www.iico-infertilitycounseling.org) as the international umbrella organisation, together with national organisations, has conducted a number of postgraduate workshops.

Several EHSRE SIGs have now developed a European-wide recognised accreditation system for their members. We hope that in the near future, ESHRE's SIG Psychology & Counselling will also be able to provide such accreditation and thus contribute towards greater recognition and accountability of their professional qualifications and skills. Such Europe-wide standards for infertility counsellors should be considered in order to enhance the professionalisation of counselling in our field. We also hope that in the next years, our SIG will be able to provide basic and advanced training workshops open to any professionals in the field of human reproduction who intend to increase their psychosocial skills.

Uschi Van den Broeck is a clinical psychologist specialising in family and couple therapy at the University Hospital, Leuven, Belgium, and Co-ordinator of ESHRE's SIG Psychology & Counselling.
Petra Thorn is a consultant fertility therapist based in Moerfelden, Germany, and was Co-ordinator ESHRE's SIG Psychology & Counselling from 2009 to 2011.

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What patient groups can do for your patients

Clare Lewis-Jones MBE, chair of Fertility Europe, a founding member of Britain's first patient organisation, and a former member of the UK's regulatory authority, finds support group benefits in access to good information, mutual help and shared experience.

'Infertility is like a bereavement which hits me afresh every month, for which I can't see a way to grieve, and from which I can't move on . . . '

The above description was sent to a volunteer organising a fund-raising event for the patient organisation I work for, Infertility Network UK (I N UK). I think it demonstrates the emotional impact infertility has for many people.

There are patient organisations throughout Europe providing practical and emotional support for those with difficulties in conceiving. Why are these organisations important? The emotional impact of infertility is well documented, with numerous studies reported over the years. The physical impact, however, is also very real, with invasive investigations and treatments often lasting for several years. For patients to feel in control and informed about what is happening to them is extremely important.

The emotional toll

The UK patient organisation Fertility Fairness (previously known as the National Infertility Awareness Campaign) surveyed patients in 1997 looking at the emotional and financial impact of infertility[1]. A second survey was performed 16 years later by I N UK to see whether the emotional impact had changed.[2] We found that those who experienced tearfulness/sadness and anger were very similar in 2013 as in 1997; 65% said that they had experienced difficulties in relationships with family and friends. However, those who had experienced loss of sex drive, guilt and shame were significantly fewer.

Unfortunately, many of those who have never experienced infertility lack understanding of just what infertility is like and can make comments which lack sympathy and insight. It's now easy to read a news piece about infertility or an interview with a patient to see the negative and some downright cruel comments from the ill-informed fertile majority - such as 'Can't scientists spend their time finding a cure for broody women who simply must procreate at any cost instead of helping them to do it?'[3]

Family and friends

People with fertility problems may find it useful to talk to family and friends about the way they feel. For some, however, this isn't an option. They may not want to share their problem with people close to them. We quite often hear that close family and friends find it hard to empathise with fertility problems. They can often be unhelpful, saying, 'Just relax and you'll get pregnant'. Well, sometimes that just isn't true.

It was for these reasons that the Clinical Guideline on Fertility published in 2013 by the UK's National Institute for Health & Care Excellence (NICE) made the recommendation in its section on Principles of Care that 'people who experience fertility problems should be informed that they may find it helpful to contact a fertility support group.[4]

The benefits of belonging to a patient organisation

Access to personal experiences. The benefit of being able to talk to others with similar experiences are plenty. It removes the feeling of isolation.

Access to good information. Patient groups can provide good quality, up to date, medically accurate information on almost every form of treatment, cause of infertility and related subjects.

Self help/mutual help. Talking to others in the same situation helps all parties involved

Knowing you are not alone. Belonging to a patient support group makes patients realise they are not alone and goes a long way to removing that feeling of isolation.

In August 2006 I N UK performed a survey of its members with 150 respondents. When asked whether they felt that belonging to the organisation had helped them in the management of their illness and treatment, 121 (81.5%) said that it had, with just 12 (8%) responding No and seven not sure.

How can clinics help?

- Hand information on local patient organisations in to each and every patient – don't just leave their leaflets in the waiting room
- Recommend the organisation to your patients

Reasons why patients may contact a patient organisation

- **They want to talk to other infertility sufferers**
- **They feel the clinic is too busy to answer their questions and/or don't know who to speak to**
- **They feel that infertility is putting pressure on their partner**
- **They feel that it reinforces a sense of failure in their partner**
- **They feel partner/family/friends are fed up of listening**
- **They feel they have to be seen to be coping by the clinic**
- **The bad news has only really hit them when they get home**
- **They want to find out why treatment was unsuccessful**

- Counselling should be available at ALL stages of treatment - before, during and after treatment
- Explain the benefits of counselling and how to access it to ALL patients
- Link your website to local patient organisations
- Give patients written information on all aspects of their investigations and treatment throughout their time at the clinic in a range of languages/formats
- Ensure patients know who to contact if they have questions or concerns
- Provide access to a counsellor - within the clinic and outside
- Provide an area or space where patients can go for privacy

And finally, patient organisations need more financial support. Otherwise, there is a danger that many cannot continue. Very few have guaranteed funding and must generate their own income, which is extremely difficult. So please support the patient organisation with funding – or help with recruiting volunteers. Even those patient organisations with paid staff would still not be able to provide all their services without the help of their wonderful volunteers.

