



**The British  
Fertility Society  
Annual Meeting 2004**

**30 March - 2 April 2004**

The Cheltenham Ladies' College, Cheltenham

[www.fertility.org.uk/meetings/annual](http://www.fertility.org.uk/meetings/annual)

# Programme

**AND ABSTRACTS**

This event, activity code number 20716 has been approved for external credit for the CPD scheme of the Federation of the Royal Colleges of Physicians of the UK.

**Valid for RCOG credit**



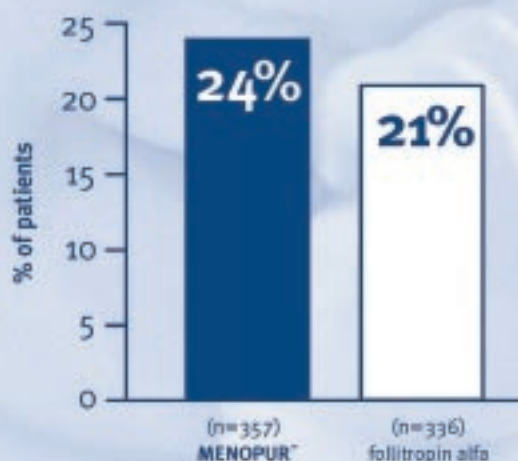
# Menopur™

menotrophin

A balanced choice

Menopur™ delivers pregnancy rates at least as good as rFSHα<sup>\*1</sup>

Ongoing pregnancy rates  
10 weeks after ovum pick-up<sup>1</sup>



\* follitropin alfa

#### Reference

1. European and Israeli Study Group on Highly Purified Menotrophin vs. Recombinant Follicle-Stimulating Hormone. *Fertility and Sterility* 2002; 78(3): 520-528.

#### MENOPUR™ PRESCRIBING INFORMATION

**Presentation:** Menopur is presented as a vial containing 75IU menotrophin BP. Also contains lactose, polysorbate 20, sodium hydroxide and hydrochloric acid. Supplied with diluent ampoules of sodium chloride solution for injections 0.9% w/v. **Indications:** **Anovulatory women:** Menopur can be used to stimulate follicle development in anovulatory women who are unresponsive to clomiphene citrate or a similar ovulation induction agent. Women undergoing superovulation within a medically assisted fertilisation programme. Menopur can be used to induce multiple follicular development in women undergoing an assisted conception technique such as in-vitro fertilisation (IVF). **Hypogonadotropic hypogonadism in men:** Menopur may be given in combination with hCG for the stimulation of spermatogenesis. **Dosage and administration:** Menopur is administered by subcutaneous or intramuscular injection. In the female: **Anovulatory infertility:** In menstruating women Menopur should be started within the first 7 days of the cycle. Treatment is determined by response, as assessed by oestrogen excretion or ultrasound. A typical regimen starts at 75 to 150IU daily or alternatively, three equal doses, each providing 225 to 375IU on alternate days. Treatment may be adjusted until an adequate response is achieved. Treatment should be abandoned if there is no response within 3 weeks. The treatment cycle may be repeated at least twice more if necessary. When adequate pre-ovulatory oestrogen levels have been reached, Menopur treatment is stopped and ovulation is induced by administration of a single injection of hCG, 5,000-10,000IU. If oestrogen levels rise too rapidly, the dose should be decreased. **Superovulation within a medically assisted fertilisation programme:** In assisted conception techniques, Menopur is used with hCG and sometimes clomiphene citrate or a gonadotrophin agonist. Stimulation of follicular growth is produced by Menopur in a daily dose providing 75 to 300IU. Treatment is continued until an adequate response is obtained. The final injection of menotrophin is followed 1-2 days later with hCG, up to 10,000IU. Spermatogenesis is stimulated with hCG (1,000-2,000IU two to three times a week) and then Menopur is given in a dose of 75 or 150IU two or three times weekly. Treatment should be continued for at least 3 or 4 months. **Contraindications:** Pregnancy;

enlargement of the ovaries or cysts not due to polycystic ovarian syndrome; gynaecological bleeding of unknown cause; tumours in the uterus, ovaries, breasts, or testes; carcinoma of the prostate; structural abnormalities in which a satisfactory outcome cannot be expected (unless superovulation is to be induced for IVF); ovarian dysgenesis; absent uterus or premature menopause. **Precautions:** The following conditions should be properly treated and excluded as the cause of infertility before Menopur therapy is initiated: dysfunction of the thyroid gland and cortex of the suprarenal glands; hyperprolactinaemia; primary ovarian failure and tumours in the pituitary or hypothalamic glands. Ovarian hyperstimulation syndrome may develop in some cases. This may be minimised by careful monitoring and withholding hCG. Patients undergoing superovulation may be at an increased risk of developing hyperstimulation in view of the excessive oestrogen response and multiple follicular development. Aspiration of all follicles prior to ovulation may reduce the incidence of hyperstimulation syndrome. Cases of ectopic pregnancy have been reported in women receiving menotrophin who have undergone assisted conception although no causal relationship to the use of menotrophin has been established. A predisposing factor for ectopic pregnancy is tubal disease/occlusion from which these patients may already be suffering. **Side effects:** Treatment with menotrophin can lead to ovarian hyperstimulation, which mostly becomes clinically relevant only after hCG has been administered to induce ovulation. Treatment should be immediately discontinued when hyperstimulation has been detected. Other adverse effects are nausea and vomiting and, rarely, fever and joint pain, hypersensitivity reactions (skin rash) and local reactions at the site of injection. In very rare cases, long-term use can lead to the formation of antibodies making treatment ineffective. There is an increased risk of miscarriage and multiple pregnancies with menotrophin therapy. **Pharmaceutical precautions:** Store at a temperature not exceeding 25°C, protected from light. **Package quantities:** 10 vials of Menopur together with 10 ampoules of sodium chloride solution for injections 0.9% w/v. **NHS Price:** £140 per pack of 10 vials. **Legal category:** POM. **Marketing Authorisation numbers:** Menopur PL 03194/0074. Sodium chloride solution for injections 0.9% w/v PL 03194/0060. **Name and address of Marketing Authorisation holder:** Ferring Pharmaceuticals Ltd., The Courtyard, Waterside Drive, Langley, Berkshire SL3 6EZ. **Date of preparation:** April 2005. Menopur is a trademark. Further information is available on request from: Ferring Pharmaceuticals Ltd, The Courtyard, Waterside Drive, Langley, Berkshire SL3 6EZ Telephone: 07533 214800.





**The British  
Fertility Society  
Annual Meeting 2004**

**30 March - 2 April 2004**

The Cheltenham Ladies' College, Cheltenham

# Programme



## Welcome

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I am delighted, as Chairman of the Meetings' Subcommittee, to welcome you to the Annual BFS Meeting in Cheltenham. This is the first time the new BFS policy of organising all meetings without a Local Organising Committee will have been tried and it certainly is trying those of us responsible! I believe, however, that we have found a superb venue in the Cheltenham Ladies' College. The town is a magnificent and compact setting for a conference. The College has a wonderful campus and transport links by road, rail and air are all easily accessible.

The programme is highly varied and caters for all, from the most scientific scientist to the most patient-orientated counsellor. We will have plenary sessions on, amongst other topics, the production of gametes from stem cells, PCOS and complementary therapy. We will have professionally aligned (but not exclusively) parallel sessions on surgery, nursing, counselling and laboratory issues and the usual panoply of prize sessions. Our HJ Jacob President's Lecturer is David de Kretser and our Steptoe Lecturer Stephen Hillier – two superb world-class sessions in the making.

Socially, we will have the usual Opening Reception. On Wednesday night the BFS Pleasure Dome will rival anything Kubla Kahn produced: be surprised. The Annual Dinner will be a culinary feast and afterwards tie your legs in knots with the help of the... Jazz Band!

I hope you will join us in Cheltenham: we believe this will be a great meeting.

**Professor Neil McClure**  
*CHAIR, Meetings' Subcommittee*

### **Conference Secretariat**

BioScientifica  
Euro House  
22 Apex Court  
Woodlands  
Bradley Stoke  
Bristol BS32 4JT, UK

Contact: Lisa Tandey and Juliet Need  
Tel: +44 (0) 1454 642217  
Fax: +44 (0) 1454 642222  
Email: [conferences@endocrinology.org](mailto:conferences@endocrinology.org)  
Web site: <http://www.bioscientifica.com>

# General Information

## Venue

The whole of the conference will take place in the unique facilities of Cheltenham Ladies' College, which is situated in the heart of Cheltenham's lively city.

## Cheltenham

Cheltenham is the most complete Regency town in England and one of the few English towns in which traditional and contemporary architecture complement each other.

Cheltenham has a vibrant, attractive town centre with a long standing reputation for quality shopping and an indefinable air of elegance. It is also an important town centre internationally, nationally and regionally, serving an extensive catchment area in central and eastern Gloucestershire and the South Midlands.



## Travel to Cheltenham

**By Road:** Situated at junctions 10, 11 and 11a of the M5, Cheltenham lies within the main motorway network and the important London, Bristol, Birmingham triangle. Visit [www.nationalexpress.com](http://www.nationalexpress.com) for long distance bus and coach services. The Ladies' College is in the centre of Cheltenham near the Town Hall and Promenade.

**By Rail:** Cheltenham Spa is well served by InterCity and British Rail Regional Railways, including direct services from London Paddington, Bristol, Birmingham, Swindon, Cardiff, Plymouth, Manchester, Leeds, Edinburgh and Glasgow. Visit [www.firstgreatwestern.co.uk](http://www.firstgreatwestern.co.uk) and [www.railtrack.co.uk](http://www.railtrack.co.uk) for rail information.

**By Air:** London Heathrow is 86 miles from Cheltenham with a drive time of 2 hours. There is a regular direct coach service with National Express and a rail/bus link via Reading.

Birmingham International and Bristol Airports - are less than 50 miles from Cheltenham with easy road access.

Gloucestershire Airport - Cheltenham's local airport is only 4 miles from the town and offers aircraft for charter, including HS125 jets and helicopters.

Road mileages to Cheltenham as provided by the AA Route master:

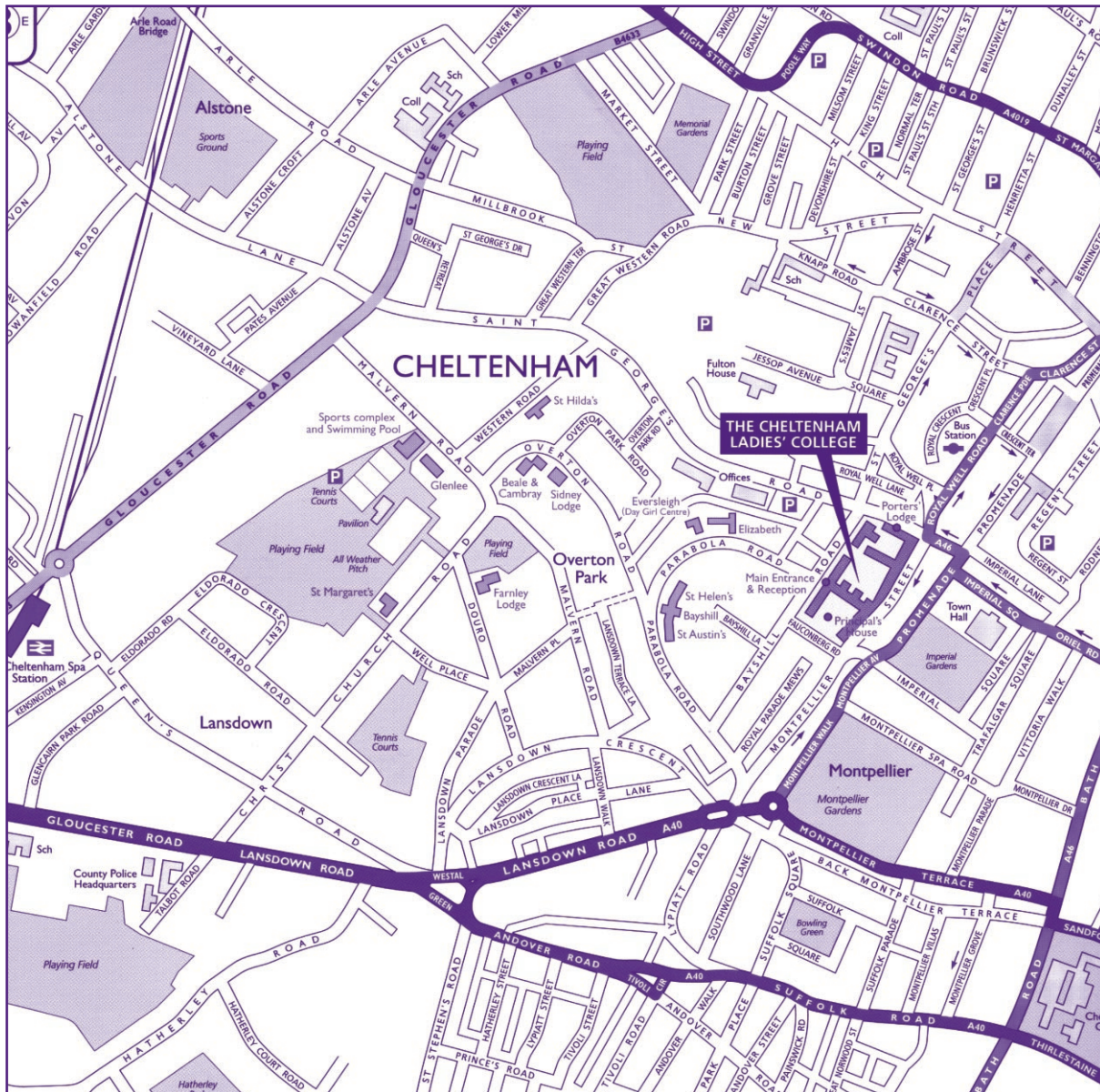
London Heathrow	86
Birmingham	56
Bristol	42
Cardiff	66
Gloucester	9
Manchester	122
Oxford	41
Portsmouth	93
Swindon	30
Worcester	24

## Parking

Parking within the grounds of the Cheltenham Ladies' College is limited, so we recommend that you park your car at your hotel. Most of the hotels we have recommended are all within easy walking distance of the conference venue.

# General Information

## Location map of The Cheltenham Ladies' College





## Meeting Information

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### Registration

On-line registration is available on the conference website at: [www.fertility.org.uk/meetings/acebfs04/](http://www.fertility.org.uk/meetings/acebfs04/) as well as via the enclosed registration form.

The registration desk will be open on Tuesday 30 March 2004 from 16.00 hours for registration for the start of the meeting then throughout the meeting from 08.00 until 18.00 on Wednesday 31 March and from 08.00 until 18.00 on Thursday 1 April from 08.00 until 15.00.

Reduced registration fees and discounted tickets to social events are available for postgraduate students who will be able to register at the student rate if evidence of student status is countersigned by the applicant's head of department. Please refer to the enclosed registration form for further information.

### Name Badges

On arrival please ensure you collect your appropriate badge. Red for speakers, blue for chairs, yellow for delegates and green for exhibitors.

### Poster Sessions

Posters will be on display during the entire meeting. There will be a poster-viewing session on Wednesday 31 March at 17.45 in the Garden Common Room and during the coffee and lunch breaks.

### The Annual General Meeting of the BFS

The BFS AGM will take place on Wednesday 31 March 2004 at 12.20-12.45 in the Princess Hall.

### Awards

Award presentations will be held at various points throughout the meeting. Prizes will be given out at the conference dinner.

### Commercial Exhibition

The exhibition will be open from 16.00 until 20.00 on Tuesday 30 March and at 08.30 until 18.00 on Wednesday 31 March and Thursday 1 April and at 08.30 until 15.00 on Friday 2 April.

### CPD Approval

CPD approval from the Federation of the Royal College of Physicians of the UK has been given for this meeting. Delegates may claim 12 points for full attendance of the meeting. If you want to claim your CPD points you must sign the register on the registration desk at the meeting before 12.30 on Friday 2 April. You will need your GMC number.

### Catering

Tea and coffee will be available during scheduled breaks throughout the meeting. Lunches will be served in the exhibition hall and are included in the cost of registration for each day. Please indicate your lunch requirements in advance using the online or paper registration form.

### Social Programme

The meeting will be opened formally on the evening of Tuesday 30 March 2004 with a Welcome Reception, kindly supported by Serono, held in the Lower Hall followed by the Exhibition Hall. This welcome evening is an opportunity to meet old (and new) friends amongst the exhibition and scientific posters.

#### Wednesday 31 March 2004

This social event promises to be an extraordinary and entertaining evening in the Princess Hall at the Cheltenham Ladies' College. Tickets cost £25.00 and will be required. We recommend that you book early to avoid disappointment. Tickets will include drinks, a medley of foods from around the world, side shows, stalls and surprise stage performances.

#### Thursday 1 April 2004

To close the Annual BFS 2004 meeting, all delegates are invited to dinner at Edwards Hall.

Tickets cost £45.00 and will be required. We recommend that you book these when you register for the meeting as there will be a very limited number available at the meeting. Your ticket includes a welcome drink, drinks during dinner, a delicious three course meal as well as entertainment and dancing. A pre-dinner drinks reception will be held at 19.00 in the Princess Hall. Transport will be provided to the dinner from the Cheltenham Ladies' College and selected hotels – last bus returning will leave at midnight. In addition, prizes will be presented during the evening.

Dress smart, not black tie.



# Programme

## Tuesday 30 March 2004

- 16.00 Registration**
- 19.00 - 20.00 Welcome Reception**  
*Generously supported by Serono*  
 LOWER HALL, CHELTENHAM LADIES' COLLEGE  
**Welcome speech**  
*Mr Leslie Kent, Head of Biology,*  
*The Cheltenham Ladies' College*

## Wednesday 31 March 2004

- 08.00 - 09.00 Registration**  
 MAIN ENTRANCE
- 09.00 - 09.05 Welcome and Housekeeping**  
 PRINCESS HALL  
*Alison Murdoch (Chairperson, BFS)*  
*and Neil McClure (Chair, BFS)*  
*Meetings' Subcommittee)*
- 09.05 - 10.50 Organon Symposium**  
 PRINCESS HALL  
**Stem Cell Biology**  
*Chair: Harry Moore (Sheffield)*  
**Stem Cells: An Overview**  
*Stephen Minger (London)*  
**Gametes from Stem Cells**  
*Niels Geijzen (Massachusetts, USA)*  
**Embryo Donation for Research**  
*Erica Haimes (Newcastle)*
- 10.50 - 11.20 COFFEE**  
 EXHIBITION HALL
- 11.20 - 12.20 Patrick Steptoe Memorial Lecture**  
 PRINCESS HALL  
*Chair: Alison Murdoch (Chairperson, BFS)*  
*Stephen Hillier (Edinburgh)*
- 12.20 - 12.45 BFS AGM**  
 PRINCESS HALL  
*Chair: Alison Murdoch (Chairperson, BFS)*
- 12.20 - 13.45 LUNCH**  
 EXHIBITION HALL
- 13.45 - 15.45 PARALLEL SESSIONS**
- Nursing**  
 COUNCIL ROOM  
*Chair: Heidi Birch (Birmingham)*  
**Setting the Scene: RCN-FNG**  
**Nursing Competencies**  
*Maggy Wallace (Newbury)*  
**The Need for Nurse Inspectors**  
*Helen Kendrew (Bath)*  
**The Future of Nursing -**  
**Where we want to be**  
 TBC

- Psychosocial**  
 WEST WING HALL  
*Chair: Sheila Pike (Sheffield)*  
**Where Infertility Meets Genetics –**  
**Where is the Patient in all of this?**  
*Sandy Raeburn (Oman), Paul Brennan*  
*(Middlesborough) and*  
*Arlene Raeburn (Edinburgh)*

- Embryology & Andrology**  
 MUSIC ROOM  
*Chair: Allan Pacey (Sheffield)*  
**Proteomics to Study Sperm**  
**Function and Dysfunction**  
*Ian Brewis (Cardiff)*  
**The Genetic and Cytogenetic**  
**Basis of Male Infertility**  
*Darren Griffin (Brunel)*  
**Fads and Foibles**  
*Geraldine Hartshorne (Coventry)*

- Medical - Fibroids**  
 LOWER HALL  
*Chair: Geoffrey Trew (London)*  
**Cochrane Database and Fibroids**  
*Inez Cooke (Belfast)*  
**Embolisation and Fertility**  
*Peter Ellis (Belfast)*  
**Endoscopic Management of**  
**Fibroids**  
*Ertan Saridogan (London)*  
**Myomectomy**  
*Tin-Chiu Li (Sheffield)*

