Results: In a consecutive series of 289 diagnostic procedures the failure rate was 4.5% with a complication rate of 1%. Failures were due to tenting of the peritoneum, mostly in the learning period or due to obesity. Complications were treated expectantly and in case of rectum perforation antibiotics were given for 6 days, without signs of infection or need for further treatment. Findings were normal in 61%: in case of abnormality endometriosis was diagnosed in 47.5% and adhesions in 35%. In 187 patients local anesthesia was used and sedation or general anaesthesia was in 35% of the patients. In another 45 patients an operative transvaginal intervention was carried out: endometriosis \( n = 30 \), adhesiolysis \( n = 5 \), drilling of ovarian capsule \( n = 8 \), functional cyst \( n = 2 \). Although till now no complications occurred, these preliminary data have to be confirmed in a larger series.

<table>
<thead>
<tr>
<th>Table I. Results of diagnostic procedures (( n = 289 ))</th>
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<tbody>
<tr>
<td>Access ( 276 (95.5%) )</td>
</tr>
<tr>
<td>Failures ( 10 ) preperitoneal</td>
</tr>
<tr>
<td>Complications ( 2 ) rectum perforation</td>
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</table>

Conclusions: In our experience TBL proved to be an accurate procedure in the exploration of the subfertile patient. In contrast to standard laparoscopy it is less invasive as it can be performed under local anesthesia. Furthermore it allows the inspection of the tubo-ovarian structures in their natural position without a need for supplementary manipulation. Our preliminary experience proves the feasibility of surgical procedures through a vaginal access. Combined with saline distention it offers the advantage of an easy access to the fossa ovarica and to the site of inversion of the endometrioma with an accurate dissection of the adhesions. The low morbidity allows patients to leave the clinic the same day and go back to work after one or two days. It also makes a two step procedure more acceptable.

Mitochondria

Monday 2 July 2001
Lausanne

O-081. Mitochondrial diseases: clinical features and defects in mtDNA
Smeets H.
Stichting Klinische Genetica Zuid-Oost N, Capaciteits groep Genetica and Celbiologie, P.O. Box 1475, 6201 BL, Maastricht, The Netherlands
Abstract not submitted

O-082. Mitochondrial DNA in mammalian reproduction.
Cummins J.M.
Murdoch University, Perth, Western Australia.

With rare exceptions, mitochondria in most living organisms are inherited uniparentally. Transmission is normally through the female germ cell line but there are examples of paternal (eg some conifers) and of mixed inheritance (mussels). The mechanisms are extremely diverse and have probably evolved separately many times. The adaptive effect is probably to minimize lethal potential competition between cytoplasmic genes. Typically, human mitochondria as ‘slave’ organelles show little evidence of genetic recombination, although recently doubt has been cast on this. This feature, together with their dangerous role in oxidative phosphorylation, lack of protective histones and relatively ineffective repair mechanisms means that they accumulate mutations much faster than nuclear genes. As mtDNA exists in multiple copies, tissues can generally compensate for defects until critical threshold loads are passed, when they typically enter age-related dysfunctional states. In general, organisms appear to be intolerant of mitochondrial heteroplasmy, and on the occasions when it occurs in humans it frequently presents as progressive bioenergetic or neurological diseases. However, there is evidence that stable or ‘benign’ heteroplasmic lineages can survive. The complex and poorly understood need for synergy between mitochondrial and nuclear genes is likely to confound cloning technology and attempts to ‘rescue’ poor quality human embryos by cytoplasmic transfer. Fortunately, all children born to date by the latter technique appear to be healthy even though they are the first examples of human germ line genetic modification. Understanding these complex interactions is essential if we are to move towards treatment of maternally inherited mitochondrial diseases. Normally the spermatozoa’s mitochondria are specifically destroyed by proteolysis in early embryonic development. Sperm mitochondria are tagged with ubiquitin during spermatogenesis, and exposure of these protein sites during the second cell division is the key trigger for destruction. The future challenge for reproductive biologists is to understand the nature of the selective destruction of paternal mitochondria, as it appears to be a strictly species-specific recognition phenomenon.