Clare Lewis-Jones: 'For patients to feel in control of what is happening is very important.'

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fertility europe fe.eu

More talking with the patient than about the patient

This is a big year for Fertility Europe. It's been three years since our last election of members to the Executive Committee and it's time for new elections. This time we've looked to other societies and associations, such as ESHRE, and are changing our election process. Instead of electing the entire committee once every three years, we will be having annual elections where only one or two members will be elected, ensuring continuity in the work being done.

We have also noticed in our work that more and more attention is being paid to the voice of the patient. Last year we were asked to co-chair an ESHRE precongress course on 'new generation patients'. It was a great experience and important to see such respect for the voice of the patient during the course. In the past our feeling has been that those working in the field have been talking *about* their patients, but not so much *with* them. So this is a noticeable change and ESHRE and its members should be acknowledged for their part in it.

Fertility Europe continues with its policy work, which is greatly appreciated by our member countries and other parties. Some of our members have successfully used our policies to influence their governments in matters related to fertility treatments.

The Special Families Campaign and Wall of Hope continue to be the projects that give us the greatest visibility. We have great ideas and hopes for Lisbon and look forward to sharing them with you. It's been great to see the Wall of Hope growing from 250 postcards in Stockholm to more than 1000 in our online galleries. These postcards have stories from all sorts of people from all over the world. Our main focus has been on Europe, but the word has spread and we now have cards from both Canada and Brazil and one never knows where the next one will come from. Many people gather around the Wall of Hope during ESHRE's Annual Meeting, looking at the postcards and taking pictures. It's great acknowledgement of the work we've done so far.

Hopefully we can continue to inspire you with more stories and pictures from the people behind the treatments. This year Fertility Europe's stand will be with the Wall of Hope in the entrance hall – so do come and see us.

Elín Einarsdóttir
Secretary of Fertility Europe

Update on PGS fails to deliver consensus

A Campus meeting organised by the SIG Reproductive Genetics and PGD Consortium aimed for consensus, but even some of the world's leading experts in the field found little unanimity in their choice of technique or timing of biopsy.

Those hoping for definitive conclusions from the Update on PGS Campus meeting held in Rome in March would have been somewhat disappointed. Even the current 24-chromosome screening 'consensus' now drifting over the Atlantic (blastocyst biopsy, whole genome amplification techniques) was by no means accepted by all, and consensus here in Rome was not built in a day.

One of the course organisers, former PGD Consortium Chair Joyce Harper, said she hoped all attending 'would be convinced that PGS is a viable procedure', but by the end of this two-day meeting even she admitted that 'we're not at that point yet'. The techniques themselves, the timing of the interventions, and the patient groups most likely to benefit were all topics for clarification.

Indeed, it was a sign of the uncertainty still surrounding PGS that so many took part in the event. More than 150 registered for the meeting, which was organised by the PGD Consortium and SIG Reproductive Genetics.

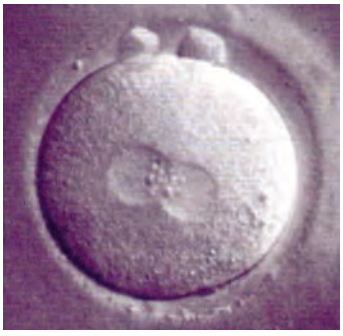
The meeting kicked off with the premise that 'we've moved away from cleavage-stage biopsy' and that blastomere analysis by FISH 'is redundant'. There was not much doubt about that, even though the latest data from the PGD Consortium suggest that cleavage stage biopsy is still commonly applied. Nevertheless, while Edith Coonen, Chair of the Consortium, methodically explained why FISH 'had failed' (technical artefacts, mosaicism), one after another speaker reviewed their data from the next WGA phase of PGS: Nathan Treff on quantitative PCR on trophectoderm cells ('inexpensive, fast, flexible and simple'), Joep Geraedts on array CGH on polar bodies, and Francesco Fiorentino on array CGH and next-generation sequencing.

However, it was Treff, in his presentations on qPCR and trophectoderm biopsy who explored the question of timing and the best stage of embryo development for analysis. Treff's case in favour of blastocyst biopsy rested largely on one RCT, although he noted too that the three RCTs so far showing a benefit of comprehensive chromosome screening were all with blastocyst biopsy (albeit in good responder patients).[1] Results from this trial suggested that cleavage-stage biopsy is detrimental to the implantation potential of the embryo, which is not evident in trophectoderm biopsy. Results of the study showed that only 30% of biopsied embryos had implanted and developed into live births, against 50% of unbiopsied controls; in contrast, implantation rates were equivalent (51% vs. 54%) for both the biopsied and control blastocysts, reflecting an implantation benefit for the biopsied blastocysts over the day 3s.