- 15.45 - 16.15 Afternoon Tea**  
 EXHIBITION HALL
- 16.15 - 17.45 FREE COMMUNICATIONS**
- Best Young Scientist Prize Session**  
 LOWER HALL  
*Chair: Lisa Thurston (London)*  
**Canadian Nurse Exchange**  
**Prize Session**  
 COUNCIL ROOM  
*Chair: Debbie Barber (Oxford)*  
**Best Abstract for Counselling and**  
**Psychological Aspects of Infertility**  
**and Reproductive Medicine Session**  
 WEST WING HALL  
*Chair: Sheila Pike (Sheffield)*

- 17.45 Poster Session**  
 GARDEN COMMON ROOM
- 19.30 - 22.00 A Night at the Pleasure Dome**  
 PRINCESS HALL, CHELTENHAM LADIES' COLLEGE



# Programme

## Thursday 1 April 2004

**08.00 - 09.00 Registration**

**09.00 - 09.05 Housekeeping**

*Neil McClure (Chair, BFS Meetings' Subcommittee)*

**09.05 - 10.05 Serono Symposium  
Polycystic Ovarian Syndrome**

PRINCESS HALL

*Chair: Neil McClure (Chair, BFS Meetings' Subcommittee)*

**The ESHRE/ASRM Consensus**

*Adam Balen (Leeds)*

**Novel Approaches to  
Ovulation Induction**

*Roy Homburg (Amsterdam,  
The Netherlands)*

**10.05 - 10.30 COFFEE**

EXHIBITION HALL

**10.30 - 12.30 PLENARY SESSION 3**

**Hazards or Hype**

PRINCESS HALL

*Chair: Adam Balen (Leeds)*

**Embryo Freezing**

*Maureen Wood (Aberdeen)*

**Blastocyst Culture**

*Lorraine Young (Nottingham)*

**ICSI**

*Willem Verpoest (Belgium)*

**12.30 - 14.00 LUNCH**

EXHIBITION HALL

**14.00 - 14.30**

**Canadian Nurse Exchange  
Prize Winner Lecture**

PRINCESS HALL

*Chair: Alison Murdoch (Chairperson, BFS)  
Diane Tkalec (Montreal, Canada)*

**14.30 - 15.00**

**Fertility Society of Australia  
Prize Lecture**

PRINCESS HALL

*Chair: Alison Murdoch (Chairperson, BFS)  
Neil Johnson (Auckland, New Zealand)*

**15.00 - 15.30**

**AFTERNOON TEA**

EXHIBITION HALL

**15.30 - 17.00**

**FREE COMMUNICATIONS**

**Best Young Clinician Prize Session**

LOWER HALL

*Chair: Ian Cooke (Sheffield)*

**Female Issues in Infertility**

COUNCIL ROOM

*Chair: Mark Hamilton (Aberdeen)*

**BICA Workshop**

WEST WING HALL

*Chair: Arlene Raeburn (Edinburgh)*

**Living with Uncertainty – The  
Legacy of Male Factor Infertility**

*Sheila Pike (Sheffield)*

*and Kate Grieve (Coventry)*

**19.00**

**Pre-Dinner Drinks**

PRINCESS HALL, CHELTENHAM LADIES' COLLEGE

**19.30**

**Carriages to Edward's Hall,  
Cheltenham**

**Gala Dinner**

EDWARD'S HALL



# Programme

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## Friday 2 April 2004

**09.00 - 09.05 Housekeeping**

**09.05 - 09.50 Ferring Symposium Debate**  
PRINCESS HALL

'Complementary Therapies are Valid Options in the Treatment of Infertility.'

*Chair: Richard Kennedy (Coventry)*

*For: Michael McIntyre (Oxford)*

*Against: Steve Smith (Glasgow)*

**09.50 - 10.50 Ferring Symposium**

Accreditation - are you up to it?  
PRINCESS HALL

*Chair: Richard Fleming (Glasgow)*

Quality in Tissue Banking and ART  
*Richard Fleming (Glasgow)*

The Impact and Implications of the European Framework  
*Alison Murdoch (Newcastle)*

Introduction of Quality to the Laboratory  
*Cecilia Sjoblom (Nottingham)*

**10.50 - 11.20 COFFEE**  
EXHIBITION HALL

**11.20 - 12.20 PARALLEL SESSIONS**

## Research Design

COUNCIL ROOM

*Chair: Steve Smith (Glasgow)*

Statistical Analysis and Pseudo-analysis

*David Torgerson (York)*

Ethical Approval – A Nightmare of Bureaucracy

*Terry McMurray (Belfast)*

## Ethical Conundrums

LOWER HALL

*Joanne McManus (Belfast)*

## Sperm in a World of Drugs

MUSIC ROOM

*Chair: David de Kretser (Australia)*

Cannabinoids and the Body

*Roger Pertwee (Aberdeen)*

Recreational Drugs and Fertility

*Sheena Lewis (Belfast)*

Smoking, Alcohol and Sperm Function

*Michael Zitzmann (Germany)*

**12.20 - 13.20 HS Jacob's President's Lecture**

PRINCESS HALL

*Chair: Ian Cooke (Sheffield)*

*David de Kretser (Australia)*

**13.20 - 14.20 LUNCH**

EXHIBITION HALL

**Close**



# Timetable - Wednesday 31 March 2004

	PRINCESS HALL	COUNCIL ROOM	LOWER HALL	WEST WING HALL	MUSIC ROOM
08.00	<b>REGISTRATION</b> (FOYER)				
08.15					
08.30					
08.45					
09.00					
09.00	<b>WELCOME &amp; HOUSEKEEPING</b>				
09.15	<b>Organon Symposium:</b> Stem Cell Biology				
09.30					
09.45					
10.00					
10.15					
10.30					
10.45					
11.00	<b>COFFEE</b> (EXHIBITION HALL)				
11.15					
11.30	<b>Patrick Steptoe Memorial Lecture</b> Stem Cell Biology				
11.45					
12.00					
12.15					
12.30	<b>BFS AGM</b>	<b>LUNCH</b> (EXHIBITION HALL)			
12.45					
13.00					
13.15					
13.30					
13.45	<b>Plenary Session:</b> Nursing		<b>Plenary Session:</b> Medical - Fibroids	<b>Plenary Session:</b> Psychosocial	<b>Plenary Session:</b> Embryology & Andrology
14.00					
14.15					
14.30					
14.45					
15.00					
15.15					
15.30					
15.45					
16.00	<b>AFTERNOON TEA</b> (EXHIBITION HALL)				
16.15					
16.30		<b>Free Comms:</b> Canadian Nurse Exchange Prize Session	<b>Free Comms:</b> Best Young Scientist Prize Session	<b>Free Comms:</b> Best Abstract for Counselling & Psychological Aspects of Infertility and Reproductive Medicine	
16.45					
17.00					
17.15					
17.30					
17.45	<b>POSTER SESSION</b> (GARDEN COMMON ROOM)				
Evening		<b>A Night at the Pleasure Dome</b> PRINCESS HALL, THE CHELTENHAM LADIES' COLLEGE			



# Timetable - Thursday 1 April 2004

	PRINCESS HALL	COUNCIL ROOM	LOWER HALL	WEST WING HALL	MUSIC ROOM
08.00	<b>REGISTRATION</b>				
08.15	<i>(FOYER)</i>				
08.30					
08.45					
09.00	<b>HOUSEKEEPING</b>				
09.15	<b>Serono Symposium:</b>				
09.30	Polycystic Ovarian Syndrome				
09.45					
10.00					
10.15	<b>COFFEE</b>				
10.30	<i>(EXHIBITION HALL)</i>				
10.45	<b>Plenary Session 3</b>				
11.00	Hazards or Hype				
11.15					
11.30					
11.45					
12.00					
12.15					
12.30	<b>LUNCH</b>				
12.45	<i>(EXHIBITION HALL)</i>				
13.00					
13.15					
13.30					
13.45					
14.00	<b>Canadian Nurse Exchange</b>				
14.15	Prize Winner Lecture				
14.30	<b>Fertility Society of Australia</b>				
14.45	Prize Lecture				
15.00	<b>AFTERNOON TEA</b>				
15.15	<i>(EXHIBITION HALL)</i>				
15.30					
15.45		<b>Free Comms:</b>	<b>Free Comms:</b>	<b>BICA</b>	
16.00		Female Issues	Best Young	<b>Workshop</b>	
16.15		in Infertility	Clinician Prize		
16.30			Session		
16.45					
17.00					
17.15					
17.30					

Evening

**Pre-Dinner Drinks – 19.00**  
*PRINCESS HALL, CHELTENHAM LADIES' COLLEGE*

**Gala Dinner – Carriages at 19.30**  
*EDWARD'S HALL, CHELTENHAM*

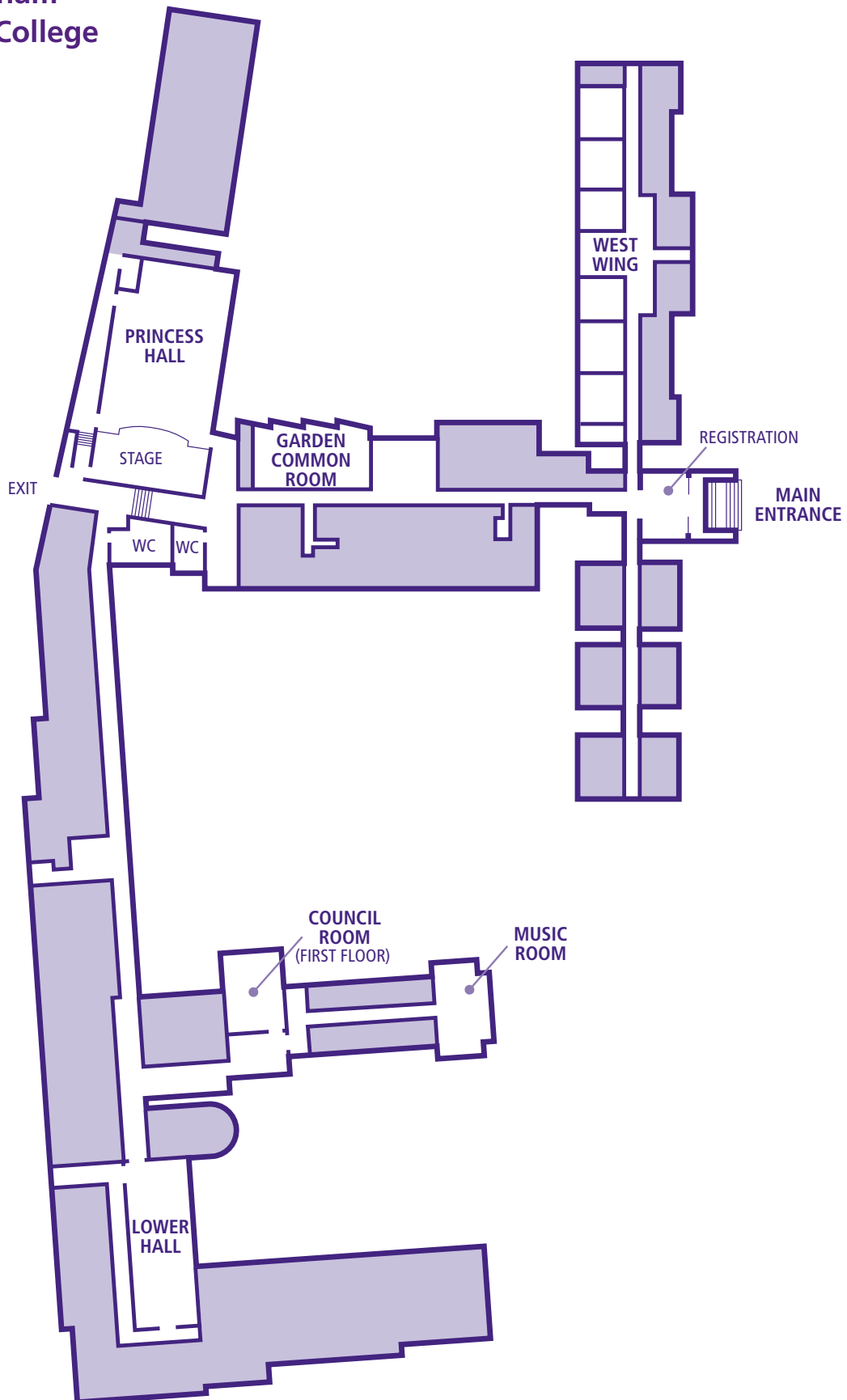


# Timetable - Friday 2 April

	PRINCESS HALL	COUNCIL ROOM	LOWER HALL	WEST WING HALL	MUSIC ROOM
08.00	<b>REGISTRATION</b> (FOYER)				
08.15					
08.30					
08.45					
09.00	<b>HOUSEKEEPING</b>				
09.15	<b>Ferring Symposium Debate:</b> Complementary Therapies are Valid Options in the Treatment of Infertility				
09.30					
09.45					
10.00	<b>Ferring Symposium:</b> Accreditation - are you up to it?				
10.15					
10.30					
10.45					
11.00	<b>COFFEE</b> (EXHIBITION HALL)				
11.15					
11.30		<b>Parallel Session:</b> Research Design	<b>Parallel Session:</b> Ethical Conundrums		<b>Parallel Session:</b> Sperm in a World of Drugs
11.45					
12.00					
12.15					
12.30	<b>HS Jacob's President's Lecture</b>				
12.45					
13.00					
13.15					
13.30	<b>LUNCH</b>				
13.45					
14.00					
14.15					
14.30					
	<b>CLOSE OF MEETING</b>				

# Floor Plan

## Cheltenham Ladies' College



## Speaker Abstracts

### S1

#### Derivation, Characterisation and Differentiation of Human Embryonic Stem Cells

Stephen Minger, Peter Braude, Minal Patel, Hannah Taylor and Susan Pickering

There has been intense interest in the potential therapeutic application of human embryonic stem (ES) cells. However, only a limited number of human ES cell lines throughout the world have been derived and characterised, and many of these are difficult to propagate. Under license from the Human Fertilisation and Embryology Authority and with ethical approval from King's College London, we have been endeavouring to generate new human ES cell lines. We have recently derived a novel human ES cell line, WT-3, that expresses a number of characteristic genes and proteins indicative of human ES cells, including Oct-4, Nanog, SSEA-3 and SSEA-4. These cells also differentiate into cells of all three primitive germ layers, including cells that express characteristic markers of neurons, liver cells, pancreatic beta cells, muscle and heart tissue. We have also established two additional new human ES cell lines, one of which was derived from an embryo screened by preimplantation genetic diagnosis and shown to harbour Cystic Fibrosis. This line represents the first known human ES cell line containing a known genetic lesion, which should provide a valuable resource for biomedical research,

#### REFERENCES:

Pickering SJ, Braude P, Patel M, Burn CJ, Bolton V, Minger S. 2003. Preimplantation genetic diagnosis as a novel source of embryos for stem cell research. *Reprod BioMed*, 7, 353-364.

### S2

#### Semenal discoveries and embryonic stem cells

N Geijsen

*Massachusetts General Hospital, Center for Regenerative Medicine and Technology.*

ES cells hold great promise for future treatment of human degenerative disease. ES cells are totipotent, they can be expanded indefinitely and can be directed to differentiate into a number of cell-types with potential therapeutic value in vitro. We and two other groups have recently demonstrated that ES cell cells can also be coaxed to form germ cells in vitro (1-3). In a groundbreaking paper, Hubner et al demonstrated that when ES cells are grown in monolayer culture in the absence of the anti-differentiation factor LIF, they form primordial germ cells that differentiate into aggregates resembling primordial follicles (2). These structures we shown to contain oocytes surrounded by stromal supporter cells. Remarkably, both female as well as male ES cells yielded oocytes in these experiments. This demonstrates that when cellular communication is confined to the two-dimensional monolayer culture, primordial germ cells enter the 'default' pathway of female differentiation. Here we compare this data to our own recent studies on ES cell differentiation toward the male lineage. When ES cells are cultured in three-dimensional structures called Embryoid Bodies (EBs), the induction of embryonic germ layers is faithfully recapitulated (4). In the context of EB differentiation, the fate of numerous cell types is specified in a choreographed, stepwise process (5) and therefore EBs provide a means to investigate otherwise inaccessible cell populations of the early murine embryo. Utilizing the EB differentiation system we were able to demonstrate the in vitro development of male gametes from ES cells. We will discuss these results and the implications they might have for future research and treatment of infertility.

#### LITERATURE:

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## Speaker Abstracts

### S3

#### Studying potential embryo donors' views on stem cell therapies

E Haines

PEALS, Newcastle, UK.

Embryo experimentation has raised many ethical questions but has been established as an acceptable practice in the UK by the Human Fertilisation and Embryology Act 1990. Developments such as preimplantation genetic diagnosis (PGD) and embryonic stem (ES) cell research have raised additional questions. Nonetheless, PGD is regarded as having much to offer families confronted with the possibility of a child affected by a serious genetic disorder and ES cell research promises much for therapeutic interventions in conditions resulting from the degeneration of certain cell types (e.g. Alzheimer's, Parkinson's). However, both PGD and ES cell research require further research and are dependent on IVF couples to donate their spare embryos for that research. Rarely is the role of these donors acknowledged let alone studied. One aspect of particular concern is whether couples feel under any obligation to donate embryos because of their gratitude for the IVF treatment they have received.

This paper will report on, and put in a wider context, an ongoing study that is investigating the similarities and differences between the views and values of those IVF couples who agree to donate embryos for research and those who refuse to donate embryos, in order to assist practitioners and policymakers in assessing the social and ethical contexts of this very important aspect of current and future scientific developments.

### S4

#### Ovulation, inflammation and innovation

SG Hillier [1], MT Rae [1], D Niven [1], HODC Critchley [1], CR Harlow [1], PYK Yong [2] & KJ Thong [2]

[1] Centre for Reproductive Biology, University of Edinburgh, Edinburgh, UK; [2] Assisted Conception Programme, Royal Infirmary of Edinburgh, Edinburgh, UK.

Before the introduction of laparoscopic oocyte collection for IVF, pioneered by Patrick Steptoe, all human life depended on ovulation, and most still does. The monthly release of a fertilisable egg by the ovary is one of nature's wonders, whose complexity is only now being unravelled by the tools of postgenomic science. As a consequence of the 400 or so ovulations they normally undergo, women's ovaries are highly prone to malignant and non-malignant disease. Greater than 90% of ovarian cancers in women are believed to originate in the ovarian surface epithelium OSE. The OSE is subject to serial injury and repair as it is breached during ovulation, which is a natural inflammatory process. It follows that a compensatory anti-inflammatory mechanism exists, possibly involving locally produced steroid hormones. Using gene-array analysis we have determined the steroidogenic signatures of 'inflamed' and 'uninflamed' human OSE cells cultured in the presence and absence of interleukin-1a (IL-1a), a pro-inflammatory cytokine produced during ovulation. We find 11 $\beta$ hydroxysteroid dehydrogenase type 1 (11BHS1) to be abundantly expressed in human OSE cells, and up-regulated by IL-1a. This translates functionally into increased rates of conversion of cortisone to cortisol in vitro, consistent with the intracellular steroidogenic properties of 11BHS1. Based on the ability of cortisol to suppress inflammatory (e.g. COX2) gene expression in IL-1a-stimulated HOSE cells, we postulate an anti-inflammatory role for 11BHS1 in creating a steroidal milieu conducive to the resolution of ovarian inflammation. Furthermore, since cortisol itself dose-dependently amplifies IL-1a-stimulated 11BHS1 expression, the means is available to sustain the regeneration of this anti-inflammatory signal at the site of ovulation. The discovery of this natural anti-inflammatory process has implications for the diagnosis and treatment of disease states involving chronic or excessive ovarian inflammation, including endometriosis and ovarian cancer. Supported by MRC Programme Grant 0000066.



## Speaker Abstracts

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### S5

#### **Setting the Scene RCN-FNG Nursing Competencies**

M Wallace

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This session will look at the work currently being undertaken on competencies by specialist nurses working in the field of fertility. It will describe the approaches being taken on competencies by the RCN and how this activity fits within that overall framework. Changing professional boundaries are a fact of life and if handled positively can bring great benefit to patients and professionals alike. Any change however has to be based on clear lines of accountability, effective education and training, together with positive and supportive team working. Defining explicit professional competencies will support change in the most positive manner, clarifying the range and capacity of nursing's knowledge and skills base and ensuring that nursing gets appropriate recognition for work done. The links with other national initiatives such as Agenda for Change; The NHS Knowledge and Skills Framework (NHS KSF); European Working Time Directives and the new consultant contract will also be considered.