Paramedical Free Communication
Session – ‘Nursing’

Monday 2 July 2001
Albertville

O-083. Establishing a quality management system (International Standards Organization ISO 9001/2000) in a Reproductive Medicine Unit’s clinical programme
Brown S.J., Opie S., Stables R. and Norman R.J.
The Reproductive Medicine Unit, The University of Adelaide, The Queen Elizabeth Hospital, 28 Woodville Road, Woodville, South Australia, Australia 5011

Introduction: Quality management systems are routinely used in international industry practice and are increasingly being used in medicine. Quality management systems have also been used in IVF laboratory facilities but have not been easily introduced into a clinical medicine programme. There are many advantages of a quality management system, including risk reduction, improved customer service, and efficiency gains. As patients are increasingly demanding reassurance about quality control in IVF programs, a quality management system can assist in meeting this demand. The international industry practice is to use the ISO9000 management system to gain quality accreditation. There is limited experience of ISO in reproductive medicine units, yet there are enormous gains to be made by instituting this practice. ISO is a series of international standards, conforming to which provides assurance to an organization’s management and clients that a system of quality management is established and is effective. The standards focus on documentation of operational procedures and management practices to meet the client’s expectations.

Aims: The aim of this paper is to show how a nurse-instigated quality management system (ISO 9001/2000) can change practice in a reproductive medicine unit. The paper will also discuss the logistics and consequences of instigating a quality management system in a clinical IVF unit based on the ISO standard.

Method: A small committee was established to oversee the project. A senior nursing staff member was seconded to supervise the project and
to adapt the ISO system from an industry standard to one suited to an infertility unit’s clinical programme. There were three separate fully functional infertility units that required co-ordination to meet ISO standards. Over the past 12 months the unit has undergone a quality accreditation process, which has resulted in Quality Assurance Service (QAS) granting ISO 9001/2000 quality accreditation to the unit.

Results: ISO 9001/2000 accreditation has had a major impact in several areas including: improved documentation, minimization of medico-legal risk, improved customer service, increased staff collaboration and morale, cost savings, continuous improvements to management practices initiated and suggested by staff, and reassurance that the unit meets standards well beyond Australian infertility units’ accreditation requirements.

Conclusion: Our unit is the first reproductive medicine unit in Australia to become quality accredited under the ISO standard and the first in the world to receive this new ISO9001/2000 standard. Quality accreditation system provides a great asset to the company and ensures that correct procedures are followed throughout all stages of the business.

17.15–17.30

O-084. Subcutaneous injection techniques for recombinant gonadotrophins: Puregon® Pen versus Gonal-F® conventional syringe
Van den Branden K., van de Winckel E., Platteau P., Debrabanter A. Massant G. and Devroey P.
Centre for Reproductive Medicine, The Dutch-speaking Brussels Free University, Belgium

Introduction: Over the last decade, the convenience of fertility treatment has been improved with the introduction of purified and recombinant gonadotrophin preparations suitable for subcutaneous injection. Until now, most patients in Belgium have received their daily FSH injections from a nurse who comes to the patient’s home. We therefore started a study in the Centre for reproductive medicine of the Dutch-speaking Brussels Free University, to look at the feasibility, and to compare the convenience of subcutaneous injection of the Puregon® Pen with Gonal-F® freeze-dried cake ampoules to be self-injected by women undergoing ovarian stimulation for IVF/ICSI.

Materials and methods: In total 200 infertile women will be selected for this trial. One hundred patients will be randomized to the treatment with the Puregon® Pen and one hundred will be randomized to the treatment with Gonal-F®. Since October 2000, 92 patients have been included in the study, 27 of whom have finished their stimulation. Patients are instructed on how to use the Puregon® Pen and Gonal-F® injections by two nurses, during their down-regulation.

Throughout the recombinant FSH stimulation, the subjects record daily local symptoms (pain, bruising, redness, swelling, itching) on a diary card. At the end of the cycle the patients score the local tolerance and the overall convenience of Puregon® Pen versus Gonal-F® ampoules on a visual analogue scale (VAS).

Aim: The aim of the study is to analyse the feasibility of self-injections by the patient and the convenience and local tolerance of the Puregon® Pen versus the subcutaneous injections of Gonal-F® with syringe.

Temporary results: After one instruction session all the patients managed to self-inject the medication.