However, it seemed somewhat disconcerting for many in the audience to learn that at least two large groups (IVI in Spain and IVF Melbourne) continued to rely on day 3 biopsies - and with good results. The danger of blastocyst biopsy, as several speakers pointed out, is that some embryos will simply not make it to day 5, with the result that many patients will have no transfer. Dagan Wells noted that some 50% of IVF patients over 40 would not reach embryo transfer in day 5-biopsy programmes. And Fiorentino himself, while reporting updated results

Speakers at the Rome meeting. From left, Florence Belva, Edith Coonen, Luca Gianaroli, Joris Vermeesch, Dagan Wells, Cristina Magli, Francesco Fiorentino, Joep Geraedts, Nathan Treff, Maaike Haadsma, Ursula Eichenlaub-Ritter.

Questions remain for aneuploidy screening by polar body analysis



This was not an encouraging meeting for aneuploidy screening by polar body analysis. First, Nathan Treff argued with evidence from several studies that polar body analysis is less predictive of reproductive potential than other CCS approaches. Further, with reference to one of his own studies of 2010 (though not an RCT), he claimed that the safety of polar body biopsy had not yet been 'rigorously established' - despite the assumptions of their natural extrusion. Treff thus concluded that trophectoderm biopsy is preferable to polar body in terms of cost, convenience, predictive value and outcome.

It was therefore especially disappointing for all in the audience to hear from Joep Geraedts that recruitment in the ESTEEM trial - the one and only study currently able to establish the credentials of polar body biopsy for aneuploidy screening - was running behind schedule. A pilot study had already provided a proof of principle, but the current multicentre trial in seven centres had so far performed just 212 transfers, considerably behind target. As a result, said Geraedts, continued funding from the trial's main sponsor, ESHRE itself, was now in question. More discussion - with ESHRE and other potential sponsors - would now be necessary to secure the trial's future.

There was strong feeling in the audience that without the ESTEEM trial the place of polar body testing for aneuploidy would remain in doubt, and a move to support continuing funding for the trial had overwhelming agreement.

from a small trial of array CGH on day 3 embryos, agreed that the procedure still 'had potential to improve IVF efficiency', though he was cautious about over-interpretation ('I can't say that these results demonstrate anything').

In response, Cristina Magli from SISMER in Bologna argued that day 3 biopsy should not be abandoned, while Leeanda Wilton from Melbourne, speaking from the floor, insisted that 'the best labs should be able to do both [day 3 and day 5] biopsies well'.

This flexibility of approach seemed also the case proposed by Dagan Wells, who set out the advantages and disadvantages of polar body biopsy (least invasive, ethically acceptable, more time for analysis, no mosaicism - but no paternal anomalies, and only 95% predictive value), cleavage-stage biopsy (more embryos for testing, but risk of damage, with prevalent mosaicism), and blastocyst biopsy (more cells for testing, less mosaicism, but fewer embryos available and a shorter time for analysis if not freezing). But, said Wells, blastocyst biopsy is the current 'trend for the field', with 'a luxury of genetic material'.

However, while noting that trophectoderm testing is 'probably ideal', Wells reported that 'there still remains a role for all biopsy stages' - though despite a diagnostic failure rate of 0%, he still emphasised the importance of training in the blastocyst biopsy technique, and shocked many in the audience by disclosing that as many as 18% of cells sent to his Oxford lab for testing were not suitable for analysis.

Joint course organiser Joyce Harper: Consensus on PGS still elusive.

Wells seemed also equivocal about the best testing method, but was quite clear (unlike many) about the generic value of PGS and its superiority over morphology as a gold standard in embryo selection (for SET). The evidence, he said, was 'accumulating', and, whatever the arguments against PGS as a means of embryo selection (as once again delivered by Sjoerd Repping, see page 10), PGS would avoid the cryopreservation of aneuploid embryos, would reduce time to pregnancy, lower the miscarriage rate, and lower the risk of Down's syndrome and other anomalies. This opinion was also voiced by former ESHRE Chairman Luca Gianaroli, who noted benefits of overall cost and time to pregnancy in the concept of PGS.

However, despite such claims, by the end of the meeting there was still no consensus on PGS. Both voting and opinions expressed reflected pros and cons for all methodologies and an emerging feeling that any generalisation about patient groups may not be the way to best treatment. That, most agreed, will require the evidence of further RCTs, and a few more years yet to wait.

Simon Brown
Focus on Reproduction

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A new data collection system 'more fit for purpose'

New online database to be introduced during Lisbon Annual Meeting

Steering Committee at its meeting in March. From left: Celine Moutou, Jan Traeger-Synodinos (Past Chair), Georgia Kokkali, Sioban SenGupta (Chair-elect), Veerle Goossens (ESHRE Science Officer), Edith Coonen (Chair), and Martine de Rycke.