### S6

#### **The need for nurse inspectors**

H Kendrew

*Clinical Nurse Manager, Bath Assisted Conception Clinic*

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In the early days of IVF and in an effort to address societies anxieties about this new and exciting field of medicine the Voluntary Licensing Authority, invited clinics and centres to be inspected and reviewed.

Two areas of new service development were identified as requiring particular scrutiny. They were embryology and counselling.

The nurses role in IVF clinics whilst not actually ignored at that time has now developed into one which is diverse and variable. The role of the nursing teams has been considered as part of the HFEA inspection process but this has generally been as part of the treatment service provision. It is timely that the HFEA in collaboration with the RCN fertility nurse group are devising protocols for the inspection of nursing teams in IVF units. Nurses should be appropriately trained and patients should expect high standards of expertise and care whilst undergoing treatments which are becoming more and more complex.

This talk will examine the impact that the 6th Code will have on the function of the nurse within an IVF unit.

## Speaker Abstracts

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### **S7**

#### **Genetic counselling in infertility: a family affair**

P Brennan

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In the UK, genetic counselling for infertility issues is largely separate from ART counselling. While some of the issues may be common to both, genetic diagnoses often raise a whole set of challenges that the patient may need to deal with in addition to their infertility. A person seeking advice in a genetics clinic provides a window into an extended family: aside from the process of genetic assessment - which may involve genetic testing, a process which carries its own set of ethical issues - familial implications often need to be discussed. No genetic condition is perhaps more difficult to discuss with one's relatives than infertility. The discussion will be illustrated by two cases of male infertility in which the genetic implications - and their ART management - were completely different. They serve to underline the complexity of genetic diseases, their differing impacts and the importance of collaborative working in achieving optimum experience and outcome for our patients.

### **S8**

#### **Counselling support during ART assessment**

A Raeburn

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Couples who are infertile have often been buffeted by the circumstances of their problem, over a considerable period of time. They are still more stressed when there is a possible genetic cause; this is because it may confirm their fears of an absolute inability to have their own children, with accompanying elements of guilt. They may be angry at the time period for the genetic diagnosis to be considered and may have feelings of hopelessness at their dilemmas. At such times they are vulnerable both to optimistic advice about what they and the ART centre can achieve and also to "ex cathedra" pessimism (you are never going to be able to conceive). Truth and psychological balance for them lies in being able to understand the diagnosis and test results and use these to make the best decisions in their own situation. So counselling support must go beyond the provision of "an understanding chat" and be a basis for informed, autonomous client choice. This is an approach, which must be central to each ART unit's management plan and integral to medical, nursing and embryological consultations, not just the prerogative of counselors.

## Speaker Abstracts

### S9

#### Ethical Dilemmas at the Genetics/Art Interface: How to solve them

JA Raeburn

*Genetics Unit, College of Medicine, Sultan Qaboos University, Muscat, Oman.*

Ethical issues occur within all specialties of medicine. The guiding principles are autonomy, confidentiality, beneficence, non-maleficence, equity and justice. Fertility services applying these principles can design an ethical pathway of care for each infertile couple. When two or more specialties work together (e.g. ART and Genetics) all must be committed to an ethical approach. If one team wishes couples to display independence and to make autonomous decisions whilst another organises treatment within an inflexible system, there are going to be difficulties. The solution is to recognise potential 'culture' clashes and agree how to resolve them individually. Sometimes the legal background can provide problems. For example, the HFEA Acts require that fertility units must always prioritise 'the best interests of the child'. How should the best interests of a future child be assessed against the alternative of non-existence or be balanced against the rights of a couple to choose (and often pay for) IVF treatment? Do blindness, deafness, or severe genetic or other risks form contraindications to fertility treatment? How severe is severe? These are not easy decisions. They are often passed to the Research Ethics Committees of IVF units, where the major commitment is to evaluate research proposals. Ethical issues about treatment for individual couples, however, relate to the 'Ethics of Clinical Practice'. This requires different guidelines and different skills of committee members (and chairpersons) from those of research. Therefore the work of ethics committees should be separated into two different elements, one for research and one for clinical practice. Lay representatives at each ethical discussion are mandatory for both types of committee. Such changes will show that the ethical principles above are not out of date. They will also facilitate appropriate responses to the future dilemmas of fast-growing specialties.

### S10

#### Proteomics to study sperm function and dysfunction

IA Brewis

*The Reproductive Biology and Genetics Group, Division of Medical Sciences, The University of Birmingham, Birmingham B15 2TT, UK; The Assisted Conception Unit, Birmingham Women's Hospital, Birmingham B15 2TG, UK; Department of Medical Biochemistry, University of Wales College of Medicine, Cardiff CF14 4XN, UK; Biostatistics and Bioinformatics Unit, UWCM, Cardiff CF14 4XN, UK.*

Proteomics (the study of proteins in a genome) is an important area of emerging research in the post-genomic era. As proteins, or more correctly protein-protein interactions are responsible for cellular function, it is critical that comprehensive identification and quantification of the proteins expressed in cells and tissues is undertaken to gain new insights into these processes. However, proteomics represents a considerable challenge as there are considerably more proteins than genes and much less developed methods for automated analysis than in genome mapping. The most common technique for the separation of proteins is two-dimensional electrophoresis and recent advances in mass spectrometry for peptide sequencing to facilitate more sensitive protein identification have been significant. These workhorse approaches, other methodologies and the latest developments in the technology will be introduced. Several groups have successfully used proteomic approaches to study normal sperm function and there have also been some studies addressing immunological infertility. However, there have been almost no studies that have used proteomics to directly investigate human sperm dysfunction or male infertility. In Birmingham (co-supervised by Prof. Christopher Barratt) we have been interested in whether there are differences in protein expression between normozoospermic fertile men and selected men with defined infertility (such as fertilisation failure at IVF or globozoospermia). To enable these studies we have profiled the sperm proteome in normozoospermic (fertile) donors in detail and have addressed intra- and inter-donor variability. Overall these studies have revealed some interesting data but have also highlighted the limitations of this technology for such studies. We have also used proteomics to study normal sperm function. Specifically we have probed human sperm capacitation and, in a successful collaboration with Dr. Bart Gadella (Utrecht University, The Netherlands), we have used proteomics to directly identify multiple sperm zona-binding proteins in the pig. Please address correspondence to [brewisia@cardiff.ac.uk](mailto:brewisia@cardiff.ac.uk).

## Speaker Abstracts

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### S11

#### The Genetic and Cytogenetic Basis of Male Infertility

DK Griffin

*Biological Sciences, Brunel University, Uxbridge, UK.*

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It can be difficult to assess accurately the overall magnitude of the contribution of genetics to male infertility since most, if not all conditions are likely to have a genetic component e.g. susceptibility to infection, obesity and psychological problems. Nevertheless, various genotypes, karyotypes and genes have been linked with particular phenotypes. Indeed the genetic basis of male infertility can be due to chromosomal abnormalities, single gene disorders and phenotypes with a multifactorial nature. With regard to chromosomal disorders, constitutional abnormalities such as inversions, translocations, sex chromosome trisomy and Y chromosome deletions are all reported. Chromosomal abnormalities that appear in the sperm only, that is elevated levels of sperm disomy, have also received significant attention in recent years. Several male infertility phenotypes have been associated with specific genetic anomalies such as Cystic Fibrosis, Prader-Willi Syndrome and Myotonic Dystrophy. Moreover several hundred genes have been associated with infertility (<http://www.nature.com/fertility/content/suppinfo/ncb-nm-fertilitys41-s1.html>) and these, most likely, contribute to the multifactorial nature of the disorder in many cases.

### S12

#### Fads and Foibles - but what is the evidence?

GM Hartshorne

*Department of Biological Sciences, University of Warwick, CV4 7AL.*

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The acronym ART for assisted reproductive technology is apt. The science underpinning our discipline is often difficult to establish because of the difficulties in working with the basic elements of human reproduction. Hence, some of the 'evidence base' relies upon extrapolation or interpretation of results from relatively small studies or other species.

In the absence of robust data upon which to base clinical decisions, sometimes procedures 'evolve', without the research that might normally be expected in fields where such research is (a) feasible, (b) less highly regulated, (c) less emotive and (d) government funded. Such evolution of methods has led to variability among different centres on diverse topics, including, for example, the threshold sperm criteria for ICSI treatment, the optimal numbers and stages for embryo cryopreservation, and the relative merits of different embryo selection criteria.

It seems peculiar that modifications to treatments (for example, a change in culture media) can be introduced if they are not expected to influence safety or efficacy negatively, however, prospective research (to demonstrate whether one or other media is superior) requires formal authorisation, patient consent and considerably more resources.

This talk will explore some of the more and less contentious issues in ART, highlighting aspects of the evidence available on the safety and efficacy of certain methods, for example, the pros and cons of introducing unknown or unphysiological factors into culture systems and the need to choose appropriate model systems for human embryology.



## Speaker Abstracts

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### S13

#### Cochrane and Fibroids

Inez Cooke

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Obstetrics was the first specialty to collate the information of separate randomized controlled trials of medical interventions as systematic reviews and meta-analyses in any formalized way, in the form of 'Effective Care in Pregnancy and Childbirth' edited by Chalmers, Enkin and Keirse which was published in 1989 together with the first version of the 'Oxford Database of Perinatal Trials'. Following from this the Cochrane Collaboration was formed in 1992, with the resulting publication of the Cochrane Library, whose aim is to be 'the best single source of reliable evidence about the effects of healthcare.'

An estimated 25% of women have uterine leiomyomas (fibroids) with 20 – 50% of those women presenting with symptoms warranting treatment. Fibroids have represented one of the most frequent indications for major surgery in pre-menopausal women with the standard treatment in the past being either a hysterectomy or, in women who wished to retain their fertility, a myomectomy. However, with the increasing average maternal age at delivery, increased assisted conception numbers and requests for prenatal investigations together with post-menopausal women using hormonal treatments, fibroids are causing more frequent dilemmas of clinical management. The Cochrane Library aims to be an information source for health care givers and consumers. This presentation will summarize the information available within the Cochrane Library which could help both clinician and patient decide best management of one of the commonest gynaecological pathologies, uterine fibroids.

### S14

#### Fibroid Embolisation and Fertility

PK Ellis [1] & N McClure [2]

[1] Dept of Radiology, Royal Victoria Hospital, Belfast, N.Ireland;

[2] Dept. of Obstetrics and Gynaecology, Royal Victoria Hospital, Belfast, N.Ireland.

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The technique of fibroid embolisation has been employed since the mid 1990's. Approximately 90% of patients achieve some or complete resolution of symptoms. Fibroid volume reduction, decreased bleeding and increased quality of life have all been measured in this group of patients. However, the issue of fertility following embolisation treatment remains relatively controversial. Some authors claim that fibroid embolisation can be used safely for patients wishing to maintain fertility, whilst others feel that it is not appropriate to use this technique in this particular group of patients. In this talk the technique and results of fibroid embolisation will be discussed. In addition, a review of the current literature, in particular with regard to maintenance of fertility, will be undertaken.

## Speaker Abstracts

### S15

#### Endoscopic management of uterine fibroids

E Saridogan

*Reproductive Medicine Unit, University College London Hospitals, London, United Kingdom.*

**Introduction:** Uterine fibroids are very common, approximately 70-80% women develop fibroids before menopause. There is convincing evidence that submucosal fibroids reduce fertility and the success rates of fertility treatment, however, the impact of intramural or subserosal fibroids on these outcomes is controversial.

**Methods:** This presentation will give an overall view of hysteroscopic and laparoscopic management of uterine fibroids.

**Results and Discussion:** Hysteroscopic removal has been accepted as the standard treatment for submucosal fibroids. The operative techniques include resection using monopolar or bipolar energy and ablation using laser or bipolar energy. Submucosal fibroids are usually classified according to the ratio of the intracavitary and intramural parts; a commonly used system classifies them as type 0, type I and type II. Details of management of these subtypes, as well as potential complications will be presented. Treatment of submucosal fibroids is usually associated with better reproductive outcomes. While myomectomy is one of the first gynaecological procedures described, laparoscopic myomectomy is a relatively new technique. Although it is commonly used for subserosal and intramural fibroids, it can also be used for some fibroids with a small intracavitary portion. The surgical principals of laparoscopic myomectomy are similar to those of open myomectomy; enucleation of fibroid(s), uterine reconstruction with haemostasis and removal of fibroid(s) using an abdominal morcellator or through a posterior colpotomy incision. The potential advantages of laparoscopic myomectomy over open procedures include less adhesion formation, shorter hospital stay, quicker recovery and better cosmesis. Its disadvantages include longer operating time and future risk of uterine rupture in pregnancy or labour. Laparoscopically assisted myomectomy and laparoscopically assisted vaginal myomectomy techniques have also been described by some authors.

### S16

#### Myomectomy

TC Li & Dr M McIlveen (Sheffield)

The relationship between fibroid and reproductive failure, including infertility and miscarriage is a very interesting one. The relationship depends on the location and size of the fibroid. Removal of a sub-mucous fibroid is best carried out via the hysteroscope. In selected cases of sub-serosal and intramural fibroids, a laparoscopic approach should be considered but it requires special training and expertise. Most reproductive surgeons are comfortable with open myomectomy if removal of fibroid is considered necessary to improve reproductive outcome.

In many cases, the indication for surgical intervention, i.e., myomectomy is not clear cut. In such cases, the reproductive history is an important consideration. The pros and cons of myomectomy ought to be carefully explained to patients before a decision is made.

Careful pre-operative preparation and counselling is required. The use of GnRH analogue to shrink the fibroid prior to myomectomy is controversial. Bloods should always be cross-matched prior to undertaking myomectomy. The risk of hysterectomy needs to be mentioned as a potential complication of myomectomy. The various surgical techniques used in carrying out myomectomy will be presented, including the use of an omental graft to prevent adhesion formation.

**INFERTILITY – WHAT CAN WE DO AND WHEN SHALL WE DO IT?**  
Mr T.C. LI

In women with infertility due to tubal disease, there are two basic approaches to the management, namely IVF or tubal surgery.

Salpingostomy carried out by a gynaecologist without special training has a 5% take home baby rate, however, the outcome of microsurgical salpingostomy in specialist centres produces a pregnancy rate of around 30%.

Salpingo-ovariolysis produces an even higher pregnancy rate in the region of 40-50%.

Microsurgical reversal of previous sterilisation by Filshie clips or Falope ring has a success rate of 80%.

More recently the presence of significant hydrosalpinx, i.e., detectable by ultrasound, is found to reduce implantation and conception rate in IVF treatment. Surgical removal of the hydrosalpinx does improve the implantation and take-home baby rate in IVF treatment.

Surgery also has a role in the treatment of endometriosis associated with infertility. Medical treatment has now been found to be of little value in the management of such a condition. Sub mucous fibroids reduce the fertility rate and increases the miscarriage rate. Recent evidence suggests that intramural fibroids, even <5cm in size, also compromises the implantation rate in IVF treatment cycles. There is a strong argument to discuss the removal of fibroids prior to IVF treatment, and in women who have repeated miscarriages, in addition to infertility.

To conclude, reproductive surgery has an important complimentary role to IVF in the management of patients with tubal/peritoneal infertility. What is needed is improved, structured training in reproductive surgery to ensure optimal outcome in women with infertility problems.

## Speaker Abstracts

### S17

#### Polycystic Ovary Syndrome: New definitions and diagnostic features

Adam Balen MD, FRCOG, Department of Reproductive  
Medicine

*The General Infirmary, Leeds, LS2 9NS, UK*

The polycystic ovary syndrome (PCOS) is a heterogeneous collection of signs and symptoms that gathered together form a spectrum of a disorder with a mild presentation in some, whilst in others a severe disturbance of reproductive, endocrine and metabolic function. The pathophysiology of the PCOS appears to be multifactorial and polygenic. The definition of the syndrome has been much debated. Key features include menstrual cycle disturbance, hyperandrogenism and obesity. There are many extra-ovarian aspects to the pathophysiology of PCOS yet ovarian dysfunction is central. At a recent joint ESHRE/ASRM consensus meeting a refined definition of the PCOS was agreed: namely the presence of two out of the following three criteria: 1) Oligo- and/or anovulation; 2) Hyperandrogenism (clinical and/or biochemical); 3) Polycystic ovaries, with the exclusion of other aetiologies (The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group, 2004). The morphology of the polycystic ovary, has been redefined as an ovary with 12 or more follicles measuring 2-9 mm in diameter and/or increased ovarian volume (>10 cm<sup>3</sup>) (Balen et al, 2003).

There is considerable heterogeneity of symptoms and signs amongst women with PCOS and for an individual these may change over time. The PCOS is familial and various aspects of the syndrome may be differentially inherited. Polycystic ovaries are commonly detected by ultrasound or other forms of pelvic imaging, with estimates of the prevalence in the general population being in the order of 20% - 33%. However, not all women with polycystic ovaries demonstrate the clinical and biochemical features which define the polycystic ovary syndrome (PCOS). There are a number of interlinking factors that affect expression of PCOS. A gain in weight is associated with a worsening of symptoms whilst weight loss may ameliorate the endocrine and metabolic profile and symptomatology.

Genetic studies have identified a link between PCOS and disordered insulin metabolism, and indicate that the syndrome may be the presentation of a complex genetic trait disorder. The features of obesity, hyperinsulinaemia, and hyperandrogenaemia which are commonly seen in PCOS are also known to be factors which confer an increased risk of cardiovascular disease and non-insulin dependent diabetes mellitus (NIDDM). There are studies which indicate that women with PCOS have an increased risk for these diseases which pose long-term risks for health, and this evidence has prompted debate as to the need for screening women for polycystic ovaries.

Balen AH, Laven JSE, Tan SL, Dewailly D. Ultrasound Assessment of the Polycystic Ovary: International Consensus Definitions. *Human Reproduction Update* 2003;9:505-14.

The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group. Authors: Fauser B, Tarlatzis B, Chang J, Azziz R, Legro R, Dewailly D, Franks S, Balen AH, Bouchard P, Dahlgren E, Devoto, Diamanti E, Dunaif A, Filicori M, Homburg R, Ibanez L, Laven J, Magoffin D, Nestler J, Norman R, Pasquali R, Pugeat M, Strauss J, Tan SL, Taylor A, Wild R, Wild S. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Human Reproduction* 2004; 19: 41-47.

### S18

Roy Homburg

Abstract Not Available

## Speaker Abstracts

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### S19

#### How safe is embryo freezing?

MJ Wood

*Department of Obstetrics and Gynaecology,  
University of Aberdeen, Aberdeen, Scotland.*

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Embryo freezing is an established element of assisted reproduction. Nonetheless, patients still ask about the associated risks to the embryos and to children conceived from the embryos. The aim of this paper is to summarize the evidence available and indicate where knowledge is lacking.

Some embryos do not survive freezing and many of the survivors sustain damage that has been shown to reduce their viability. HFEA statistics suggest that frozen embryos are less likely than fresh embryos to establish a successful pregnancy, but these may reflect factors such as selection of the 'best' embryos for fresh transfer, rather than the effects of freezing. There is a small risk of viral cross contamination of samples stored in liquid nitrogen. Routine screening of patients before embryos are stored and changes in cryopreservation methodology are being introduced to address this fear.

Follow-up of conceptions from frozen embryos has been reassuring, with no evidence of increased birth defects or abnormal early development, but the studies are far from definitive. The possibility of genetic modification, induced by freezing but manifest only later in life, cannot be ruled out until a large cohort of children matures. A recent study reported modified expression of a gene in frozen embryos but the significance of this is unknown. Evidence accumulated over three decades generally suggests that animals conceived from frozen embryos, and their offspring, exhibit no evidence of genetic change. However, one study reported subtle morphological, developmental and behavioural variations in mice derived from frozen embryos.

In conclusion, randomized trials to determine optimal procedures for freezing and post-thaw management of embryos are long overdue. More extensive molecular studies of frozen embryos, animal and human, will allow further assessment of the risks of cryopreservation. Prospective long-term follow-up of frozen embryo conceptions is needed.