<table>
<thead>
<tr>
<th></th>
<th>Convenience</th>
<th>Local tolerance</th>
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</thead>
<tbody>
<tr>
<td>Puregon® Pen (n = 10)</td>
<td>8.7</td>
<td>8.5</td>
</tr>
<tr>
<td>Gonal-F® (n = 17)</td>
<td>8.3</td>
<td>8.8</td>
</tr>
</tbody>
</table>

Conclusion: Subcutaneous administration of recombinant FSH is easy for the patient to learn. Until now there has been no significant difference in the convenience and local tolerance between Puregon® Pen and Gonal-F® with a syringe, but this is probably due to the low number of patients recorded. More complete results (200 patients) will be known and presented in July 2001.

17.30–17.45

O-085. Exploring the difficulties for couples to access ART in rural Western Australia
Gael McLean
Fertility West, Suite 47, 146 Mounts Bay Road, West Perth, Australia, 6005

Introduction: Western Australia (WA) has a land area of 2.5 million square kilometres and a population of less than 2 million people. By comparison, WA has 10 times greater land area than the United Kingdom, but only 3% of its population! One-third of Western Australia’s population live in rural, remote, and isolated areas outside the capital city of Perth. Whilst there are five clinics offering assisted reproductive technology (ART) treatments in Perth, there are no clinics, either permanent or satellite, available in rural outreach centres. Therefore, for rural patients to access ART they must travel, anywhere up to 3000 kilometres for fertility treatment. What are the additional costs and difficulties these couples encounter in seeking treatment, and may this reduce their access to ART treatment? What greater role does the co-ordinating nurse have in assisting these couples in their care by distance?

Patients: Six couples living in different rural locations were asked to complete a questionnaire. Their distance from Perth varied from 500 to 2500 km.

Results: Financially, the largest expenses were travel (by car or plane) and accommodation. All of the couples had taken time off from work as sick leave, annual leave, or leave without pay, staying in Perth for an average of 10 days. These costs are compounded by the number of treatments they have had. It was recorded by all the couples that the cost, interference with work, and loss of wages delayed their treatments and in some cases prevented further treatment. Geographical difficulties arose with the couriering of blood samples, delayed results, nil access to transvaginal ultrasound, delays in obtaining drugs, and the weather (excessive heat or cyclones!). Psychologically, emotions escalated whilst staying away from the home environment. Those in paid accommodation lacked personal comforts, whilst those staying with family, lacked privacy. For financial or work reasons, some women attended without their partners and felt very alone throughout their treatments. At home in the rural setting, isolation was the main stress, as was gaining support within the community, without losing privacy and confidentiality. Co-ordinating treatment cycles by distance is challenging for the nursing staff, which have very little personal contact with the patient and have to provide the majority of information and care via the telephone. Communication is a lifeline for these couples and providing some extra phone contact, support, and understanding is of paramount importance for reducing their isolation and stress. Giving negative or sad news is always difficult, and more so over the phone to rural patients who have undergone so much more to access ART. No matter how great the distance, extra care and communication need to be given to rural patients to help them acquire ART treatment and reduce the difficulties associated with their isolation.

17.45–18.00

O-086. PureSperm: a good alternative to Percoll for sperm preparation
Kraenborg N.E., Ouchoorn-Roessen E.M.J., van der Westerlaken L.A.J. and Naaktgeboren N.
Department of Gynaecology & Obstetrics, Leiden University Medical Centre, The Netherlands

Introduction: PureSperm (Silane-coated silica particles) was evaluated as an alternative to Percoll (polyvinylpyrrolidone (PVP)-coated silica particles) for separation of spermatozoa. Sperm concentration, motility, total sperm count, and recovery as well as fertilization results and embryo quality after IVF were recorded after using Percoll and PureSperm for the sperm preparation.

Methods: From a total of 53 fresh sperm samples, the concentration, motility, and total motile sperm count was recorded. They were divided into three different groups according to the total number of motile sperm in the sample (<5×10^6, >5 and <15×10^6, >15×10^6). All sperm...
samples were diluted with HEPES-buffered Earle’s medium containing 20% human serum albumin (HSA) (Earle’s Flush) and divided into two equal parts. The diluted semen was layered on top of 1 ml Percoll or PureSperm solution (70 or 80%) respectively and centrifuged for 10 min at 1500 r.p.m. The supernatant and interface were removed. After the Percoll or PureSperm treatment the isolated spermatozoa was washed twice with Earle’s Flush. Finally the concentration, sperm motility, total sperm count, and recovery were recorded. In addition the fertilization results and embryo quality resulting from 22 IVF cycles were compared for Percoll- and PureSperm-treated semen; half of the collected oocytes of each patient was inseminated with Percoll-treated spermatozoa and the other half was inseminated with PureSperm-treated spermatozoa.