The primary task of the ESHRE PGD Consortium is to collect PGD data. In 15 data collections so far (data XV including PGD cycles carried out between January-December 2012 with babies delivered up to 2013) data from over 58,000 cycles have been submitted to the database. As such, this comprises the world's largest collection of PGD/PGS data, providing an extremely valuable resource for data mining and for following trends in PGD practice.

However, the submission of data is a difficult process for our members and the Steering Committee wishes to acknowledge the effort of all contributing centres. As a result of a huge increase in the number of reported cycles each year, the Steering Committee has found it extremely difficult and time-consuming to mine the data and produce accurate tables. Moreover, the nature of PGD/PGS treatments has changed significantly over recent years and today we face complexity in IVF cycle management and genetic analysis techniques.

As a result, the Steering Committee has found it timely to rejuvenate our data collection and make it more fit for purpose. To do so, we have invested time in strategic initiatives, first to determine what technologies are being used or introduced into genetic diagnosis, and also how IVF cycles are being managed for PGD. This information has allowed us to restructure data collection and mining and has led to the creation of a new online PGD database.

The design of the new database will allow centres to input and analyse their own data in real time. So, with the database now ready, our focus will be to inspire and encourage all PGD centres to submit their data. We cordially invite you to the launch of this new online database during the Annual Meeting in Lisbon. Join the Consortium and find out more about the advantages of the online database. Add your data prospectively from oocyte retrieval to analysis, from embryo transfer to pregnancy and live birth. Keep track of your fresh and cryopreserved PGD/PGS cycles. Audit your centre's pregnancies and live births according to ART and genetic analysis techniques. And last but not least, network with PGD practitioners, discuss trends and identify good practice.

Working groups

By their nature, our current data collections do not represent real-time trends in PGD or PGS. For this reason the Steering Committee has formed a working group to monitor new technologies in PGD and to gather up-to-date information on developments in all aspects of PGD. A manuscript describing the results of a survey performed in 2013 was sent to *Human Reproduction*, but reviewers suggested a further survey to allow comparison between the two investigated periods. To that end, a second questionnaire will be sent out in the weeks to come.

Another WG plans to look at collaborative working practices between Genetics and IVF teams when delivering a PGD service. After a pilot evaluation by the Steering Committee, it was decided to re-evaluate the format of the questionnaire.

The WG on HLA has made good progress. An e-mail was sent out to all potential participants, inside and outside the PGD Consortium, inviting them to participate in a multicentre study that aims to evaluate the overall clinical utility of HLA-PGD. We feel that an evaluation of the true clinical utility of HLA-PGD is timely and important so that prospective patients and medical practitioners can be informed accordingly. A database was set-up to facilitate retrospective (and potentially prospective) cohort studies to investigate aspects of PGD cycles which influence a positive outcome (birth of a genetically suitable donor-baby) and to investigate clinical outcomes of bone marrow transplant from PGD-selected donors. A good number of PGD centres have responded positively, but we would once more like to encourage centres that have not yet responded to do so.

The ESHRE PGD Consortium continues to promote a high standard of PGD. With your help and input we can make it work.

Edith Coonen
Chair ESHRE PGD Consortium

All set for first nurse/midwife certification exams in Lisbon

The Paramedical Board ran a very successful **Basic training course for Paramedics working in reproductive medicine** in Lisbon in March. This is the first time the course has been run in Portugal and 76 delegates attended. Feedback has been very positive and I would like to thank all the speakers and organisers for their support with this Campus course.

Lisbon will be the venue for the first Nurses and Midwives Certification examination which will be held on Saturday 13 June. Prospective candidates have submitted their Log Books and will have received notification by e-mail about the examination process. We wish all candidates the best of luck for the forthcoming examination.

Sadly, we will say goodbye to Jolieneke Schoonenberg-Pomper in Lisbon, who will come to the end of her second term on the Board. As a previous Chair, Jolieneke has been a great advocate for Paramedical members of the Society and has always worked hard for ESHRE. We are very pleased to say that she will continue to be involved as Chair of the steering committee for the Nurse and Midwife Certification Course, which she has helped to develop.

On that note I am delighted to tell you that Valerie Blanchet has been appointed to the Paramedical Board as a nurse representative. Her position will be confirmed at the Annual Meeting and we welcome her to our Board. Valerie was a member of the local organising committee for the basic training course held in Paris in May last year and I am sure she will be a very active board member.

As mentioned before, we are always keen to hear from ESHRE Paramedical Group members and would be pleased to see you at our AGM on Monday 15 June at 13.00. If there are any burning issues or topics which you would like us to address or courses that you feel would be valuable. please feel free to contact me directly.

Helen Kendrew (helen.kendrew@bathfertility.com)
Chair Paramedical Board

Go ahead for Europe-wide survey on oocyte cryopreservation

STEERING COMMITTEE

Françoise Shenfield (GB), Co-ordinator
Paul Devroey (BE), Deputy
Ana Pia Ferraretti (IT), Deputy
Virginie Rozée (FR), Junior Deputy

We are pleased to confirm that our European egg-freezing project in collaboration with EIM has started after its approval by the Executive Committee in January. It has taken a lot of energy during our first year of activity, to finalise the protocol and questionnaires. We are now gathering information on the statutory or practical requirements and status of current data collection for oocyte storage and their eventual use in most EU countries. Results are likely to be fairly heterogeneous and we hope the study will stimulate the prospective recording of data on the reasons and conditions for oocyte freezing in Europe, whether for medical or non-medical reasons.