### S20

#### Blastocyst Culture: Cause for Concern or Hype?

LE Young

*Division Of Obstetrics and Gynaecology;  
University of Nottingham; Nottingham; UK.*

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The question of whether extended culture of human embryos to the blastocyst stage will result in unforeseen risks has been the subject of recent debate. Reports from clinics adopting blastocyst culture are positive in terms of pregnancy outcome in comparison to transfer of cleavage stage embryos. Evidence from animal systems, where transfer of blastocyst stage embryos can result in developmental problems, has been cited as a cautionary note. However these embryos are transferred at blastocyst stage as a routine and so it is not yet clear whether it is the early or late stages of embryo culture (or both) that contribute to the resulting developmental defects, such as Large Offspring syndrome in cattle and sheep. Indeed work with these animal species suggests that procedures emanating from the oocyte source, including superovulation and maternal nutrition, may have a role in predisposing to developmental defects. The role of the sperm is unknown. Making no apologies for only taking the scientific viewpoint, this presentation will suggest that the only way to safely evaluate changing procedures in human ART is to begin to unravel the molecular mechanisms that are perturbed and to develop reliable screening methods. Progress being made towards this aim will be reviewed.

## Speaker Abstracts

### S21

#### ICSI: hypes versus hazards

WMJA Verpoest & H Tournaye

*Reproductive Medicine, Free Dutch-speaking University of Brussels, Belgium.*

Ever since its introduction in clinical practice more than 10 years ago, intracytoplasmic sperm injection (ICSI) has been the subject of ongoing debate about its indications and safety. Many theoretical issues have been raised, but most concerns related to the technique of ICSI have not manifested.

ICSI was, and still is, hyped because of its potential to give those couples with severe male factor infertility, a chance to conceive, and because of its apparently low fertilisation failure rate compared with 'classic' in vitro fertilisation (IVF).

Concerns about ICSI are related to technical, biological and genetic hazards. ICSI can potentially damage the second meiotic spindle apparatus and provoke chromosome breakage. Potential hazards include the injection of contaminating foreign material, microbiological contaminants, and foreign DNA. Faulty genomic imprinting, injection of diploid rather than haploid germ cells and abnormal fertilisation are additional hazards.

It has emerged that ICSI can pass on genetic abnormalities, creating a generation of less fertile men. ICSI patients may have a slightly higher prevalence of potentially heritable, non-reproductive disorders.

Obstetric hazards include low birthweight and increased perinatal mortality.

Follow-up studies on a substantial number of children born after ICSI at our centre, have failed to show an increased risk of congenital abnormalities. Mental and psychological development is not different in IVF versus ICSI children. Many external and often uncontrollable factors, such as sperm morphology, sperm motility, or the presence of reactive oxygen species, do not seem to have any major impact on the outcome of ICSI. Risks of major congenital abnormalities are not higher after ICSI than after IVF.

Follow-up studies are essential to the technique of ICSI. Patients will have to decide for themselves whether the concerns outweigh the benefits of ICSI, and it is our duty to counsel them about the latest data on safety available.

### S22

#### Evening inseminations are more convenient for couples and are equally successful to inseminations performed during morning hours

D Tkalec

*Montreal Fertility Centre, Montreal, Canada.*

Evening inseminations are more convenient for couples and are equally successful to inseminations performed during morning hours

**Background:** Patients prefer having intrauterine insemination (IUI) in the evenings as they perceive the process less anxiety producing. They do not have to miss work and can relax better after the procedure. However, the evidence in the literature suggests that the quality of semen samples produced in the afternoon hours is superior to morning samples. In this study we investigated whether evening inseminations have a positive effect on semen parameters and pregnancy rates when compared to morning inseminations.

**Methods:** This prospective analysis included patients with unexplained infertility who did not achieve a pregnancy with anti-estrogens alone. The patients were undergoing IUI treatment with 5.0 mg of letrozole administered from cycle day 3 to day 7 and gonadotropins in a dose of 120 IU every alternative day starting from day 5 of the menstrual cycle. Ultrasound scans were performed prior to the initiation of treatment, on cycle day 9, and as required thereafter in the morning or evening depending on patient's response, until the dominant follicle reached 18 mm in diameter. Ovulation was then triggered with 10,000 IU hCG and an IUI was performed exactly 36 hours later.

**Results:** During a period of 12 months a total of 118 inseminations were performed in the morning (median (M)= 8:00 hours interquartile difference (IQD)= 8:00-9:00) and 121 in the evening (M= 20:00 hours IQD=19:00-20:30). No difference was observed in the age of patients (35.8 vs. 35.8 p=0.7), quantity of gonadotropins used (550 iu vs. 480 iu p=0.44), number of follicles >14mm (5 vs. 5 p=0.6), quality of semen sample (volume (3.0 vs. 3.0 ml p=0.72), concentration (44.5 vs. 44.7 mil/ml p=0.85), and motility (45 vs 48% p=0.69)) or pregnancy rates (14.4 vs. 14.9% Odds Ratio =1.04 95%CI=0.47-2.27) between the two groups.

**Conclusions:** Evening inseminations are a more convenient treatment option for patients without posing a detrimental effect on the quality of semen or pregnancy rates.

## Speaker Abstracts

### S23

#### Fertility Society of Australia Prize Lecture: The Auckland FLUSH Trial - RCT of Flushing with Lipiodol for Unexplained (and endometriosis-related) Subfertility by Hysterosalpingography

NP Johnson [1, 2, 3, 4], W Hadden [3, 5], J Suckling [1, 3],  
Y Yu [1], L Sadler [1] & CM Farquhar [1, 2, 3]

[1] University of Auckland, New Zealand; [2] Fertility Plus,  
Auckland, New Zealand; [3] National Women's Hospital,  
Auckland, New Zealand; [4] University Specialists, Mercy Specialist  
Centre, Auckland, New Zealand; [5] Auckland Radiology Group,  
New Zealand.

**Introduction:** We aimed to assess the effectiveness of flushing with the oil-soluble contrast medium lipiodol in women with unexplained infertility.

**Methods:** An open randomised controlled trial compared lipiodol flushing with no intervention in 158 women with unexplained infertility. Two populations, including 96 women with pure unexplained infertility and 62 women with mild endometriosis where fallopian tubes and ovaries were unaffected in the context of otherwise unexplained infertility, were assigned to receive lipiodol flushing or no intervention. The primary outcomes were clinical pregnancy assessed at 6 months following randomisation and live birth.

**Results:** In women with endometriosis, pregnancy occurred in 12 out of 25 women with lipiodol flushing (48.0%) versus 4 out of 37 women with no intervention (10.8%) (relative risk [RR] 4.44, 95% confidence interval [CI] 1.61-12.21) and live birth in 10 out of 25 women with lipiodol flushing (40%) versus 4 out of 37 women with no intervention (10.8%) (RR 3.70, 95% CI 1.30-10.50). In women with unexplained infertility, pregnancy occurred in 16 out of 48 women with lipiodol flushing (33.3%) versus 10 out of 48 women with no intervention (20.8%) (RR 1.60, 95% CI 0.81-3.16) and live birth in 13 out of 48 women with lipiodol flushing (27.1%) versus 8 out of 48 women with no intervention (16.7%) (RR 1.62, 95% CI 0.74-3.56)

**Discussion:** Lipiodol flushing in women with mild endometriosis results in a significant increase in the pregnancy and live birth rate. Although this trial did not demonstrate a significant increase in pregnancy rate for women with unexplained infertility, meta-analysis of available data from randomised trials of lipiodol flushing also demonstrates a significant increase in pregnancy rate in women with unexplained infertility. Lipiodol flushing should be offered as a fertility treatment option for these women.

### S24

#### Living with uncertainty - the legacy of male infertility

CMC Grieve [1, 2] & SJ Pike [1, 3]

[1] British Infertility Counselling Association; [2] Centre for Reproductive Medicine, University Hospitals, Coventry and Warwickshire NHS Trust, Walsgrave, UK; [3] Assisted Conception Unit, Jessop Wing, Sheffield Teaching Hospitals NHS Trust, Sheffield, UK.

Today, a wide number of male factor infertility problems can be diagnosed and treated with increasingly sophisticated and successful technological procedures. In recent years treatment options such as ICSI, PESA and TESE have become available. However, as in other infertility therapies, it is still the woman who undergoes the greater part of treatment even though her own fertility may not be impaired. This focus on the woman and marginalizing of the man may heighten any sense of blame and consequent guilt he may be feeling. This in turn may lead him to ignore or deny the reality of any risks or longer term concerns relating to proposed treatment in his desire for atonement.

For many couples with male factor infertility, ICSI, PESA and TESE represent treatment options that make a genetically-shared pregnancy more achievable than ever before, but not without significant demands and implications for both the couple and for the child born to them. In the pre-eminent desire to become parents one or both partners may minimize the importance of other considerations (for example, the medical and genetic risks and other potential health issues for themselves and future generations of children). They may press on with reproductive solutions that fulfill their psychological need but ignore other concerns or consequences.

How well informed are the men and women who are considering these treatments?

How well prepared are they for the complexities and challenges involved?

What contribution has counselling to make in helping individuals and couples explore all the implications of male factor infertility, its treatment and the uncertainty of outcomes, short and long-term?

This workshop will provide the opportunity to examine these and other issues surrounding the provision of ART for male infertility. It will also provide the opportunity to reflect on the similarities and differences in legacy between donor-assisted and genetically-shared parenthood.

## Speaker Abstracts

### S25

#### The Impact and implications of the European Framework

Alison Murdoch

*Professor of Reproductive Medicine, Mary Herbert, Scientific Director, Newcastle Fertility Centre at Life.*

In 2003, the European Parliament directed that assisted reproductive technologies would be included within the current regulations for the donation, procurement, testing, processing, storage and distribution of human tissue and cells. The Directive will be adopted in April 2004 and will become legally binding in the UK by April 2005. At present the precise details of what this will mean for the practice of ART is still under discussion. A Working Group was set up by the HFEA and DH to determine the implications primarily for laboratory practice but also for clinical practice since the regulations will include all parts of the IVF process from initial patient assessment to the use of the embryo. In this talk I will review the main issues that have been discussed.

The Code of Practice for Tissue Banks providing tissues of human origin for therapeutic purposes (DH 2001) was used as the basis upon which the standards have been devised. The Code has been reviewed to identify which elements of the ART process can be practically compliant with the standards. The Code covers quality systems, facilities, responsibilities of personnel and training, donor selection, control of tissues, services and materials, process control, packaging, labelling and transport and documentation. Many of these issues are familiar to those in the NHS who work within Clinical Governance principals. The process of accreditation will require that units provide documentation to identify that they have set and maintained appropriate standards under these headings. It is anticipated that the accrediting body will inspect the Centre against these standards.

The scope of the new regulations is wide and includes any situation in which cells or tissue are 'processed' before transfer to a patient. In the context of fertility treatment this will almost certainly include the preparation of semen for IUI.

As an illustration of the practical implications of these new regulations, the upgrade in facilities needed for Newcastle Fertility Centre at Life will be considered.

### S26

#### Accreditation – are you up for it?

Cecilia Sjoblom

*Director of Embryology, University of Nottingham*

Quality assurance and accreditation are concepts that seem to touch on a wide range of functions in our society. Quality control systems are specially needed in ART units to ensure reproducibility of all methods and competence in all duties performed by the personnel. The necessity of a quality control system becomes even clearer when considering the possible risks of ART.

An accreditation or certification according to recognized international standards, such as the ISO 9001:2000 and ISO 17025, is an efficient and effective tool to demonstrate both technical competence and the existence of a good quality control system.

Laboratory accreditation according to the ISO 17025 standard is the formal recognition of the laboratory's technical competence. Certification of the clinic in accordance to the ISO 9001:2000 standard will guarantee a good total quality management system.

For the years ART has been practiced clinically in both large and small scales much knowledge has been gained on how to run ART clinics and what methods to use to achieve ultimate success. Facing the future we encounter other parameters like the safety and efficiency of the clinic and quality control becomes a key feature. In such systems the clinic as well as the laboratory can be audited by a third party authority. A system for regular auditing of an ART unit makes it possible for our society to get an insight into how units practice the technique according to legislation and professional guidelines. Furthermore, the audit also provides a possibility for feed back between the authority and the ART clinics. Thus, in general it is positive to have a system either internal or external for auditing the work performed in an ART unit.

ART units and especially IVF laboratories are now facing a future consisting of a jungle of directives, codes of practice, guidelines and standards all coming from different legislative bodies like the European Council, DH, and HFEA – all wanting to have their say in how we should run our day to day practices.

What direction should we take? How will this affect my clinic? How much will this cost us?

Are you up for it?

## Speaker Abstracts

### S27

#### Statistical analysis and pseudo-analysis

David J Torgerson

*Director, York Trials Unit, University of York, York YO10 5DD*

Although the randomised controlled trial (RCT) is rightly seen as the 'gold-standard' research method most clinical research does not use this design when trying to infer causality. Even when the RCT is used its reliability can be undermined through the use of inappropriate statistical methods. In this session I will consider the following common design and statistical errors: regression to the mean; multiple comparisons; p values; and subgroup analyses. Most clinical evaluations use the pre-test post-test or before and after design. This is where patients are selected on the basis of having an extreme value, given an intervention and then re-tested. Such an approach is 'confounded' by the regression to the mean phenomenon, where extreme values will, on average, tend back towards the population mean. This phenomenon leads the credulous into believing the intervention has worked. RCTs are the most robust method of controlling for regression to the mean. Nevertheless, inappropriate statistical techniques may result in an inference of either causality, when none exists, or erroneously accepting the null hypothesis. A common mistake is the use of multiple comparisons. A statistically significant result (e.g.,  $p = 0.05$ ) will almost always occur, by chance, if 20 different statistical tests are undertaken on the trial data even if, in truth, no difference really exists. A similar problem occurs when undertaking a 'clinically relevant' sub-group analysis. Such tests have weak power to demonstrate a 'real' effect and again because of multiple testing the chances of obtaining a falsely significant result is high. On the other hand, the obsession with a p value of 0.05 will lead to the unwarranted rejection of effective treatments merely because they do not pass an arbitrary value.

### S28

#### Ethical Approval. A Nightmare of Bureaucracy

TJ McMurray

*Queens University; Belfast.*

Over the next few months the research ethics process will transform from the voluntary self-regulation, which has characterised bio-medical research in the United Kingdom (UK), to regulation by statute.

The new regulatory processes are a consequence of the advent of the European 'Clinical Trials' Directive 2001/20/EC[1] that is to be incorporated into United Kingdom law by May 2004. The essential aims of the directive are to harmonise the various national, administrative procedures necessary to start a clinical trial and to set pan-European legal standards of protection for all clinical trial participants, including healthy volunteers.

While the directive was initially drafted to facilitating commercial drug development in Europe, the different nature of non-commercial research was not recognised. In the UK, clinical trials funded publicly (i.e. by charities, the Medical Research Council and the NHS) make an essential contribution to areas of medicine that are not supported by the pharmaceutical industry e.g. aspirin in patients with circulatory disease, and magnesium sulphate in the treatment of pre-eclampsia of pregnancy.

The heart of the problem with this directive lies not only in the increased bureaucracy but also in the increased obligations the directive places upon the 'sponsor' of the trial. The sponsor may be an individual, company, institution or organisation who must accept total legal responsibility for the initiation, management and/or funding of a clinical trial. This requirement for a single legal sponsor, takes no account of the partnership collaborations that characterise publicly-funded clinical trials and single organisations within academic partnerships will find acting as a sponsor for a single-centre trial difficult, and for a multi-centre trial potentially impossible. Legal compliance with Good Clinical Practice for all trials will also be mandatory, which means that publicly funded investigators face the same intensive site monitoring and source-data verification as are currently standard in industry.

If the government and MHRA fail to make the necessary changes and provisions for publicly funded clinical research before final approval of the draft regulations by parliament later this year, the UK will have substantially fewer high-quality clinical trials to offer patients and progress in clinical research will be curtailed.

## Speaker Abstracts

### S29

#### Cannabinoids and the Body

RG Pertwee

*Institute of Medical Sciences, University of Aberdeen, Aberdeen, Scotland.*

Mammalian tissues contain at least two types of cannabinoid receptor, CB1 and CB2, both G-protein coupled. CB1 receptors are expressed at the terminals of central and peripheral neurones, where they modulate transmitter release, and by some non-neuronal cells. CB2 receptors are found mainly on immune cells, one of their roles being to alter cytokine release. Endogenous cannabinoid receptor agonists have also been discovered. These 'endocannabinoids' are all eicosanoids and are synthesized on demand. They include arachidonoyl ethanolamide (anandamide), 2-arachidonoyl glycerol and 2-arachidonoyl glyceryl ether. Endocannabinoids and their receptors constitute the 'endocannabinoid system'. Potent cannabinoid receptor agonists and antagonists/inverse agonists, including several with marked CB1 or CB2-selectivity, have been developed. So too have agents that can modulate extracellular concentrations of endocannabinoids by inhibiting their tissue uptake or enzymic hydrolysis. Pharmacological evidence is now emerging for the existence of additional targets both for anandamide and for other cannabinoids that include not only certain established non-eicosanoid CB1/CB2 receptor ligands but also the non-psychotropic plant cannabinoid, cannabidiol, and its synthetic analogue, abnormal-cannabidiol. In addition, there is strong evidence that anandamide and some of its metabolites can activate peripheral and central vanilloid TRPV1 receptors. CB1 receptors and/or endocannabinoids have been detected in various parts of the reproductive system including hypothalamus, pituitary gland, ovary, testis, vas deferens, prostate gland, sperm cells, uterus, embryo, blastocyst and reproductive fluids. Indeed, the endocannabinoid system appears to contribute to the regulation of fertility, for example through effects on luteinizing hormone release, male and female sexual behaviour, the oestrous cycle, the motility and fertilizing capacity of sperm, embryo implantation, and trophoblast differentiation and proliferation. There is also evidence that sex steroids can alter the expression level of central CB1 receptors.

### S30

#### Recreational Drugs and Male Fertility

SEM Lewis, L Whann, DRJ Glenn & N McClure

*Obstetrics and Gynaecology, Institute Clinical Science, Grosvenor Road, Belfast BT12 6BJ.*

In recent years, recreational drugs have been added to the list of potential lifestyle hazards to human fertility. An estimated 3.3 million people smoked cannabis in the UK in 2002 and this figure is set to increase with the declassification of the drug from Class B to Class C this year. Surprisingly, this law was passed with a paucity of information available about the effects of cannabis use on health generally and none on its effects on fertility. Our group has examined the in vivo and in vitro effects of tetrahydrocannabinol; THC the primary psychoactive cannabinoid in marijuana on human sperm fertility potential using biomarkers such as quantitative motility and acrosome reaction.

Another recreational drug that has become instantly popular is Viagra. Although initially restricted to older men with impotence problems, its use has now spread to men of all ages for both medicinal and recreational purposes. This includes men of reproductive age and particularly men undergoing infertility treatment. Indeed, in our audit of all the UK fertility centres, 42% were prescribing Viagra to help patients produce semen samples. Yet its effects on sperm function are not fully understood. Since Viagra is a phosphodiesterase (PDE) inhibitor, and other PDEs have been shown to have variable effects on semen and deleterious effects on early embryo development there are justifiable concerns about these trends. We have determined the effects of Viagra on sperm function and early embryo development using human and animal models. These two studies will be reviewed and their implications discussed.

## Speaker Abstracts

### S31

#### Smoking, Alcohol and Sperm Function

Michael Zitzmann and Eberhard Nieschlag

Cigarette consumption increases the risk of both atherogenic and cancerogenic disease. Similarly, inhalation of cigarette smoke also impairs fertility. In women smoking decreases the chance for spontaneous conception and doubles the risk of failure in assisted reproduction.

In males, smoking attacks several aspects of fertility:

- 1 By impairing the vascular endothelium, smoking causes erectile dysfunction which can be considered an early sign of atherosclerosis. The risk of developing erectile dysfunction is almost doubled for smokers compared to non-smokers. Thus, semen deposition may be compromised.
- 2 Despite several studies on semen variables in smokers and non-smokers, this issue is still controversial. Even recent studies carried out among subjects from similar cultural background found either no effects or significant decreases in sperm count and motility in smoking vs. non-smoking men.
- 3 Sperm DNA is significantly damaged by benzopyrenes, a toxic ingredient of cigarette smoke.
- 4 In male smokers, the natural conception rate seems to be slightly impaired.
- 5 Several studies demonstrate a negative effect of male smoking on IVF results.
- 6 Recently, it was also demonstrated that male smoking significantly decreases the success rates of ICSI. The effect is associated with the number of daily consumed cigarettes. Cessation of smoking has a positive influence after approximately two years.
- 7 Finally, embryos surviving DNA damage may develop to children with low birth weight and infants with higher malignancy rates.
- 8 It is difficult to assess the effects of excessive alcohol consumption on fertility, since it is often accompanied by cigarette smoking, but experimental approaches suggest altered genomic imprinting caused by reduced DNA methylation, which, in turn, may lead to the expression of normally silent paternal alleles and may be a mechanism for paternal alcohol effects, such as affection of growth and behavior of offspring.

### S32

#### Issues in the management of male infertility

David de Kretser

*Monash Institute of Reproduction and Development, Monash University, Melbourne, Victoria, Australia.*

This presentation will address two fields that impact significantly in the management of male infertility today. One involves men with vasectomies who seek to achieve a pregnancy with a new partner. While ICSI can circumvent many of the issues concerned in the management of these men, successful fertility by reversal needs to recognise the impact of spermatogenic damage post-vasectomy and the issue of sperm antibody formation resulting from alterations of the immunological environment of the testis and epididymis. Basic studies reveal that the so-called immune privileged environment of the testis is maintained by altered macrophage function in the testis and the production of a substance(s) that may modulate the responsiveness of immunological mechanisms. These processes may be perturbed in the 3-6% of men who spontaneously develop sperm antibodies that impair fertility.

The second involves the 40% of infertile men with disorders of spermatogenesis, in whom the cause of their impaired sperm production is unknown. There is an increasing recognition that a significant number of such men have a genetic cause for this disorder. Support for this concept comes from the demonstration that approximately 6-10% of men with sperm counts of less than 5 million/ml have significant deletions in the long arm of their Y chromosome. The basis of other genetic lesions are becoming apparent as studies of genes involved in known regulatory mechanisms of spermatogenesis are studied. For instance, mutations in genes related to the gonadotrophic and androgenic control of spermatogenesis have been shown to result in lowered sperm production. In others novel pathways of interrupting spermatogenesis are emerging as infertility results from targeted disruption of genes in the mouse.

In some cases, there will be a family history of an identifiable syndrome with a genetic basis such as the immotile cilia syndrome which results in infertility caused by immotile sperm lacking a key structural feature of the sperm tail such as dynein arms. The genetic basis of these disorders is now emerging from comparative studies of the genomes from as widely disparate species as *Chlamydomonas*, mice and humans.

The identification of new genetic causes of disordered sperm production will emerge from a careful selection of which genes, identified from mouse studies, are selected for mutational analysis in infertile men. With increasing knowledge of genetic causes of male infertility, it will become expensive to undertake multiple tests and the clinician will need to carefully choose the relevant investigation by the use of clinical and ancillary laboratory data. Eventually, a genetic "male Infertility" chip will be developed to enable a single test to evaluate several thousand potential genetic causes of male infertility.

## Oral Abstracts

### O1

#### The significance of positive chlamydia serology in women with normal tubes at laparoscopy

VA Akande [1], LP Hunt [2], PG Wardle [3] & JM Jenkins [1]

[1] *Obstetrics and gynaecology, University of Bristol, UK;* [2] *Institute of Child Health, University of Bristol;* [3] *Department of Women's Health, Southmead Hospital, Bristol.*

**Introduction:** Chlamydia trachomatis poses a potential threat to the fertility of women by causing tubal damage. Many women with serological evidence of past chlamydia infection have normal tubal appearances on laparoscopic assessment. Could subtle endo-tubal damage cause sub-fertility in such women? Our aim was to assess if serological evidence of past chlamydial infection affects the likelihood of conception in women with normal tubes.

**Methods:** Infertile couples in whom the female partner was under the age of 40 years, with normal ovulatory function and a male partner with normal sperm function were studied. All women had normal tubes as assessed by laparoscopy. Serum chlamydia antibody titres were assayed using the immunofluorescence test (IFT). Pregnancy rates were related to grouped Chlamydia antibody titres [ $<64$ ;  $64-256$ ;  $\geq 512$ ]. The Log rank test was used to compare the Kaplan-Meier estimated cumulative pregnancy rates at three years following laparoscopy. Multivariate analysis was carried out using Cox's proportional hazards regression method to control for the influence of variables such as age, duration of infertility, smoking, and type of infertility.

**Results and Discussion:** 174 women studied. The cumulative pregnancy rates (SE) according to titres of  $<64$ ;  $64-256$ ;  $\geq 512$ ; were 45.1% (6.2); 42.6% (9.3); 59.1% (11.8) and the risk ratios (95%CI) were 1; 1.59 (0.82-3.07); 1.04 (0.52-2.08) respectively. Risk ratios (multivariate) were risk for pregnancy adjusted for other factors, as opposed to cumulative rates which were unadjusted (univariate). The differences were not statistically significant. Three women subsequently had ectopic pregnancies; two of these women had negative titres of  $<64$ , while the third had a high titre of  $\geq 512$ . Therefore in women with normal looking tubes, serological evidence of past Chlamydial infection does not appear to have an adverse effect on pregnancy rates. These findings suggest that laparoscopic findings and not Chlamydia serological titres are the key to fertility prognosis.

### O2

#### The influence of positive Chlamydia antibody titres on natural conception in infertile women

VA Akande [1], LP Hunt [2], DJ Cahill [1], PG Wardle [3] & JM Jenkins [1]

[1] *University division of Obstetrics and Gynaecology, Bristol, UK;* [2] *Institute of Child Health, University of Bristol;* [3] *Department of Women's Health, Southmead Hospital, Bristol.*

**Introduction:** Chlamydia trachomatis infection can cause pelvic inflammatory disease leading to tubal damage. Our objective was to assess if serological evidence of past chlamydial infection was predictive of the likelihood of conception in infertile women trying to conceive naturally.

**Methods:** We conducted a study of 796 fully investigated infertile couples. Women  $>40$  years of age and couples with male factor infertility were excluded. Chlamydia antibody titres were assayed using the Whole-cell immunofluorescence test. Multivariate survival methods and competing risks analysis were employed to determine the likelihood of conception within 3 years of laparoscopy and to control for biologically plausible factors affecting the chance of pregnancy and its outcome; such as diagnosis, age, duration of infertility, smoking, and primary infertility.

**Results and Discussion:** Increasing antibody titre were strongly associated with tubal damage ( $P < 0.001$ ). The overall Kaplan-Meier estimate of the pregnancy rate was 42.9% (95% CI 38.8-47.0%). Of the 263 women who conceived 160 (60.8%) were live births, 44 (16.7%) ectopic pregnancies, 38 (14.4%) miscarriages and the outcomes for 21 pregnancies (8.0%) were unknown. There was no relationship between antibody titres and pregnancy overall ( $P = 0.937$ ), but the chance of a live birth in women with a titre of  $>512$  was 60% (95% CI 30-70%) lower than amongst women with a titre of less than 64; and the chance of ectopic pregnancy 4.7 (95% CI 1.6-13.9) higher. Although both high antibody titres and tubal damage were associated with the lowest probability of live birth, and highest risk of ectopic pregnancy, further analysis revealed antibody titres not to be significantly associated with pregnancy outcome once infertility diagnosis was accounted for. Therefore while the proportion of live births declined with increasing titres and the proportion of ectopic pregnancies increased, it was the infertility diagnosis that determined outcome and not the Chlamydia antibody titre.

## Oral Abstracts

### 03

#### Modes of conception and multiple pregnancy: A national survey of babies born during one week in 2003 in the UK

N Bardis [1], M Deivanayagam [1], H Cuckle [2] & AH Balen [1]

[1] Department of Reproductive Medicine, Leeds General Infirmary, Leeds, U.K.; [2] Department of Reproductive Epidemiology, Leeds General Infirmary, Leeds, U.K.

**Introduction:** We report what we believe to be the first attempt to study the mode of conception of all babies born during a specified period of time related to multiplicity.

**Methods:** Invitation letters were sent to 245 maternity units in the United Kingdom. The aim was to collect data on every baby born during the week of 6th to 12th April 2003.

**Results and Discussion:** Information was collected by 178 maternity units (72.7%). Data was received on 6,913 deliveries: 6,812 (98.54%) were singleton, 100 (1.45%) twin and 1 (0.01%) triplet. A total of 7,015 babies were born. Of the 6,913 pregnancies 6,638 (96%) were conceived spontaneously, 133 (1.9%) with assistance and information was not provided for 142 (2.1%). The only triplet pregnancy was conceived spontaneously. The rate of multiple pregnancy was significantly greater in assisted (13.5%) compared with spontaneous (1.2%) conceptions ( $p < 0.001$ , difference=0.123, 95% C.I.=0.102-0.144). Of the multiple pregnancies from fertility treatment, 3 (16.7%) were as a result of clomiphene citrate therapy, 13 (72.2%) from in vitro fertilization (IVF) or frozen embryo replacements (FET) and 1 (5.6%) from superovulation with intrauterine insemination (IUI). There were no multiple pregnancies from ovulation induction with gonadotrophins. In the assisted conception pregnancies, the multiple pregnancy rate after clomiphene citrate therapy (7.3%) was significantly lower from that after IVF/FET (26%) [ $p = 0.040$ , difference=(-0.187), 95% C.I.=(-0.344)-(-0.0296)]; the multiple pregnancy rate after superovulation with IUI (12.5%) was not significantly different from that after clomiphene citrate or IVF/FET. The median maternal age at delivery of those who conceived spontaneously (29.7 years, interquartile range=33.7-24.6) was significantly less than those who received fertility treatment (33.7 years, interquartile range=37.5-30.1) ( $p < 0.001$ ). The median gestational age at delivery was 40 weeks (interquartile range=40.9-38.9) for singleton and 36.7 weeks (interquartile range=38.1-34.1) for multiple pregnancies ( $p < 0.001$ ). The live birth rate was higher for singleton (98.2%) than multiple pregnancies (93.6%) ( $p < 0.001$ ).

### 04

#### Does the site of sperm retrieval affect the outcome of intracytoplasmic sperm injection in azoospermia? A comparison of epididymal and testicular sperm

S Bhuiya, P Ray, M Mallya & V Sharma

Assisted Conception Unit, St James University Hospital, Leeds, UK.

**Introduction:** Azoospermia is found in 10% of male infertility cases. Obstructive azoospermia commonly results from genitourinary infections, congenital bilateral absence of the vas (CBAVD) and scrotal surgery. Surgical sperm retrieval and IVF with ICSI enables azoospermic men to have their own genetic offspring. The site of surgically retrieved sperm may influence the outcome of the treatment (Bachtell et al-1999). In this study we compared the fertilization, cleavage and pregnancy rates between epididymal and testicular sperm.

**Methods:** A retrospective analysis was done of 82 consecutive sperm retrievals in azoospermic men between May 1995 and October 2003. This included 17 vasectomised men, 36 patients with failed vasectomy reversal, 8 men with CBAVD, 12 men with post infective obstruction and 9 patients were in the miscellaneous aetiology group.

Our protocol was to perform a single stage procedure timed with egg collection where PESA was performed for all patients in the first instance. Failure to retrieve sperm by PESA progressed to MESA and failed MESA was followed by TESA. Sperm was retrieved by PESA in 36 patients, MESA in 13 and TESA in 7 patients. 25 patients were excluded from the study due to insufficient notes.

We also looked at other parameters like female and male partners age, which could have a significant impact on success rates.

**Results and Discussion:** The fertilization, cleavage and pregnancy rates of ICSI following epididymal sperm retrieval were 59.59%, 82.33% and 44% respectively and following testicular sperm retrieval were 59.01%, 83.33% and 28.5% respectively. The differences were not statistically significant in any of the above parameters of the two groups. ( $P = 0.9305$ ,  $P = 0.881$  and  $P = 0.4387$  respectively).

We were also unable to find a statistically significant impact of patient and partner's age on the outcome parameters.

ICSI with sperm retrieval has shown to produce a good fertilization, cleavage and pregnancy rate. Even though the pregnancy rate was higher with epididymal sperm, it did not attain statistical significance compared to testicular sperm. We propose that TESA should be attempted in all cases of failed PESA and MESA as ICSI following TESA gives comparable pregnancy outcomes.

## Oral Abstracts

### 05

#### Does repeated assisted ejaculation improve semen quality in spinal cord injured men?

S Das [1], S Dodd [2], SD Sharma [3], R Gazvani [1] & DI Lewis-Jones [1]

[1] *Hewitt Centre for Reproductive Medicine, Liverpool Women's Hospital, Liverpool, L8 7SS, UK;* [2] *Centre for Medical Statistics and Health Evaluation, University of Liverpool, Liverpool, L69 3GS, UK;* [3] *Southport and Formby NHS Trust, Southport, Merseyside, PR8 6PN, UK.*

**Introduction:** One of the major consequences of spinal cord injury (SCI) in male patients is infertility. It is estimated that about 50% of these injuries in the United States involve young men in the age group of 18-45 years. Less than 5% of these men can procreate without medical intervention. Defective scrotal temperature regulation and failure of clearance of the contents of the vas due to neurological dysfunction are thought to be important factors contributing to poor semen quality in men with SCI. There have been varying reports in the literature regarding the effect of repeated ejaculations on semen quality in this group of men.

**Methods:** Approval for the study had been taken from the local ethics committee. The aim of the study was to evaluate the effect of repeated electro-ejaculation on the semen quality in men with chronic spinal cord injuries. Sixteen men with chronic SCI of duration ranging from 5-25 years underwent three successive electro-ejaculations at two- four week interval. Both antegrade and retrograde ejaculates were collected at each sitting. Data was collected regarding the semen volume, sperm concentration, sperm motility, viability and the total motile count. The difference in these parameters between the first and third semen samples was analysed to ascertain improvement in the sperm concentration and quality.

**Results and Discussion:** Differences between the first and third sample were calculated for each patient, and the antegrade and retrograde samples were analysed separately. Wilcoxon signed rank test was used to determine the significance of these variables in both antegrade and retrograde samples. The difference in volume of antegrade ejaculate between the first and third samples had a median of 0, range from -18,10.5 with p-value of 0.6 and that in the retrograde samples had median 1.45 and range -8.5,78.3 with p-value 0.05. Negative values indicate a higher value of the variable in the third sample as compared to the first. Improvement in the volume of retrograde ejaculate just reached significance at p-value of 0.05. Since the retrograde volume is dependent on the volume of medium instilled before the procedure, this improvement is of doubtful clinical importance. No other parameters showed any significant improvement following three consecutive assisted ejaculations.

The mechanisms responsible for poor semen quality in SCI males is possibly multifactorial and poorly understood. Hypothetically, repeated assisted ejaculation would improve the semen quality by clearing possible noxious effects of stasis of prostatic fluid and sperm autoantibodies. However, other contributory factors i.e. scrotal hyperthermia and neuro-endocrine dysfunction continue to operate thereby, negating any positive effect that repeated assisted ejaculation may have. This study only involved a small number of patients and provided no firm conclusions and a larger study may help to provide a more definite answer.

### 06

#### Is the absence of an early pregnancy maternal inflammatory response associated with lower ongoing pregnancy rates?

SA El-Shawarby, L Seyani, SA Lavery, GH Trew & GP Sacks

*The IVF unit, Department of Reproductive Medicine and Science, Hammersmith Hospital, Imperial College School of Medicine, London, U.K.*

**Introduction:** We have recently shown that a systemic maternal inflammatory response is detectable at 4 weeks gestation with raised circulating C-reactive protein (CRP) levels, and have developed the novel hypothesis that an absence of such a response may result in early pregnancy failure. Those data were based on fresh IVF/ICSI cycles. The aim of this study was to assess CRP levels in early pregnancy following frozen embryo replacement cycles. These do not have the pro-inflammatory stimuli of fresh cycles, and are well recognized as having lower pregnancy rates.

**Methods:** Frozen embryo replacement cycles entailed ovarian suppression using gonadotrophin releasing hormone agonist followed by endometrial preparation using oestrogen patches and progesterone suppositories. 84 consecutive women had CRP levels measured on the day of the pregnancy blood (BhCG) test at 4 weeks gestation. Women with positive pregnancy tests were followed up by serial transvaginal ultrasound scans until 8 weeks gestation.

**Results and Discussion:** CRP levels were not significantly raised in either pregnant or non-pregnant women. In contrast to our findings in fresh cycles, there were no significant differences in CRP levels in women with ongoing pregnancy (n=19), pregnancy loss (n=25), and women who were not pregnant (n=40). There were no significant differences in the 3 study groups in age, cause of infertility, parity, body mass index, smoking status, and infection screening. Also, there were no significant differences in the treatment cycle peak estradiol levels, endometrial thickness, number of days of oestrogen therapy, embryo developmental stage, duration of storage, number and quality of embryos transferred.

Fresh cycles involve numerous potentially pro-inflammatory stimuli, which are not encountered in frozen cycles such as gonadotrophin administration and oocyte retrieval. We hypothesise that the pro-inflammatory environment of fresh cycles may be one important factor causing the generally higher pregnancy rates in fresh cycles when compared to frozen ones.

## Oral Abstracts

**07**

### **Pregnancy following monofollicular ovulation induction with recombinant FSH, recombinant LH, and timed coitus in an amenorrhoeic woman with long-standing hypogonadotrophic hypogonadism**

SA El-Shawarby, CF Turner, N Reddy, RA Margara, GH Trew & SA Lavery

*Department of Reproductive Medicine and Science, Hammersmith Hospital, Imperial College School of Medicine, London, U.K.*

**Introduction:** We describe the successful use of recombinant FSH (rFSH) and recombinant LH (rLH) to induce monofollicular ovulation, and achieve a viable pregnancy in an amenorrhoeic patient with hypogonadotrophic hypogonadism (HH).

**Methods:** A 31-year-old patient presented to our infertility unit with primary infertility and HH. Induction of ovulation was achieved using 50 I.U rFSH and 75 I.U rLH, with transvaginal ultrasonography and hormonal assay used for cycle monitoring. The dose of rFSH was increased to 75 I.U on day 12 as there was no follicular growth. 5000 units of human chorionic gonadotrophin were administered when a dominant follicle was seen on day 26 of treatment, and sexual intercourse was advised. The patient became pregnant but unfortunately had an early miscarriage.

A similar treatment protocol was followed in the second cycle except that the starting dose of rFSH was increased to 75 I.U, and luteal support in the form of progesterone suppositories was given until the day of pregnancy test. The patient became pregnant, and ultrasound scan performed 6 weeks later revealed a single viable pregnancy. Luteal support was continued until 12 weeks of an ongoing pregnancy.

**Results and Discussion:** The efficacy of the combination of rFSH and rLH has been recently shown to be similar to that of human menopausal gonadotrophin and gonadotrophin releasing hormone in induction of ovulation in HH. The case has confirmed that a daily dose of 75 I.U rLH is sufficient for promoting optimal monofollicular development and adequate endometrial growth.

To our knowledge, this is the first U.K report of consecutive pregnancies using rLH (Luveris) for monofollicular ovulation induction in a patient with HH. This line of treatment is acceptable, effective, and increases the treatment options available to this group of patients.

**08**

### **An investigation of what parents would like to know about their IVF conceived child's health**

L Fisher-Jeffes & AG Sutcliffe

*Department of Child Health, Royal Free Campus, RFUCMS, Rowland Hill Street, London, NW3 2PF.*

**Introduction:** We wished to investigate in a national cohort of IVF families (now with seven year old children) what specific concerns they had about their children's present or future health.

**Methods:** A longitudinal cohort study of 253 families whose children were ICSI or IVF conceived, were sent a questionnaire asking if they wished to participate in future studies of a) general child development b) child physical development; and were invited to add specific questions that were of concern to them about their child's present or future health.

**Results and Discussion:** We received 167 replies of which 166 considered the general questions (a) and (b) important. 48 families posed additional questions, of which 19 were concerned with their child's future fertility. Other questions related mostly to neurodevelopmental conditions that their child had. Others asked how to go about telling their child of their conception type. It seems the most pressing issue for families is future fertility of their children. Our group (Chrysostomou, Peters and Sutcliffe) have written a booklet (How I was conceived) to be provided for families which is child friendly on 'how to tell' aimed at eight year olds. This will also be demonstrated at this presentation.

For purposes of counselling it is important to know parents' specific concerns so they can be accurately addressed. This study goes some way to providing an insight into what parents regard as important.

## Oral Abstracts

### 09

#### Viagra Affects Sperm Function In-Vitro

DRJ Glenn, N McClure & SEM Lewis

*Obstetrics and Gynaecology, School of Medicine, Queen's University of Belfast.*

**Introduction:** In an audit of HFEA licensed units, we have demonstrated that 42% prescribe Viagra to aid patient semen production. Its effect on sperm function is unknown. However, as Viagra is a phosphodiesterase inhibitor, and these have been shown to affect sperm function, legitimate safety concerns have been raised. The aim of this study is to investigate the effect of Viagra on sperm motility and acrosome reaction.