Among the many questions raised are whether the technique will have an impact on the further postponement of child bearing, a theme which certainly has caught public attention. Indeed, the offer to their female work force by several companies may be considered a real social advance for women, or alternatively a ploy to ensure keeping them employed when young and productive.

Another international issue of great societal concern in our field is surrogacy, even though its European practice is also very heterogeneous, as many countries ban it. Our junior deputy Virginie Rozée, a sociologist, organised last November a meeting in Mumbai on cross-border socio-cultural issues in ART, with the special dimension of North-South interaction, or high-and-moderate income countries with low-income countries. In Europe, surrogacy is legal in the UK, Greece and the Netherlands, while unregulated but allowed in Belgium and the Czech Republic. In low income countries, commercial surrogacy looms large, and is used by many foreign citizens living in countries where the technique is either banned or regulated within 'non-commercial' boundaries.

The ethical issues concerning the possible intrumentalisation of women have already been well rehearsed (ESHRE TF Ethics & Law, FIGO), but the socio-cultural aspects are also worthy of more detailed analysis, which will appear in the planned publication related to the Mumbai meeting. Virginie further plans a meeting on surrogacy next year in Paris, and we are looking forward to a collaboration between our SIG and INED (the French National Institute of Demographic Studies).

We will also take part in a workshop organised by the SIGs Andrology and Ethics & Law next December in Leuven on **Donor sperm banking: medical, socio-cultural, ethical and legal considerations**, and a precongress course at the 2016 Annual Meeting in Helsinki with the SIG Early Pregnancy on **What happens in utero lasts a lifetime: A multi-disciplinary approach to improving preconception and early pregnancy care**.

We look forward to seeing many members at these forthcoming events, as well as to your feed-back and suggestions for future work.

Françoise Shenfield
Co-ordinator SIG Socio-Cultural Aspects of (In)fertility

Recurrent implantation failure on Lisbon agenda

A Campus meeting on **Old and new in reproductive endocrinology** took place in Helsinki in April. The programme covered the hormonal environment during pregnancy and early stages of reproductive development, from the fetal period to adulthood, with a focus on developmental disturbances of reproductive organs during early and late reproductive life.

This year's precongress course in Lisbon is titled **When IVF fails: optimal management of recurrent implantation failure**. The course will provide a critical appraisal on recurrent implantation failure, one of the most difficult problems in IVF for both patients and physicians.

Future activities

In 2016 the SIG RE is preparing two Campus events: one in Istanbul on **The ageing woman and her ovary**, for which the programme has already been finalised, and a joint workshop with the SIG Reproductive Surgery in Thessaloniki, which is currently in preparation. The Istanbul meeting aims to increase understanding in female reproductive changes across the lifespan, with current and future perspectives on treatment options for women of advanced reproductive age, and on the management of premature ovarian insufficiency and menopause.

The 2016 precongress course in Helsinki is titled **Managing the difficult IVF patient: Facts and fiction**. The course will provide a guide to managing the patient with advanced age, with extremely low or high BMI, and presenting with a thin endometrium. The course will also address recurrent implantation failure and conception complicated by medical disorders. Attention will also be given to controversial topics, such as the management of IVF patients with endometriomas or intramural fibroids as well as the prevention of discontinued IVF treatment.

Stratis Kolibianakis
Co-ordinator SIG Reprodcutive Endocrinology
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STEERING COMMITTEE

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Frank J. Broekmans (NL), Deputy
Daniela Romualdi (IT), Deputy
Terhi Piltonen (FI), Junior Deputy
Georg Griesinger (DE), Past Co-ordinator

Strong stem cell representation in Lisbon - despite competition

We have had some trepidation this year about stem cell abstract submissions to the Annual Meeting, Just a few days after Lisbon, the International Society for Stem Cell Research will hold its meeting - in Europe for the first time, and with high potential for low participation in ESHRE. So we are very happy to announce that this year we scored 35 abstracts in stem cell research for Lisbon, and that the quality of the work presented was very high, covering both pluripotent and progenitor cells, with a nice balance between basic and preclinical applied research.

Our precongress course ahead of the scientific sessions in Lisbon has been organised with the SIG Early Pregnancy and will cover the role of stem cells in the pathogenesis, modelling, and possible treatment of several aspect of early pregnancy, from Asherman's syndrome to altered placentation.

Steering committee

Our meeting in Lisbon will also mark a change in the constitution of the SIG SC. I will step down from my position as Co-ordinator, to be replaced by Björn Heindryckx from the University of Ghent. Björn has been a very active member in the SIG for the last two years, participating in all activities and committed to improving the visibility of stem cell research in ESHRE. Filippo Zambelli will move on from Junior Deputy to SIG Deputy, a very apt promotion given his energy and commitment. A new junior deputy will be elected shortly, following a round of nominations soon to be under way.

This is also the last report that I write as SIG Co-ordinator, and I wish to leave thanking those who made it possible - the staff at ESHRE's Central Office for their patience in explaining the workings of the Society, and all the member of the SIG for their trust and confidence in me. I would like to close by thanking my predecessors Karen Sermon and Anna Veiga for their strong commitments to stem cell research and leadership in the field. They have been a great support and their work has enabled the very existence of a vibrant stem cell community in ESHRE.

Rita Vassena
Co-ordinator SIG Stem Cells

STEERING COMMITTEE

Rita Vassena (ES), Co-ordinator
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Karen Sermon (BE), Past Co-ordinator

'Challenges in reproductive surgery' for Lisbon PCC

Meeting reports

The latest biannual endoscopy workshop was successfully completed in Leuven in March. Of particular interest were the several hours of live surgery performed by Stephan Gordts, Sylvie Gordts, Rudi Campo and Patrick Puttermans, which included cases of hysteroscopic treatment of T-shaped uterus, transvaginal laparoscopic laser ovarian drilling, and laparoscopic myomectomy. Participants had the opportunity to practice laparoscopic suturing and knot tying for several hours over the three days of the course under the direction of Sylvie Gordts and Yves Van Belle. Additional lectures were included on the topics of 2D and 3D assessment of the female pelvis, which has been gaining increasing popularity recently.

Our Campus workshop in Lyon on the 17-18 April on **Complications in endoscopic surgery** was organised by Deputy Co-ordinator Antoine Watrelot. Sessions included the incidence, prevention and management of different types of complications. A special interactive hot session on the second day of the programme on 'The obituary of myoma morcellation?' included a two-hour open panel discussion led by eight specialists in the field on the risks of leiomyosarcoma dissemination with its use. In the end, it was agreed that a joint ESGE-ESHRE statement on this issue would be released soon.

Meanwhile, the current consensus of the group appeared to be that there remains a role for laparoscopic myoma morcellation providing that appropriate risk stratification, patient selection and comprehensive counselling takes place.

Interactive live surgery performed by Rudi Campo, Stephan Gordts, Sylvie Gordts and Patrick Puttermans at the endoscopy workshop In Leuven.

Future events

This Campus meeting will be suitably followed up by our precongress course in Lisbon on **Challenging reproductive surgery**. Lectures will cover the ever popular topics of large myomas, massive cysts, severe Asherman's syndrome and deep endometriosis. The audience can expect several hours of interesting images and videos from renowned lecturers. In addition there will be four sessions dedicated to case presentations and open discussion with the audience, which promises much interesting debate.

Training and education

After a successful first year, the second round of our ESHRE certification programme for the Primary Level of Reproductive Surgery and the Master Level Reproductive Surgery will be taking place in Lisbon.

Meanwhile, we are glad to announce that the ECRES Websurg electronic platform will be going live soon. This will allow online registration, as well as an evaluation of participants through their e-Logbook and through the uploading of surgical procedures for reviewer scoring and feedback.

Sotirios Saravelos
Junior Deputy, SIG Reproductive Surgery

Third year of ECRES certification in Lisbon

The third session of the ECRES certification programme for reproductive endoscopic surgeons will take place during the Annual Meeting in Lisbon. This unique programme provides an opportunity to validate hysteroscopic and laparoscopic skills and experience, to establish status, and to join an elite group of specialists.

The objectives of the certification programme are to:

- **To improve knowledge and skills in reproductive endoscopic surgery**
- **To increase patient safety and reduce unnecessary cost**
- **To develop an educational curriculum on a long term basis, which will help training centres structure their courses according to a target audience and level**

The ESHRE certification for reproductive endoscopic surgeons is a two-track qualification, at Primary level and Master level. The online registrations for both tracks of the certification programme are available until 22 May 2015 (23.59 CET) or until the maximum number of participants has been reached. One of the requirements for acceptance for the exam in Lisbon is the ECRES Winners certificate through the Websurg platform, which can be accessed via www.eshre.eu/ecres/10steps

- **More information about the ECRES programme and the application procedure is available on our website at www.eshre.eu/ecres.**

More than 200 andrology abstracts submitted for Lisbon, with highlights in the main sessions

'My term as Co-ordinator of the SIG Andrology is coming to an end and a new Co-ordinator will be elected in Lisbon. It has been an exciting responsibility, with many interesting insights, not least that the world of andrology is multifaceted. In many European countries the field is clinically dominated, often by the specialty of urology. In other countries it is running primarily under the banners of dermatology, endocrinology, sexology, gynaecology or internal medicine. Only in a very few countries - especially in the Middle East - is andrology established as a self-standing clinical and research discipline. In ESHRE andrology is perceived primarily as spermatology. Thus, with ICSI the dominant ART treatment, one sperm per egg is considered enough, and the male partner is almost reduced to his ability to provide a limited number of gametes.