**Methods:** Neat semen was incubated with Viagra (450ng/ml, equivalent to plasma concentrations after standard 100mg oral dose) and with BWV (controls). Additional semen was prepared by a 90/45% density centrifugation gradient to separate good and poor subpopulations. All samples were analyzed by computer assisted semen analysis (HTM IVOS) after 60 and 120 minutes. Prepared samples were labelled with Fluorescein Isothiocyanate Peanut Agglutinin to determine acrosome status.

**Results and Discussion:** Viagra increased the percentage sperm motility in neat semen (n=22) by 27%, percentage progressive motility by 38%, VAP by 21%, VSL by 21% and VCL by 16% at 60 minutes (all p values <0.001). These effects were sustained at 120 minutes.

Sperm isolated from 90% (n=57) and 45% (n=15) layers showed similar increases to sperm from neat semen. In addition, marked increases in ALH (16% [p=0.007]) and BCF (13% [p=0.005]) were seen in the 90% fraction after 120 minutes.

Viagra increased the proportion of fully acrosome reacted sperm in the 90% (+79%, p<0.001) and 45% (+77%, p<0.001) fractions. It also increased the proportion of partially reacted sperm in the 45% fraction (+24%, p=0.003).

This study demonstrates that in-vitro addition of Viagra to therapeutic concentrations increases sperm motility. However, Viagra clearly induces premature acrosome reaction. This study raises significant concerns for Viagra use in assisted reproduction.

Acknowledgement: Pfizer UK, Sandwich.

### 010

#### Comparative study of the use of LH and non-LH containing preparations in consecutive assisted conception cycles

UD Gordon, C Kailasam & P Wilson

*Centre for Reproductive Medicine, University of Bristol, Bristol, UK.*

**Introduction:** The use of a different gonadotrophin preparation is often considered by patients following IVF failure. Studies have indicated no clear advantage of the efficacy of LH versus non-LH preparations although this has been much debated in the literature. Few studies have, however, looked at the ovarian response with the two preparations administered in the same patient. The present study looked at the ovarian response and outcome in a select group of patients who voluntarily crossed over to a different gonadotrophin preparation (LH to non-LH and vice versa) in their subsequent cycle.

**Methods:** Retrospective study of patients who chose to alter their gonadotrophin preparation from LH (HMG: Menogon or Menopur, Ferring Pharmaceuticals) to non-LH (rec FSH: Gonal-F, Serono, UK) and vice versa. The inclusion criteria required a minimum washout period of at least one spontaneous menstrual cycle between the two treatments and the interval was no greater than twelve months. The same gonadotrophin dosage had been used in both cycles and the type of treatment undertaken (IVF or ICSI) did not differ. Long protocol gonadotrophin releasing hormone analogue regime was used in all cases. The choice to crossover to a different type of gonadotrophin was taken by the patient and was entirely voluntary. Data was analysed using parametric and non-parametric tests.

**Results and Discussion:** A total of 80 patients and 160 cycles were studied. No differences were noted in the days of stimulation, ampoules used, oocytes collected, fertilisation rates or embryos transferred. The pregnancy outcome can only be compared between the two subsequent cycles and this was no different (28.6% and 30.8% respectively, p=0.838)

When patients were treated with LH- containing and non-LH containing gonadotrophin preparations in subsequent cycles, no differences were noted in any of the ovarian response parameters studied.

## Oral Abstracts

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### O11

#### Ownership of embryos: An international comparison of attitudes to embryo ownership, use, donation and destruction

GM Lockwood

*Midland Fertility Services, Centre house, Court Parade, Aldridge, WS9 8LT, UK.*

**Introduction:** Gametes, even if donated for the benefit of other peoples' fertility treatment, have a moral 'neutrality' which is not enjoyed by embryos. In most cultures and jurisdictions (even in secular states), the fertilised oocyte is perceived to have a degree of moral significance which outweighs that of the gamete. This is the case even in countries which have liberal laws on the termination of unwanted pregnancy. The successful development of cryobiology, which has allowed a temporal separation to be made between the production of gametes, the fertilisation of oocytes and the initiation of a pregnancy, has resulted in a moral ambiguity about the status of the frozen embryo. This study was designed to identify inter-country differences in attitudes towards, and legal status of, frozen embryos.

**Methods:** Medical, ethical and legal journals were reviewed for articles relevant to the topic. Telephone interviews were conducted with clinicians, scientists, legislators and ethicists with an interest in the field. A detailed questionnaire was circulated internationally to relevant bodies including the regulatory authorities and patients' support groups.

**Results and Discussion:** Internationally, there is a wide divergence of opinion about the moral and legal status of the human embryo and the rights, duties and interests of the gamete providers. A summary of legal decisions made under different legal jurisdictions demonstrates the arbitrary nature of 'justice' in relation to the ownership and moral disposition of human embryos. I provide an argument requiring the re-appraisal of the status of the human embryo that provides an international benchmark in the face of 'reproductive tourism' and the 'globalisation' of fertility treatment.

### O12

#### Support and advice following embryo transfer

C Malone

*The Hewitt Centre for Reproductive Medicine, Liverpool Women's Hospital, Liverpool, UK.*

**Introduction:** Embryo transfer can be perceived by patients as being the most important part of their treatment cycle when undergoing in-vitro fertilisation and intra-cytoplasmic sperm injection.

**Methods:** Anecdotally it would appear that the support and advice given to patients following embryo transfer can vary from unit to unit. Given the constant drive to improve pregnancy rates whilst delivering a quality service using evidence based medicine this appeared to be an area of the treatment cycle that warranted closer scrutiny. To do this a literature search has been undertaken to review any available evidence regarding advice for patients following embryo transfer. Also a postal survey has been undertaken with a questionnaire being sent to every unit in the UK licensed to perform IVF-ET.

**Results and Discussion:** The questionnaire sought to establish the support and advice given routinely to patients following embryo transfer. The results of the questionnaire will be discussed in relation to the literature review. Areas of clinical practice will also be discussed such as when units are routinely performing pregnancy tests and pregnancy scans.

## Oral Abstracts

### O13

#### Analysis of effectiveness of revised Welfare of Child assessment for patients requesting assisted conception treatment

A McConnell & M Rajkhowa

*Assisted Conception Unit, Ninewells Hospital and Medical School, Dundee, UK.*

**Introduction:** A condition of the licence granted by the HFEA at the Unit's most recent inspection was that 'The PR must ensure that welfare of the child procedures are carried out in accordance with the Code of Practice'. The pre-existing procedure was that GPs were asked to comment on welfare of the child issues and patients' suitability for treatment; this resulted in a reply rate of only 8.2% in 2002.

A revised assessment procedure was initiated in April 2003 and included a treatment assessment form, questionnaires completed by both partners and GPs' replies to enquiries regarding welfare of the child issues. Treatment can proceed only when the assessment procedure has been satisfactorily completed.

**Methods:** An audit was carried out six months after implementation of the revised procedure with the aim of assessing the effectiveness of the system and its effect on workload and waiting times.

483 letters were sent (238 couples and 7 single women). The average delay between sending the letter and form to the GP and their return was 35 days (range 1 - 168 days); 23% required follow-up reminders. 14 replies (5.8%) from GPs mentioned potential areas of concern. Of these (3.9%) led to treatment being deferred pending a review appointment or a request for further information.

**Results and Discussion:** The revised assessment procedure has led to a substantial increase in administrative workload (an average of 1.5 hours per day and, in a significant proportion of cases, to a delay in patients starting treatment. However, in 9 cases (3.7%), replies have drawn attention to factors which could potentially be contraindicated to patients receiving treatment and which would possibly otherwise not have been revealed.

### O14

#### The effects of obstruction on spermatogenesis

CM McVicar [1], DA O'Neill [1], N McClure [1], SJ McCullough [2], LH Dalzell [1] & SEM Lewis [1]

*[1] School of Medicine, Obstetrics and Gynaecology, Queen's University Belfast, Institute of Clinical Science, Grosvenor Rd., Belfast, BT12 6BJ, UK; [2] Anatomy, Queen's University Belfast, Medical Biology Centre, Belfast, UK.*

**Introduction:** The success rate for vasectomy reversal is not high, especially if the vasectomy is longstanding. Where sperm are obtained there is an increased incidence of anti-sperm antibodies and a reduction in motility. Increasingly, sperm are obtained by testicular biopsy and used in ICSI as an alternative therapeutic approach. The aim of study was to compare the yield of round and elongated spermatids and spermatozoa from the seminiferous tubules of vasectomised males with samples from obstructive azoospermic men (OA) and from fertile men undergoing vasectomy.

**Methods:** Testicular biopsies were obtained by Trucut needle biopsy from men who had vasectomies (n=19), men with OA (n=29) and fertile men (n=37). Tubule samples were milked to calculate the number of sperm/g of biopsy and Bouins-fixed to determine the numbers of round and mature spermatids and Sertoli cells.

**Results and Discussion:** The sperm yield of fertile men was  $11.4 \pm 1.6 \times 10^6$  gbiopsy<sup>-1</sup>. This was markedly reduced in vasectomized men  $3.75 \pm 2.3 \times 10^6$  [-67%] (p<0.05, Independent t-test) and in the OA group:  $2.98 \pm 0.5 \times 10^6$  [-74%] (p<0.005, Independent t-test). There were similar reductions in mature spermatids (fertile men:  $53.3 \pm 2.8$  v vasectomy  $24.0 \pm 2.8$  per tubule, -55% (p<0.005, Independent t-test). The reduction in the numbers of mature spermatids and spermatozoa post-vasectomy and in men with obstructive azoospermia has significant clinical implications and raises concerns about the safety of vasectomy. The decreased yield may be due to an increased rate of apoptosis in the testis via the p53-Bax pathway. Ongoing studies are addressing this possibility.

## Oral Abstracts

### 015

#### Are we providing appropriate psychological and counselling care for assisted conception patients?

R Newport & U Acharya

*South West Centre for Reproductive Medicine, Derriford Hospital, Plymouth.*

**Introduction:** Infertility is a distressing problem for those who wish to have children. Assisted reproduction treatments can be a considerable source of anxiety and stress for those undergoing treatment. Traditionally counsellors provide psychological or emotional support, although audit statistics show that uptake remains low at around 20% in clinics nationally. These statistics do not fit with studies showing that the majority of patients recognise the potential benefits of psychological support services. Little is known about the factors which influence decision making regarding this issue, in explaining the apparent discrepancy between patients' interest and uptake levels. This is the first study to use an appropriate methodology to look at reviewing psychological support for patients in assisted conception centres.

**Methods:** Qualitative research methods were employed. After obtaining local ethical approval, 30 couples were interviewed on three occasions during their IVF treatment cycles: at initial consultation, following embryo transfer and at follow up visit. All participants were new IVF patients. In depth interviews were analysed using the constant comparison method of grounded theory in which textual data are carefully examined using a systematic framework.

**Results and Discussion:** Our results show that a totally different way of providing psychological support is need. The results will be discussed in depth focussing on patients psychological support needs. Recommendations about optimal care will be discussed.

Funded by Serono

### 016

#### Blastocyst development following conventional IVF or ICSI

T Pastroma, K Schnauffer, C Kingsland & S Troup

*Hewitt Centre for Reproductive Medicine, Liverpool Women's Hospital.*

**Introduction:** Embryos generated following ICSI have been suggested to display a reduced capacity for blastocyst formation in vitro compared to their IVF counterparts (Shoukir et al, 1998; Griffiths et al, 2000). In addition, ICSI-derived blastocysts have been reported to be of poorer morphology (Miller and Smith, 2001). The aim of this study was to compare the development to the blastocyst stage of surplus embryos obtained after conventional IVF or ICSI.

**Methods:** Oocytes were inseminated or injected approximately 40h post-hCG. Gametes and early embryos were cultured in P1 Medium + 10% SSS (Irvine Scientific). Embryo transfer was routinely performed on day 2. Embryos were frozen at the early cleavage stage if they were assessed as being good quality 4-cell by midday on the day of ET. Those embryos not meeting these criteria were cultured for a further 24 hours in P1, transferred to Blastocyst Medium +10% SSS (Irvine Scientific) and cultured for a further 2-3 days and blastocyst formation assessed. Data were analysed using the Chi-square test.

**Results and Discussion:** 1289 patients (535 IVF and 754 ICSI) had embryos placed in extended culture. The blastocyst formation rate per embryo was 22.1% (398/1800) following IVF and 19.4% (499/2574) following ICSI. 7.6% (136/1800) and 8.4% (216/2574) of blastocysts resulting from IVF and ICSI, respectively, were assessed as being of good quality suitable for cryopreservation. No significant difference was found between the proportion of embryos reaching the blastocyst stage obtained from IVF and ICSI or between the morphology of the blastocysts generated through both types of treatment. These data are not in agreement with previous studies, in which lower numbers of embryos were used. Our findings suggest that the development to blastocyst in vitro of ICSI-derived embryos is not adversely affected, providing reassurance for the continued use of the ICSI procedure.

## Oral Abstracts

### O17

#### Retrospective analysis of outcome following transvaginal aspiration of hydrosalpinx in patients undergoing IVF treatment

MP Perez-Clemente & M Rajkhowa

*Assisted Conception Unit, Tayside University Hospitals, Dundee, UK.*

**Introduction:** The presence of tubal disease with hydrosalpinx may have an adverse effect on the outcome of IVF treatment. Pretreatment salpingectomy has been shown to improve implantation rate in such couples. However, undergoing Salpingectomy is not always acceptable to patients who are coming through for treatment. In an attempt to improve pregnancy outcome, we developed a protocol to drain hydrosalpinges seen at the time of oocyte retrieval.

**Methods:** Couples undergoing conventional IVF treatment for tubal disease alone were included in the analysis. A retrospective analysis of the treatment data between April 2002 and March 2003 was performed. Two groups were defined: patients with hydrosalpinx at the time of egg retrieval and those without. Definition of pregnancy was the presence of an intrauterine gestational sac at the time of the pregnancy scan.

**Results and Discussion:** Sixty-seven patients with a history of tubal disease alone were identified. 18 (26.9%) had a hydrosalpinx at the time of treatment. Of these, 3 had a history of previous spontaneous conception (3/18, 16.7% spontaneous pregnancy rate). 2 patients had hydrosalpinges drained prior to starting the IVF cycle. 16 had hydrosalpinges at the time of egg retrieval and 15 were successfully drained. There were 4 pregnancies in the 18 patients with treated hydrosalpinx, giving a pregnancy rate of 22.2%. There was no postoperative infection.

49 patients had tubal disease without hydrosalpinges. Of these, 25 had previously had a spontaneous conception (51% spontaneous pregnancy rate). 16/49 achieved a pregnancy giving a pregnancy rate of 32.7%.

The overall pregnancy rate in women with tubal disease was 29.9% (20/67). Patients with hydrosalpinx achieved a pregnancy rate of 22.2% compared with 32.6% in the other group, which is not statistically significant. We are planning to perform a larger prospective randomised study to see if drainage of hydrosalpinx is an alternative to performing salpingectomies in women undergoing IVF treatment.

### O18

#### Qualitative Investigation of Staff and Patients' Opinions of a Proposed Trial of Elective Single Embryo Transfer

MA Porter & S Bhattacharya

*Obstetrics and Gynaecology, University of Aberdeen, Aberdeen, UK.*

**Introduction:** Twin pregnancy is seen as a major preventable complication of in-vitro fertilisation (IVF). Several small trials have shown that single embryo transfer (SET) can significantly reduce the incidence of twins without compromising cumulative live birth rates per couple. However before this policy can be adopted into routine clinical practice in the U.K., a large, multi-centre randomised controlled trial (RCT) comparing elective single vs. double embryo transfer is warranted. The aim of this study was to investigate staff and patient views about the feasibility of such a trial.

**Methods:** Two focus groups, involving staff and patients respectively, were planned. Consent was obtained from the local Ethics Committee. The first group comprised 10 members of an IVF Unit, including medical, nursing and embryology staff. Most couples undergoing IVF, were unwilling to be part of a focus group, but 12 agreed to be interviewed. The discussion/interviews were tape-recorded and transcripts analysed thematically.

**Results and Discussion:** Opinions among clinic staff were divided on the need for an RCT. Some patients also thought it was unnecessary. Some staff felt that all patients should have SET, whereas others welcomed the 'evidence' which a proper trial would provide. Couples saw no need to minimise their own chances of twins, but thought that other couples might find this strategy acceptable. There were a number of disparities between staff perceptions of patients' views and those of the patients themselves. Staff members felt that patients knew and accepted the 'risks' associated with twin pregnancies. In fact, patients were largely unaware. Clinic staff believed that they were discussing the 'risks' when, in fact, they were discussing the 'chances' of conceiving twins. They also thought that patients' desire for twins meant that they would never accept SET, whereas patients said they would accept SET if it were the Unit's policy but were uncertain about randomisation. Patients' views might have been different had they been able to discuss this issue with other couples. Similarly, if interviewed individually, members of staff might have offered views different from those of the majority. Erroneous perceptions of patients' views by clinic staff may affect successful planning and execution of randomised trials in IVF. (Funded by the Wellcome Trust.)

## Oral Abstracts

### O19

#### Unfulfilled expectations: a qualitative investigation of women's fertility following Caesarean section

MA Porter [1], S Bhattacharya [1], E van Teijlingen [2], D Campbell [1], M Hall [1], J Mollison [2] & A Templeton [1]

[1] *Obstetrics and Gynaecology, University of Aberdeen, Aberdeen, UK*; [2] *Public Health, University of Aberdeen, Aberdeen, UK.*

**Introduction:** It has been suggested that secondary infertility is related to mode of delivery. Caesarean section (CS) is more common in those who have problems conceiving, and those who have a CS are less likely to have further pregnancies. This study aimed to ascertain what role the CS played, if any, in women's decisions about having more children.

**Methods:** With the approval of the local ethics committee, questionnaires were sent to women who delivered their first baby by CS between 1980 and 1995 but who did not have another viable pregnancy within five years. Forty-nine respondents underwent in-depth tape-recorded interviews covering experiences of CS, decision making about subsequent pregnancies and infertility. Verbatim transcripts were analysed thematically with the aid of a computer package, NVivo.

**Results and Discussion:** Earlier analysis of questionnaires completed by 1117 women had suggested that sub-fertility could be classified as voluntary or involuntary on the basis of women's use of contraception, trying for another baby and total number of children. Sub-fertility was voluntary in 488 (69%) of those who had no more children and 169 (50%) of those who had delayed their next pregnancy by five years or more. Negative experiences during the index CS formed a prominent element in women's accounts of their reproductive choices. Particularly distressing was the recovery period, when women found themselves much less well and mobile than they had expected. In interviews it became apparent that those classified as 'voluntarily' sub-fertile had sometimes felt constrained by their circumstances or other factors not to have another child, or to leave a longer gap than they would have preferred between children. For example, many women found themselves partnerless at a time when they might have been considering having another child. The clinical categorisation of sub-fertility following CS as 'voluntary' or 'involuntary', is an arbitrary distinction which does not take account of the many factors which limit women's reproductive options. Full exploration of the complexities of women's reproductive decision-making is best performed using qualitative methods.

(Funded by Chief Scientist's Office, Scottish Executive.)

### O20

#### A postal survey of intrauterine insemination practice in the UK

N Rawal, S Wood & N Haddad

*Countess of Chester Hospital, Chester, UK.*

**Introduction:** Intrauterine insemination (IUI) is frequently indicated therapeutic modality in infertility. The overall success rate of IUI remains controversial and depends on several factors, with published pregnancy rates ranging from as low as 5% to as high as 70% per patient. We did a postal survey to determine the attitudes to the factors influencing IUI practice.

**Material & Method:** A questionnaire was devised based on a number of possible factors that can affect IUI. It was sent to 165 Reproductive medicine units in UK. Practitioners were requested to rate each parameter on the scale of 1 to 10, where 1 was least important and 10 was very important. The total score for each parameter was calculated as a percentage of the maximum score. The mean score +SD was also calculated for each variable.

**Result & Discussion:** A total of 102 practitioners replied. Over 50% of the corresponding practitioners were consultants, 32% were infertility nurse specialist and 12% were other clinicians. The factor that got the highest rating was the number of the follicles on the day of human chorionic gonadotrophine (hCG) injection. This was followed by the size of the follicle on the day of hCG and the total sperm count. The fourth critical factor voted by the respondents was the need for a standardized protocol for all unit staff regarding IUI. Use of the anti-prostaglandins to prevent contraction was voted the least important factor to influence the outcome.