Lisbon programme

Our pre-congress course in Munich was on **Treating the man with evidence based medicine,** giving attention to the general health and wellbeing of the male partner. I still consider this an important priority and hope that ESHRE continues to promote the health of the male partner as an important goal.

After scoring more than 200 andrology abstracts submitted to this year's Annual Meeting, my impression of the scientific status of andrology is cause for a little concern. The majority of studies can best be regarded as observational, usually investigating sperm quality with a large array of systems and a number of exposures. Usually, these studies are retrospective analyses of a limited number of samples from an IVF setting, whose scientific validity is marginal, though conclusions often dramatic.

Despite my concerns, we still see outstanding and highly promising breakthroughs in our field - and Lisbon will bring us up-to-date with some of these exciting developments. Sperm enthusiasts will certainly enjoy our precongress course, titled **Keep the sperm in mind when perfecting ART: news and perspectives in spermatology**. This basic course deals with many clinical and translational aspects of sperm features and functions relevant for assisted fertilisation. Basic aspects of sperm biology will be matched with novel strategies for sperm analysis and an outlook on procedures for in vitro sperm production from pluripotent stem cells. A critical evaluation of tools and endpoints used for the evaluation of sperm quality provides a useful guide for all andrologists.

In the main programme several topics will provide exciting new insights. Nils Jörgensen from Copenhagen will consider one andrological topic which is of great concern to the public as well as to all of us. Is human semen quality deteriorating? His lecture is entitled **Human semen quality in the new millennium: prospective studies of semen quality in Europe and other countries**. His concerns will be underlined in a symposium on the 'impact of environmental toxins on reproductive health'.

'Risks and benefits of being male' is a symposium on the sex-specific aspects of meiotic failures and why males on average die younger than females. RAMAN spectroscopy as a new non-invasive approach to the analysis of sperm quality and features of living sperm, eggs and embryos will highlight a new scenario for the andrologist in a session on **ICSI and beyond**.

I am sure that for the andrology-oriented researcher and clinician Lisbon will prove a fantastic opportunity for updates on scientific progress, and that the presentations continue to create much enthusiasm in our field.

I also hope all SIG Andrology members join our business meeting on Sunday to learn more about our future plans and support those people who will take over responsibilities.

Most studies investigations of sperm quality.

Future events

Those interested in sperm banking have an important event in their calendar later this year. We have developed a Campus meeting in collaboration with other groups on **Donor sperm banking: medical, socio-cultural, ethical and legal considerations**, which will take place in Leuven, Belgium, from 10-11 December 2015. The subject of sperm banking has created much discussion among ART groups but also among regulatory bodies, so this course is highly relevant and presents an update on sperm banking systems and donor recruitment. The course will provide many insights but will also propose best practice procedures and guidance.

Stefan Schlatt
Co-ordinator SIG Andrology

The first ever evidence-based guidelines on psychosocial care in infertility

New guidelines

The ESHRE guidelines on *Routine psychosocial care in infertility and medically assisted reproduction – A guide for fertility staff* is now complete and approved by ESHRE's Executive Committee. The guidelines will be made available online on the ESHRE website and a summary of this document has been submitted for publication to *Human Reproduction*. These are the first ever evidence-based psychology and counselling guidelines within the infertility field. They offer best practice advice to all fertility clinic staff (doctors, nurses, midwives, counsellors, social workers, psychologists, embryologists, and administrative personnel) on how to incorporate psychosocial care into routine infertility care.

We would like to express our sincere thanks to Sofia Gameiro, chair of the guideline development group, Nathalie Vermeulen, ESHRE's guideline expert, and to members of the guideline development group for their continuing effort and dedication to bring this exciting new work to a good end. We hope the guidelines can make a difference in clinical practice and we will keep you updated on further efforts to implement the guidelines in daily practice.

Upcoming events

Our next event on our SIG calendar is the Annual Meeting in Lisbon where we will host a precongress course on **Global (in)fertility: cross-cultural challenges for counsellors**. Many of us are confronted in our clinical work with practice and beliefs in reproductive medicine which vary greatly between cultures, countries and even regions. This course will address issues on the meaning of parenthood in different cultures, with insight into the experience of infertility in both Western and non-Western societies. What do we need to know as counsellors and reproductive specialists? What are the current and future challenges as ART becomes increasingly global?

Late September 2015 (24-25th) will bring the SIG to Leuven, Belgium, for a collaborative Campus workshop with the SIG Endometriosis on **Sexual functioning in women dealing with infertility and/or endometriosis**. This workshop aims to provide an in-depth update on the interrelationship between sexual function, infertility and endometriosis. Though sexuality and reproduction are intrinsically linked and sexual function can be affected in patients with endometriosis, sexual function and sexual health remain difficult discussion topics in clinical practice.

Leuven will also be hosting another Campus event in December (11-12th) that will focus on donor sperm banking. The field of third party reproduction is ever-changing and this workshop will bring together medical, socio-cultural, ethical and legal considerations. The second day of the workshop will provide more in-depth issues concerning third party counselling. More detailed information on the course can be found on the ESHRE website: (http://new.eshre.eu/Calendar.aspx).

Steering Committee changes

Please mark your agendas with our business meeting in Lisbon which will take place at 5 pm after Sunday's pre-congress course. This is the time when we will announce the new Steering Committee and the current Co-ordinator will step down. This is also the place to discuss your ideas concerning our SIG and to meet the current and new Committee members. We are always open to suggestions concerning educational opportunities or exciting new research to present at annual meetings and value our members' input. So please let us know what we can do for you! We hope to see many of you in Lisbon soon.

Uschi Van den Broeck
Co-ordinator SIG Psychology and Counselling

STEERING COMMITTEE

Uschi Van den Broeck (BE), Co-ordinator
Cora de Klerk (NL), Deputy
Sofia Gameiro (GB), Deputy
Mariana Martins (PT), Junior Deputy
Christianne Verhaak (NL), Past Co-ordinator

Guidelines development group: From left standing, Christos Venetis (GR), Nathalie Vermeulen (ESHRE), Tewes Wischmann (DE), Chris Verhaak (NL), Eline Dancet (BE), Sofia Gameiro (GB, chair). Sitting, Marysa Emery (CH), Cora De Klerk (NL), Petra Thorn (DE), Jacky Boivin (GB), Uschi Van den Broeck (BE).

Synthetic babies

Public attitudes to IVF are still not universally approving

I'm wondering if our fertility nurses have dumped their Dolce & Gabbana. Have embryologists (yes, men as well) sent their D&G for recycling? Indeed, have we all, standing shoulder to shoulder with Elton, risen up in protest at the Italian designers' description of IVF babies as 'synthetic'.

Domenico Dolce had told an Italian magazine: ' . . . what I call children of chemistry don't convince me, synthetic children. Wombs for hire, [semen chosen] from a catalogue. And then you have to explain to this child who is the mother. To procreate ought to be an act of love.'

Elton John, who has two surrogate children with his partner David Furnish, was furious, and on his Instagram account retorted: 'How dare you refer to my beautiful children as "synthetic". And shame on you for wagging your judgemental little fingers at IVF - a miracle that has allowed legions of loving people, both straight and gay, to fulfil their dream of having children. Your archaic thinking is out of step with the times, just like your fashions. I shall never wear Dolce and Gabbana ever again. #BoycottDolceGabbana.'

Within minutes of the outburst, people had joined the protest and were posting pictures of their IVF babies in support of Elton. Tweeters included Victoria Beckham ('Sending love to Elton David Zachary Elijah & all the beautiful IVF babies'), and Martina Navratilova ('wow- I had no idea'). And within a few days around 50 protesters, some brandishing placards, had joined the boycott call outside the Dolce & Gabbana store in central London. 'Their comments are not only an attack on same-sex parents,' said one campaigner, 'but on all parents who've had children with the aid of fertility treatment, including thousands of heterosexual couples.'

As the stand-off overflowed into a media battle of principle (to boycott or not to boycott), Dolce appeared to temper his views somewhat - and the ever resourceful *Daily Mail* even found a quote from 2006 in which Stefano Gabbana, gay like Elton John, voiced a totally different tune on ART. 'I want my own child, a biological child,- he had told asn Italian newspaper, 'a fruit of my sperm, conceived through artificial insemination. . . '

Elton John: #BoycottDolceGabbana

It's second nature for all of us working in or around IVF to assume its universal acceptance. Indeed, one conclusion to emerge from our legislation and reimbursement survey reported on page 22 is an ever increasing regulatory homogeneity throughout Europe. The deconstruction of Italy's restrictive Law 40 was, as Benagiano et al have implied, in response to legal challenges brought by members of the public.[1] For even in Italy, where in 2004 the Catholic church was instrumental in blocking the outcome of a national referendum on Law 40, public attitude seems now to have fallen largely in favour of IVF, despite the outbursts of D&G. An interesting editorial commentary in *RBM Online* on the Italian situation attributes this homogenisation of attitude (and of clinical practice) to the levelling power of public will.[2]

Yet clearly there remain dissidents. The unsuccessful (but vocal) One Of Us campaign of 2014 to restrict EU funding on stem cells was largely driven by pro-life groups. And it is still the same pro-lifers who offer token condemnation of most legitimate developments in IVF. Progress in Poland towards any legislation in IVF has been mainly thwarted by the public role of the Catholic church. Yet the Twitterers seem to find no offence in such 'political' attitudes, so why are they shocked when similar sentiments are aired by celebrity couturiers, however hauts they may be.

Simon Brown
Focus on Reproduction

1. Benagiano G, Filippi V, Sgargi S, Gianaroli L. Italian Constitutional Court removes the prohibition on gamete donation in Italy. Reprod Biomed Online 2014; 29: 662-664.
2. Ahuja KK. Patient pressure: is the tide of cross-border reproductive care beginning to turn? Reprod Biomed Online 2015, Jan 27 [Epub ahead of print].

focus on REPRODUCTION

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