We believe that the standardised protocol should cover the timing of hCG with relation to the size and number of the follicle, the minimum number of sperm required for IUI and the technique of IUI.

The wide variation in the practice of IUI partly explains the great variance in the pregnancy rates.

## Oral Abstracts

### O21

#### Does vasectomy duration affect the sperm quality and the outcome of intracytoplasmic sperm injection (ICSI) after sperm retrieval?

P Ray, S Bhuyia, M Mallya & V Sharma

Assisted Conception Unit, St James University Hospital, Leeds, UK.

**Introduction:** Epididymal sperm retrieved by PESA or MESA and testicular sperm retrieved by TESA can be used in conjunction with ICSI for treatment of azoospermic post vasectomised men and patients with failed reversal of vasectomy (Nagy et al 1995). We do not know if post vasectomy duration has any effect on sperm motility and count, which could affect the pregnancy outcome. It has also been speculated that stagnation in the chronically obstructed epididymis may affect testicular sperm DNA and have a negative impact on fertilization, cleavage and pregnancy rates (Steele et al 1999). Abdelmassih et al (2002) reported a negative correlation between pregnancy rates and time interval from vasectomy whilst Junior et al (2003) reported no effect of the duration of vasectomy on the treatment. This study was done to evaluate the effect of increasing duration of vasectomy on the outcome of treatment.

**Methods:** Retrospective case note analysis was done for 54 ICSI cycles following sperm retrieval in post vasectomy patients from May 1995 to October 2003. Sperm was retrieved by MESA or PESA in 32 cases and TESA was performed in 4 patients. The patients were divided into 4 groups depending on the duration of the vasectomy: < 6 years (Group A), 6-10 years (Group B), 11-15 years (Group C) and >15 years (Group D). Sperm count, motility, fertilization, cleavage and pregnancy rates were compared between groups.

**Results and Discussion:** The fertilization, cleavage and pregnancy rate of each group was analysed and compared using the chi square test. Spearman's Rank test was used to analyse the sperm count and motility. There was no statistically significant correlation between the cleavage rates of the 4 groups. However the fertilization and the pregnancy rates were significantly higher in-group A cycles (vasectomy duration <6 yrs) compared to the other groups ( $P < 0.0001$ ,  $P = 0.0001$  respectively). There was no statistically significant difference in the pregnancy and fertilization rates of the other three groups. The sperm count and motility did not show any significant correlation with the duration of the vasectomy.

Our study suggests that success with surgically retrieved sperm is the highest when the duration of vasectomy is less than 6 years and patients may be advised accordingly. After an initial period of 6 years we have not noticed any significant change in fertilization and pregnancy rates. Our results are different from that of Abdelmassih et al's study (2002) and of Junior et al's study (2003). In light of this contradicting data a bigger prospective randomized controlled study is warranted.

### O22

#### Combined life-style modification and metformin in obese patients with polycystic ovary syndrome (PCOS). A randomised, placebo-controlled, double-blind multi-centre study

T Tang [1], J Glanville [1], CJ Hayden [1], J Barth [2] & AH Balen [1]

[1] Reproductive Medicine Unit, The General Infirmary at Leeds, UK; [2] Department of Biochemistry, The General Infirmary at Leeds, UK.

**Introduction:** Initial reports from small studies suggested benefits from metformin therapy for women with PCOS, leading to the need for adequately powered studies.

**Methods:** A multi-centre, randomised, placebo-controlled, double blind study was carried out between 1999 and 2003. Patients with PCOS, a BMI > 30 Kg/m<sup>2</sup> and oligo-/amenorrhoea were recruited. All subjects took metformin (850mg) or placebo tablets twice daily for 6 months and received the same advice from a dietitian. They were seen for monthly review and encouragement.

**Results and Discussion:** 115 subjects, metformin group (MET) = 55 and placebo group (PL) = 60, were recruited. There were no significant differences in the median BMI (kg/m<sup>2</sup>) (MET = 38.1, PL = 36.2;  $p = 0.17$ ), the mean age (years) (MET = 29.6, PL = 29.4;  $p = 0.80$ ) and the drop out rates (MET = 18%, PL = 14%;  $p = 0.74$ ). The intention to treat approach was used in the data analysis.

At the end of the study period, both groups showed significant improvements in menstrual frequency with the median of increased menses in 6 months (MET = 1,  $p < 0.001$  and PL = 1;  $p < 0.001$ ) and improvements in weight loss with the mean weight loss (kg) (MET = 2.6;  $t = 4.08$ ,  $df = 44$ ,  $p < 0.001$  and PL = 1.35;  $t = 2.12$ ,  $df = 51$ ,  $p = 0.039$ ). However, there were no significant differences between the groups in terms of improvements of menstrual cycles ( $p = 0.98$ ) and weight loss ( $p = 0.17$ ).

A significantly higher proportion of women in both groups had lost weight among those experienced improvement of menstrual frequency compared with those with no change (MET,  $p = 0.001$ ; PL,  $p = 0.045$ ).

Serum endocrinology and metabolic assays are currently being analysed.

Metformin does not improve weight loss and menstrual frequency in obese patients with PCOS. Weight loss alone through life-style changes improves menstrual frequency.

## Oral Abstracts

### O23

#### Evaluation of Pain by using visual analogue scale at Hysterosalpingography(HSG) and Hysterosalpingo-contrastsonography (HyCoSy) performed by a single operator- a prospective study

HN Thackare, A Zosmer, M Dirnfeld, R Navratnarajah, A Tozer & T Al-Shawaf

*Reproductive Medicine Unit, Barts and the London NHS Trust, London, EC1A 7BE, UK.*

**Introduction:** HSG and HyCoSy are the most commonly used outpatient tests for the assessment of uterine cavity and tubal patency. Although women tolerate both procedures well, they are still considered as one of the most painful and distressing diagnostic procedures in infertility. Very few studies have analysed the factors affecting the degree of pain in both procedures carried out by a single operator.

**Methods:** Prospective questionnaire evaluation with a visual analogue scale for pain was used by 150 consecutive women referred to the infertility clinic for HSG or HyCoSy.

Questionnaire was filled within 30 minutes of completing the procedure and focussed on the overall pain score and at different steps of the procedure. Parameters analysed were: mean age, type of infertility, day of the cycle, volume of fluid injected and length of procedure.

Data analysis performed by using Statsdirect statistical package.

**Results and Discussion:** 96% questionnaires were completed. The mean age of women in both groups, the number of primary and secondary infertility and day of the cycle was similar in those who underwent HSG(n=75) and in those who had HyCoSy(n=69). The volume of fluid injected and length of procedure in the HSG group was 8.5+/-4.4ml, 8.84+/-3.74 minutes versus 16.5+/-8.7ml, 12.9+/- 4.9 minutes in the HyCoSy group (p<0.0001).

Overall pain score on a scale of 0 to 10 was almost identical in both groups (5.26 +/-2.6 and 5.54+/-2.49 for HSG and HyCoSy). Severe pain score (>7) was recorded by 18 and 19 women in the HSG and HyCoSy groups respectively.

Insertion of catheter and balloon inflation had the highest pain score(4.59+/-2.89 vs 5.33+/-2.86, p= 0.1, C.I. 2-5)

There was significant difference between the two groups in the pain score with regards to volume of fluid injected (p<0.001, CI 5-7).

In summary, due to larger volumes used in HyCoSy, the pain score was significantly higher as compared with HSG. Patients at infertility clinics need to be aware of the advantages and disadvantages of both procedures.

### O24

#### The effects of tetrahydrocannabinol (THC), the primary psychoactive cannabinoid in marijuana, on in vitro human sperm motility

LB Whan [1], N McClure [1, 2] & SEM Lewis [1]

*[1] School of Medicine, Obstetrics and Gynaecology, Queen's University, Belfast, Institute of Clinical Science, Grosvenor Road, Belfast, BT12 6BJ, UK; [2] Regional Fertility Centre, Royal Maternity Hospital, Belfast BT12 6BJ, Northern Ireland, UK.*

**Introduction:** Marijuana use may impair male fertility by inhibition of sperm function imperative for fertilization. In sea urchins, THC has been found to affect sperm motility and reduce the sperm's ability to bind to the egg. The aim of this study was to assess the effects of THC on human sperm motility parameters in vitro.

**Methods:** Semen samples (n=51) were obtained from men attending the Regional Fertility Centre. Sperm were separated into 45% and 90% fractions using a two-step discontinuous Percoll gradient. The prepared sperm were divided into two aliquots. One was incubated, at 37°C for 3h, with THC at 1.5 µg/ml (for comparison with work performed using sea urchin), and the other was incubated in the absence of THC. Sperm motility was assessed by computer assisted analysis (Hamilton Thorne IVOS; USA).

**Results and Discussion:** THC caused a marked decrease (-23%, P<0.001) in percentage progressive motility in the 90% fraction. The 45% fraction showed a greater decrease (-45%, P=0.01) in progressive motility in the presence of THC compared to controls. A decrease in the ALH, (-10%, P=0.007) was also observed in the 90% fraction in the presence of THC. In the 45% fraction, a 10% decrease in ALH was observed but this did not reach significance. None of the remaining motility parameters (VAP, VSL, VCL, BCF and linearity) was significantly altered by THC in either fraction. THC (at the concentration tested) leads to a decrease in the percentage and the quality of human sperm motility in vitro. This may subsequently have consequences for reproduction. Further dose dependent studies will be performed to determine if these effects persist at a range of concentrations from the therapeutic to the supraphysiological.

**Acknowledgements:** GW Pharmaceuticals UK, who donated THC for the study.

## Poster Abstracts

### P1

#### Does elective cryopreservation of embryos at pronucleate stage (freeze-all cycles) in women at risk of ovarian hyperstimulation syndrome (OHSS) affect the overall pregnancy rates?

S Vyjayanthi, T Tang, M Deivanayagam, A Fattah, N Bardis & AH Balen

*Reproductive Medicine Unit, Leeds General Infirmary, Leeds, UK.*

**Introduction:** OHSS is a life-threatening condition resulting from excessive ovarian stimulation in IVF cycles. The strategy in our unit to manage the women at risk of developing severe OHSS (when oestradiol levels exceeded 15,000pmol/l and more than 30 oocytes retrieved) is to perform an elective cryopreservation of all embryos at pronucleate stage for subsequent transfers. The aim of this retrospective study is to assess the overall outcome.

**Methods:** Details were abstracted from the unit database and the case-notes.

**Results and Discussion:** Between 1998 and 2000, 150 freeze-all cycles were performed out of 5847 IVF cycles (2.6%). The mean age was 30.6 years old (95% C.I.=29.9-31.3). The mean fertilisation rate was 51.7% (95% C.I.= 48.2-55.2%) and the median number of embryos frozen was 13 (inter-quartile range 8-19).

Overall, 260 frozen embryo transfer cycles (FET) were subsequently carried out and the median number of embryos thawed per FET was 5 (inter-quartile range 4-6). The median of FET cycles per patient was 2. The pregnancy rates (PR) and the live birth rates (LBR) per FET cycle were 31.5% and 15.8%, respectively. These rates were significantly lower than the fresh IVF cycles (PRIVF=39.7%;  $z=2.58, p=0.01$  and LBRIVF=23.1%;  $z=2.67, p=0.008$ ).

However, the overall pregnancy rates per patient (PRP) and the live birth rates per patient (LBRP) after an oocyte-retrieval attempt were not significantly different between the freeze-all cycles and the fresh IVF cycles (PRPfreeze-all = 46%, PRPIVF = 49.5%;  $z=0.763, p=0.445$ ) (LBRPfreeze-all = 26.6%, LBRPIVF = 28.2%;  $z=0.338, p=0.785$ ).

The incidence of patients who subsequently developed severe OHSS requiring hospitalisation in the freeze-all cycles was 2%. Although there is no evidence indicating that elective cryopreservation of embryos is more effective to prevent OHSS than the other strategies (coasting or prophylactic albumin infusion), this practice does not affect the overall pregnancy outcomes.

### P2

#### Association between prognostic factors and clinical pregnancy rates in donor egg recipients: A cohort study using the egg sharing model

O Olufowobi [1, 2], M Afnan [1, 2], A Coomarasamy [2, 3], O Oyesanya [1, 2], D Neelakantan [1, 2], H Mohamed [1, 2] & K Sharif [1, 2]

*[1] Assisted Conception Unit, Birmingham Women's Hospital, Birmingham, England; [2] University of Birmingham, Birmingham, England; [3] Education Resource Centre, Birmingham Women's Hospital, Birmingham, England.*

**Introduction:** The outcome of egg donation in recipients is affected by many factors. Compensated egg sharing (CES) is a programme in which, women who undergo in-vitro fertilisation (IVF) donate some of their eggs to recipients in return for reduced fee their treatment.

Here we report the prognostic factors that influence outcomes in recipients in CES.

**Methods:** We studied consecutive donors [ $n=220$  (mean age  $\pm$  (S.D) 31.0  $\pm$  2.9 years)] and corresponding recipients [ $n=218$  (mean age  $\pm$  (S.D) 38.6  $\pm$  6.9 years)] who received half of the randomly allocated eggs during July 1999 to July 2003. Donors were aged < 36 years and had basal FSH < 10 IU/L. The donors underwent pituitary down-regulation with GnRH-analogue, which was commenced in the luteal phase. After 14 days of GnRH-a therapy, down-regulation was confirmed with ultrasonography (u/s) (endometrial thickness < 4mm; absence of ovarian follicular activity). Ovarian stimulation was performed with FSH at an individually adjusted dose. Follicular development was monitored with u/s and hCG (5,000 IU) was administered when the leading follicle was > 18mm. Transvaginal egg recovery (TER) was performed 36 hours after hCG administration. Recipients had two or three embryos transferred 2-3 days after TER in the donors, following a programmed E2 and progestogen therapy, which was synchronised with respective donor cycle.

**Results and Discussion:** The mean  $\pm$  (S.D) number of eggs retrieved was 15.7  $\pm$  5.5 and 8.7  $\pm$  4.9 was donated. The mean  $\pm$  (S.D) fertilisation rate for recipients was 67.0  $\pm$  32.6 % while the mean  $\pm$  (S.D) endometrial thickness was 9.9  $\pm$  2.2 mm. The mean  $\pm$  (S.D) number of embryo transferred to recipients was 2.1  $\pm$  0.4. Their urine pregnancy, clinical pregnancy and implantation rates per cycle started were 37%, 28% and 20% respectively.

Logistic regression analysis demonstrates a trend towards an improved pregnancy success in recipients less than 35 years of age, endometrial thickness of > 8mm, fertilisation rate > 50%, patients with residual ovarian function and those whose donors had basal FSH < 8 IU/L.

## Poster Abstracts

### P3

#### Seasonality and the role of sunlight in Assisted Conception cycles

SJ Wood [1, 3], A Quinn [2, 3], CR Kingsland [2] & DI Lewis-Jones [2, 3]

[1] Dept Obstetrics & Gynaecology, Countess of Chester Hospital, Chester UK; [2] Hewitt Centre for Reproduction, Liverpool Womens Hospital, Liverpool UK; [3] Dept of Obstetrics & Gynaecology, University of Liverpool, Liverpool, UK.

**Introduction:** The evidence for seasonal difference in pregnancy rates has been well documented in animal and human populations. The evidence for a seasonal variation in in vitro fertilisation (IVF) results is more contentious. In papers that have demonstrated seasonal variations the commonest finding is an increase in conceptions occurring during the summer months possibly explained by photoperiodic effects modulated by melatonin secretion. We wished to confirm if this seasonal variation exists, and what is the effect of daylight hours on outcomes in IVF cycles

**Methods:** This was a retrospective analysis of 3,568 consecutive IVF/ICSI cycles over 3 years. Only cycles utilising urinary gonadotrophins under a standard long protocol regimen were included for study. In these 2709 cycles, data was collected for age, FSH level, diagnosis, oocytes retrieved and fertilised, the number of units of gonadotrophin utilised, implantation and pregnancy rates. These results were correlated against the season in which the cycle occurred (winter Dec-Feb, Spring Mar-May, Summer Jun-Aug, Autumn Sep-Nov). Further analysis was performed to assess differences occurring during cycles performed during Summer daylight hours BST and those during winter time GMT.

**Results and Discussion:** No differences were found with regard to female age, previous parity, FSH levels or diagnosis between cycles performed at different times of the year. The analysis of variance did however indicate a significant difference in the seasonal outcomes in terms of an increased requirement of gonadotrophins per oocyte retrieved during the winter months over the summer 882 v 728 ( $p=0.026$ ). There was no significant difference in implantation or pregnancy rates with regard to season. When cycles were analysed with regard to the influence of daylight hours the differences were more marked with a significant decrease in the amount of gonadotrophins required per oocyte collected during the lighter summer cycles 766 v 880 ( $p=0.006$ ), there was also significant increases in implantation rates per embryo transferred 11.4 v 9.3  $p=0.03$  and clinical pregnancy rates 328/1642 (20%) v 165/1067 (15%)  $p=0.003$ . These results appear to confirm a significant increase on the response of the ovary to gonadotrophin stimulation due to prolonged exposure of the patient to daylight. It is known that the anatomical and molecular substrates and receptors of the system that encodes changes in photoperiodism are preserved in primates including humans and that this system appears intact from the retina to the cortex, pineal gland and hypothalamus. It is also thought that melatonin secretion may interact with the neurones controlling GnRH secretion in the hypothalamus. Whilst this may explain the increased gonadotrophin requirement during winter cycles the effect on implantation and clinical pregnancy rate suggests that endometrial receptivity may also be affected by sunlight duration.

### P4

#### Is endometriosis responsible for difficult embryo transfer?

S Basu, A Sizer & G Jose

Cardiff Assisted Reproduction Unit, University Hospital of Wales, Cardiff.

**Introduction:** Many studies have been done to prove the hypotheses that there is a causal relationship between endometriosis and subfertility. The possible explanation extends from reduced tubal motility to poor oocyte and embryo quality. Though research has been done to find out the effect of medical or surgical treatment of endometriosis on pregnancy outcome in this group, so far no studies had looked into the relative ease or difficulty during embryo transfer in patients with severe endometriosis.

**Methods:** A retrospective analysis of all embryo transfers over a period of one year in a tertiary referral centre. All patients with difficult embryo transfer and with a diagnosis of endometriosis (primary or secondary) were identified from our unit database. Experienced research fellows and clinical specialists did all the transfers, by clinical touch technique using Rocket catheter. Ultrasound guided transfer was only done in very difficult cases.

**Results and Discussion:** One hundred forty three cases were identified, out of which one hundred eighteen embryo transfers were easy in comparison to twenty-five cases where difficulty was encountered. Out of all the easy transfers only fifteen (12.7%) patients had evidence of endometriosis where four patients out of twenty-five patients (16%) difficult transfers, had endometriosis. When these two groups were compared, the difference was not statistically significant. It seems logical to think that if the uterus is acutely retroverted or anteverted or undergone axial rotation due to adhesion, that should lead to difficult embryo transfer, eventually affecting the implantation rate. Though the abovementioned study failed to prove severe endometriosis could be a factor for difficult transfer, the sample number simply was not large enough for sound statistical calculation. Probably a multicentre study or retrospective analysis over many years will be a way forward.

## Poster Abstracts

### P5

#### Should pretreatment frozen semen or post-treatment fresh semen be used in Assisted Reproduction in men who have been treated for cancer?

M O'Donovan [1], RF Harrison [1, 3], E Donnelly [2], D Keane [1] & R Conroy [3]

[1] Human Assisted reproduction Ireland; [2] Institute of clinical science royal Victoria Hospital Belfast.; [3] Royal College of Surgeons in Ireland.

**Introduction:** A couple with a diagnosis of cancer may achieve a pregnancy after treatment by a number of methods. These include cryopreservation of ejaculated semen prior to therapy and subsequent use in assisted reproduction or in some cancers gonadal function may return after therapy is finished. In these cases is it better to use the cryopreserved semen which has not been exposed to antineoplastic agents?

Or is it more appropriate to use fresh semen if spermatozoa have returned in the ejaculate? This study attempted to answer this question.

**Methods:** Men having semen cryopreserved at our assisted reproductive unit were recruited. For ethical reasons only men whose sperm count was greater than  $10 \times 10^6$  ml/ml were admitted to the study. Sample were analysed using the Comet assay before and at least three months after completion of chemotherapy. Control samples were also analysed from men of proven fertility.

**Results and Discussion:** Thirty three men with cancer and fourteen men with proven fertility took part in the study. There was no significant difference in comet values in the spermatozoa of men with cancer before and after therapy ( $p=0.04$ ). The median %head DNA intact in pretreatment men who recovered spermatozoa in their ejaculate was 49.87% (95% CI 37.21-88.49) compared to a post-treatment value of 50.66%. The median %head DNA intact for control patients was 86.91% (range 75.76-93.65 CI 84.40-89.42). Men were followed up for 18 months after completion of therapy.

**Conclusion;** In men who recover spermatozoa in their ejaculate, there was no significant difference in DNA integrity when compared to pre-treatment spermatozoa when assessed using the Comet assay.

### P6

#### The aetiology of subfertility in HIV-infected couples

LCG Frodsham & C Gilling-Smith

Assisted Conception Unit, Chelsea & Westminster Hospital, London, UK.

**Introduction:** The demand for assisted conception in HIV-infected couples is rising in line with increased efficacy of antiretroviral medication which has dramatically improved life expectancy and reduced vertical transmission risk. Retrospective data from sub Saharan Africa and Australia indicates relative subfertility in HIV positive women. To date, the aetiology of their subfertility is unknown. HIV positive men are known to have reduced sperm motility and volume.

**Methods:** 52 HIV positive women were reviewed in the Chelsea and Westminster research fertility clinic. 27 were in HIV discordant relationships and 25 had HIV positive partners. Routine fertility investigations were ordered including Day 2-5 endocrine profiles and pelvic ultrasound prior to review. Following consultation and satisfactory semen analysis, a hysterosalpingogram/laparoscopy was arranged according to history.

**Results and Discussion:** Median (range) patient age was 35 (23-42) years. All median endocrine profile results were within the normal range. 21 (40%) patients had evidence of partial or complete tubal blockage and 20 (39%) had bilateral tubal patency. In 11 (21%) cases tubal status was not determined. 20 (37%) of the partners had normal semen analysis, 15 (28%) were suitable for ICSI and 5 (10%) for IVF. 10 (50%) of the HIV positive partners had semen analysis suitable for ICSI compared to 5 (25%) of the HIV negative partners. HIV positive women in our clinic have a higher rate of tubal factor infertility (40% v 14%) and HIV positive men, severe male factor (50% v 24%) infertility than demonstrated by Hull (et al;1985). This is the first study to analyse causes of subfertility in HIV infected women and their partners. The aetiology of infertility demonstrated is likely to further increase the demand for assisted conception in these patients.

## Poster Abstracts

### P7

#### Audit of James Paget - Bourn Hall Clinic Transport IVF Programme - June 1998- October 2001

PA Greenwood, B Sharma & D Currie

*Subfertility Clinic, James Paget Healthcare Trust, Great Yarmouth,  
Norfolk. UK.*

**Introduction:** The Audit was carried out to monitor practise and evaluate Unit performance against National standards and outcomes. The intention being to modify practise to the benefit of couples. The transport IVF programme works to criteria set by the Suffolk Area Health Authority. Female age must be 40 years or less and the female BMI <30 and the woman a non-smoker with a baseline FSH <10 Units/l. 123 cycles of treatment were analysed.

**Methods:** A prospective data form has been routinely kept for each cycle of IVF treatment since the inception of the Transport IVF programme in 1994. This records female age, diagnosis, dosage of gonadotrophin and outcome of the cycle of treatment. These forms were entered into a database and the original notes hand searched for any details omitted from the record forms.

**Results and Discussion:** The pre-treatment diagnosis was 32% tubal factors, 29% unexplained infertility, 23% male factors, 12% mixed diagnoses and 4% other. The female age range was 23-40 with a median age of 33. 123 cycles of treatment were commenced in the study period, 12% were cancelled prior to Oocyte Retrieval, 8% the oocytes failed to fertilise and all the embryo's were frozen in 7%. 73% Of cycles led to an embryo replacement procedure. 19% of the embryo replacement cycles involved ICSI. The Clinical pregnancy rate was 29%/cycle commenced and 40.5%/embryo transfer. The live birth rate was 27%/embryo transfer and 36% of those livebirths were twin pregnancies. There were no triplet pregnancies. The age related outcome was analysed and the live birthrate was 25%/cycle prior to 35 and 8.3% thereafter. Analysis showed that 11.5ampoules (75IU) of gonadotrophin were necessary per embryo in women aged 35 and over but only 6 ampoules per embryo below that age. A separate analysis showed that 14 ampoules were needed per embryo where the baseline FSH was 8 or more and that the clinical pregnancy rate in that group was only 10.8%. The clinical pregnancy rate according to diagnosis were 33%/cycle for tubal disease. 39% for male factor cases and only 11% for unexplained. Our conclusion was that these results demonstrated the cost effectiveness of a transport IVF programme when compared to national outcomes. The poor results in the women 35 and over and where the baseline FSH was 8 or more has led to an improvement in our pre-treatment counselling of couples. It is interesting to note that this aspect is highlighted in the 6th Edition of the Human Fertilisation and Embryology Authority Code of Practise. Changes in the criteria for treatment are currently in abeyance until finalisation of the NICE Infertility Guidelines.

### P8

#### Audit of Clomiphene citrate treatment - outcome and adherence to good practise

PA Greenwood, R Joseph & D Currie

*Subfertility Department, James Paget Healthcare Trust.*

**Introduction:** Subfertility treatment in our specialised clinic in a District general Hopsital ranges from reassurance and counselling up to sperm retrieval and Transport ICSI IVF. Couples are selected for Clomiphene citrate treatment according to diagnosis, semenology, length of subfertility, absence of risk factors for tubal disease and satisfactory BMI. The Audit of 50 consecutive couples assessed adherence to good practise, fecundity rate and pregnancy outcome.

**Methods:** A Register of patients started on Clomophene citrate treatment is kept on the Subfertility unit. A record of start date for treatment and date of confirmation of pregnancy is part of this record. 50 consecutive cases from 2001 onwards were selected for the Audit. The records were analysed and data extracted for age at commencement of Clomid, BMI, length of subfertility, previous treatment semen analysis, history of pelvic inflammatory disease, outcome of assessment Trans-vaginal Ultrasound scan, parity, result of tubal patency test, Clomid dosage and number of cycles of treatment, pregnancy and outcome of pregnancy. Audit standards had been set including recording BMI in the patient notes, presence of a semenanalysis, performance of an Ultrasound scan in the first cycle of treatment and cessation of Clomod treatment if unsuccessful after 12 cycles.

**Results and Discussion:** The Audit has demonstrated good compliance with good practise Guidelines. The pregnancy rate was 64% although there were 7 1st trimester pregnancy failures including one ectopic. 16 patients who had not conceived were still taking Clomod and 2 patients had progressed to IVF treatment. It is important to consider relatively simple treatment for couples where there is a chance of successful outcome prior to more invasive, intensive and complicated treatments. This allows pregnancies to occur in a more natural way for couples and reduces the overall cost to the NHS per pregnancy achieved. This approach is re-affirmed in the 2nd Draft of the NICE Guidelines for management of the subfertile couple.

## Poster Abstracts

### P9

#### Corticotrophin Releasing Hormone (CRH) promotes murine blastocyst rate and increase total cell number

LN Lim [1, 2, 3], YQ Yao [1, 2], IL Sargent [1, 2], JE McVeigh [1, 2, 3], DH Barlow [1, 2, 3] & EA Linton [1, 2]  
 [1] NDOG, University of Oxford, Oxford, UK; [2] Oxford Fertility Unit, Oxford, UK; [3] John Radcliffe Hospital, Oxford, UK.

**Introduction:** Our previous work showed that murine preimplantation embryos and oviducts expressed Corticotrophin Releasing Hormone (CRH) and its R1 receptor. In this study, we examined whether CRH plays any role in the development of preimplantation embryos.

**Methods:** In vivo fertilized zygotes from superovulated CBAB6 F1 mice were cultured in vitro with CRH (10nM, 100nM), CRH receptor antagonist, antalarmin (1µM) or in M16 culture medium alone (control). Blastocyst formation rates 120 hours post hCG injection were evaluated under an inverted microscope, then the total cell numbers of DAPI-stained and mounted blastocysts were counted under a fluorescence microscope. Each experiment was repeated three times, providing a minimum of 100 embryos/group.

**Results and Discussion:** CRH at 10nM and 100nM induced a significant increase in the blastocyst formation rate (60.4% (61/101) and 45.0% (45/100), respectively, compared to that of the control group (36.3% (37/102);  $p = 0.003$  and  $0.015$  using the two-tailed t test). Antalarmin alone caused a small but insignificant reduction in the blastocyst formation rate as compared to the control group (29.7% (30/101) vs. 36.3% (37/102);  $p = 0.06$ ). CRH at 10nM also induced a significant increase in the mean total cell number of the blastocysts compared to that of the control group (50.9 vs. 41.7,  $p = 0.001$ ) but there was no difference in blastocyst cell numbers in the other groups.

**Conclusion:** CRH significantly increased the in vitro murine blastocyst rate and total cell number. Further work is underway to determine the specificity of the CRH effect and to investigate which signaling pathways may be involved in mediating the CRH-induced effect on embryo development.

### P10

#### Ectopic pregnancy management in an early pregnancy clinic: women's perceptions of care

DJ Cahill

Centre for Reproductive Medicine, University Div. of Obstetrics and Gynaecology, St Michael's Hospital, Bristol, UK.

**Introduction:** Early pregnancy clinics improve the quality of care and produce financial and staff resource savings. Delay in diagnosis and over-diagnosis of ectopic pregnancies both occur. We evaluated the effects of this management approach on women undergoing it.

**Methods:** Following diagnosis, women attending an early pregnancy clinic were invited to participate in a short questionnaire evaluation of their management and 46 women gave written informed consent to the collection of data. We asked whether adequate and timely information was provided, and who provided it, whether they had to take time off work and whether during the time they were being monitored, they experienced fear, tension, indecision, inability to relax or a fear of the ectopic pregnancy rupturing. They also provided free text feedback on their experience.

**Results and Discussion:** Most considered that they were given adequate information, and this was given generally by phone (78% of cases). Over 90% considered this was acceptable. The professional imparting the information had no particular importance, and again most considered this to be acceptable. Of women who worked, most (78%) took little or no time off work. All indices of anxiety were exhibited in at least 60% of women as was fear of ectopic rupture.

For most, the information was provided by telephone and considered adequate and acceptable. No particular preference was expressed as to who provided this information. Most continued working throughout this time, an important aim of EPAC management. All the indices of anxiety were reported and the majority reported tension. As well as these, women reporting concerns of ectopic pregnancies rupturing were in the majority. This small study shows that while systems generally work well to transfer hard information to patients about the clinical condition, and most women can stay at work, they exhibit considerable signs of anxiety during this time.

## Poster Abstracts

### P11

#### First year of a rapid-access outpatient hysteroscopy service in a London teaching hospital: Effectiveness, efficiency and impact

D Nikolaou & R Richardson

*Department of Obstetrics and Gynaecology, Chelsea and Westminster Hospital, London, UK.*

**Introduction:** A rapid access Gynaecology service was launched at Chelsea and Westminster hospital in January 2003, offering, among else, trans-vaginal ultrasound and outpatient hysteroscopy on a see-and-treat basis. Our aim was to evaluate the effectiveness of this service and assess its impact on other hospital resources.

**Methods:** We carried out a detailed audit of all aspects of the new service for the first 12 months. Also, we examined the workload of main theatres and day surgery theatres over 2 years. Finally, we carried out a detailed audit of all hysteroscopies under general anaesthetic over a 2-month period.

**Results and Discussion:** We did 42 clinic sessions and saw 123 different patients, of whom one was seen 3 times and one was seen twice. We carried out TV scans in 67% of the patients and performed hysteroscopies in 81%. Hysteroscopy was attempted and not possible in only 3 cases (2.8%). Pathology was identified in 53% of hysteroscopies. Polyps were removed in 30 patients. The median number of patients seen per clinic was 3 (1-5), which is 71.5% of the planned for this year and just under 50% of the maximum capacity. 56.15% of the referrals came straight from GPs, of which 50.9% were discharged back to the GP. The same year there was a 14.92% reduction in the total number of hysteroscopies performed under GA in the Department (11.69 % reduction in main theatres and 17.97 % reduction in day surgery). The average patient who had a hysteroscopy under GA in day surgery needed 3 clinic appointments, one USS appointment and one day in theatre. The rapid access service is effective. It frees up important theatre and clinic resources. Its efficiency can be improved by filling in all patient slots, and discharging patients to their doctor. Local GPs need to be made aware of this facility and refer directly.

### P12

#### How good are we at recruiting sperm donors? The Newcastle experience 1994-2003

S Paul [1] & JA Stewart [2]

*[1] Newcastle Fertility Centre at Life, Newcastle upon Tyne, UK;*

*[2] Newcastle Fertility Centre at Life, Newcastle upon Tyne, UK.*

**Introduction:** The demand for sperm donors has continued in reproductive medicine despite the introduction of artificial reproductive techniques such as ICSI. Decline in sperm parameters and removal of donor anonymity may have an impact on both the demand for and recruitment of sperm donors. This study was undertaken to evaluate the current recruitment process of sperm donors at Newcastle Fertility Centre at Life.

**Methods:** Retrospective analysis of unit records of potential sperm donors between the period of January 1994-August 2003.

**Results and Discussion:** Over a period of 10 years, 1101 men applied as potential donors. The majority were aged <36 years (88.07%,  $p < 0.0001$ ), students (54.88%,  $p < 0.0001$ ), without a partner (53.47%,  $p = 0.0015$ ), unmarried (85.38%,  $p < 0.0001$ ) and without proven fecundity (78.67%,  $p < 0.0001$ ). The common information sources were the media (36.50%), student sources (35.11%) and word of mouth/friends (21.07%).

Only 3.63% of the applicants were released as donors, 0.64% are currently in quarantine and 0.45% are under investigation. 30.79% defaulted during the process, whilst 64.48% were rejected on the basis of selection criteria.

The main reasons for rejection were exclusion by phone call history (12.11%) such as past history of sexually transmitted diseases (47.67%), adoption (15.12%), homosexual relation (9.30%) and medical problems (6.98%); and suboptimal semen quality (83.10%) such as poor concentration plus grade A+B motility (51.19%), grade A+B motility (17.46%), concentration (12.88%) and post-thaw motility (08.47%).

A total of 22640 straws were stored from an average of 45 ejaculations per donor (range 6-101). The overall clinical pregnancy rate, during this period, was 23.52% (330 pregnancies in 1403 cycles), 30.18% for intrauterine insemination, 30.07% for in-vitro fertilisation and 18.75% for donor insemination.

This study shows that in a successful sperm donor programme only a small proportion of the applicants are released as donors. This may have serious resource implications for future donor treatment.

## Poster Abstracts

### P13

#### Sperm preparation prior to freezing and storage: Risk reduction practice which also improves post thaw sperm motility

SL Drury, SM Costello, M Afnan & MJ Tomlinson

*Assisted Conception Unit, Birmingham Women's Hospital, Birmingham, UK.*

**Introduction:** Preparation of sperm prior to freezing offers the following potential benefits: 1. Reduction of viral load in stored samples of seropositive patients 2. Reduced workload when treating patients with frozen samples, 3. Allows storage of smaller, more concentrated volumes and, 4. Allows manipulation of sperm function to improve post-thaw survival. Few units prepare sperm prior to freezing due to concerns with post-thaw quality and the initial extra work involved. This study was designed to examine whether such concerns were justified or that perhaps sperm preparation prior to freezing may represent a significant risk reduction method, particularly in relation to the storage of the seropositive patient.

**Methods:** 1.0mL of patient sample was halved and either a. Prepared using density gradient centrifugation (DGC) prior to freezing or b. Frozen in seminal plasma and prepared by DGC after thawing. Initially 29 samples were compared using manual semen analysis methods followed by 14 samples analysed using CASA. Controlled rate freezing was used for all experiments. A further 26 samples were prepared by DGC and incubated in capacitating conditions for up to 2 hours prior to freezing. Capacitation was confirmed by the presence of hyperactivated motility and phosphotyrosine residues.

**Results and Discussion:** Samples prepared prior to freezing gave significantly better post thaw motile concentration when compared to those prepared post-thaw, whether assessed manually (0.9 v 2.6 millions/ml,  $p < 0.001$ ) or by CASA (0.6 v 1.6 millions/ml,  $p = 0.019$ ). Samples prepared and then incubated to induce capacitation for 2 hours gave significantly better post-thaw returns when compared to those not incubated (2.9 v 4 millions/ml  $p = 0.012$ ). DGC prior to sperm storage not only confers the benefits mentioned above but also provides better sperm survival. Modulation of sperm function in future e.g. by capacitation may help to extend survival after freezing further.

### P14

#### Outcome of Intracytoplasmic sperm injection (ICSI) with surgically retrieved sperm and ejaculated sperm: a comparative study

P Ray, S Bhuiya, M Mallya & V Sharma

*Assisted Conception Unit, St James University Hospital, Leeds, UK.*

**Introduction:** Intracytoplasmic sperm injection is known to benefit men with profound oligospermia and asthenoteratospermia, using both ejaculated and surgically retrieved sperm. Epididymal and testicular sperm may lack structural maturity due to the site of origin. This study was done to compare the reproductive efficacy of surgically retrieved sperm with ejaculated sperm, both used in conjunction with ICSI.

**Methods:** Retrospective analysis was done of 174 patients who had ICSI done between May 1995 and October 2003. They were divided into two groups: Group A comprised of 87 patients who underwent ICSI using surgically retrieved sperm for obstructive azoospermia and Group B comprised of female age-matched controls of 87 patients who had ICSI treatment with ejaculated sperm. For group A patients our protocol was to perform a single stage procedure timed with egg collection where PESA was performed for all patients in the first instance. Failure to retrieve sperm by PESA progressed to MESA and failed MESA was followed by TESA.

The fertilization rate, cleavage rate, and pregnancy rates of the two groups were compared.

**Results and Discussion:** The fertilization, cleavage and pregnancy rates were 60.59%, 82.04% and 42.52% for surgically retrieved sperm and were 65.88%, 81.49% and 35.63% respectively with the ejaculated sperm in the control group. Though we achieved a higher pregnancy rate with surgically retrieved sperm, there was no statistically significant difference between the outcomes of the two groups. Amongst group A patients the fertilization, cleavage and pregnancy rate were 59.59%, 82.33% and 44% for epididymal sperm and 59.01%, 83.33% and 28.57% for testicular sperm respectively. The differences between the two sub-groups were statistically insignificant.

Our study shows that ICSI overcomes the limitation of poor sperm motility and low count irrespective of the source of the sperm and achieves comparable results with ejaculated sperm and surgically retrieved sperm.

## Poster Abstracts

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### P15

#### **Surgical sperm retrieval as the last resort for infertility due to retrograde ejaculation**

TR Aust [1], S Das [1], E Barsoum-Derias [1], CR Kingsland [1] & DI Lewis-Jones [1, 2]

[1] *Hewitt Centre for Reproductive Medicine, Liverpool Women's Hospital, Liverpool, UK;* [2] *University of Liverpool, Liverpool, UK.*

**Introduction:** Retrograde ejaculation (RE) is a rare cause of male factor infertility characterised by semen at ejaculation passing into the bladder through a patent bladder neck, rather than down the urethra and into the vagina. Assisted conception may be performed using sperm retrieved from post-coital urine (PCU) but this is not always successful.

**Methods:** We present the case of a 38 year-old man with retrograde ejaculation for whom all attempts at retrieving live sperm from voiding the bladder after masturbation had failed. Testicular sperm extraction was carried out under general anaesthesia resulting in 16 straws of sperm being frozen and a cycle of ICSI is planned.

**Results and Discussion:** To our knowledge this is the first time surgical sperm retrieval (SSR) has been reported as a treatment for infertility secondary to RE. In most cases of retrograde ejaculation spermatogenesis will be normal. Thus for patients with RE for whom conventional methods to restore antegrade ejaculation or retrieve sperm from PCU have failed, SSR should be offered.



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**Conference Secretariat**

BioScientifica  
Euro House  
22 Apex Court  
Woodlands  
Bradley Stoke  
Bristol BS32 4JT, UK

Contact: Lisa Tandey and Juliet Need  
Tel: +44 (0) 1454 642217  
Fax: +44 (0) 1454 642222  
Email: [conferences@endocrinology.org](mailto:conferences@endocrinology.org)  
Web site: <http://www.bioscientifica.com>