Results: No significant differences between Percoll- and PureSperm-inseminated oocytes were found in the fertilization percentage ($P = 0.527$) or in the percentage good quality embryos ($P = 0.182$).

Table 1. Sperm characteristics after preparation with Percoll and PureSperm (median ± SD)

<table>
<thead>
<tr>
<th>Before treatment TMSC ≤5 ($\times 10^6$)</th>
<th>After treatment</th>
<th>Percoll n = 15</th>
<th>PureSperm n = 15</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conc. ($\times 10^6$)</td>
<td>3.2 ± 0.7</td>
<td>2.2 ± 0.15</td>
<td>0.414</td>
<td></td>
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<tr>
<td>Motility (%)</td>
<td>9.8 ± 17.6</td>
<td>17.6 ± 21.7</td>
<td>0.059</td>
<td></td>
</tr>
<tr>
<td>TMSC ($\times 10^6$)</td>
<td>0.1 ± 0.2</td>
<td>0.2 ± 0.1</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>Recovery (%)</td>
<td>10.2 ± 12.3</td>
<td>14.2 ± 19.3</td>
<td>0.022</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Before treatment TMSC &gt;5 and ≤15 ($\times 10^6$)</th>
<th>After treatment</th>
<th>Percoll n = 13</th>
<th>PureSperm n = 13</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conc. ($\times 10^6$)</td>
<td>12.0 ± 12.3</td>
<td>15.0 ± 9.7</td>
<td>0.937</td>
<td></td>
</tr>
<tr>
<td>Motility (%)</td>
<td>35.0 ± 21.1</td>
<td>39.0 ± 22.6</td>
<td>0.100</td>
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<tr>
<td>TMSC ($\times 10^6$)</td>
<td>0.9 ± 0.8</td>
<td>0.9 ± 1.2</td>
<td>0.045</td>
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<tr>
<td>Recovery (%)</td>
<td>20.4 ± 20.4</td>
<td>26.7 ± 32.2</td>
<td>0.117</td>
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</table>

<table>
<thead>
<tr>
<th>Before treatment TMSC &gt;15 ($\times 10^6$)</th>
<th>After treatment</th>
<th>Percoll n = 18</th>
<th>PureSperm n = 18</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conc. ($\times 10^6$)</td>
<td>33.0 ± 19.4</td>
<td>31.0 ± 25.1</td>
<td>0.301</td>
<td></td>
</tr>
<tr>
<td>Motility (%)</td>
<td>65.0 ± 28.5</td>
<td>73.0 ± 28.1</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>TMSC ($\times 10^6$)</td>
<td>4.2 ± 8.9</td>
<td>4.2 ± 10.3</td>
<td>0.307</td>
<td></td>
</tr>
<tr>
<td>Recovery (%)</td>
<td>17.9 ± 14.0</td>
<td>23.9 ± 17.5</td>
<td>0.174</td>
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</tr>
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</table>

TMSC, total motile sperm count.

Conclusion: Sperm preparation by PureSperm resulted in a significantly higher motility, a significantly higher total sperm count, and a higher recovery compared with Percoll when all three groups were pooled. The difference in total motile sperm count (TMSC) after sperm preparation and recovery between treatment with PureSperm and Percoll respectively seems to increase with decreasing TMSC before sperm preparation. Overall, PureSperm appears to be at least as effective as Percoll for sperm preparation.

No significant differences in IVF results regarding fertilization and embryo quality were found. However, numbers are small, and therefore the insemination experiments with IVF will be continued. Extended data will be presented.

O-088. Obesity and reproduction
Pasquali R.
Endocrinology, Dept. Internal Medicine, S. Orsola-Malpighi Hospital, Univ. Bologna, Italy.

There is both clinical and epidemiological evidence that obesity may impair ovulation and fertility in women. Polycystic ovary syndrome (PCOS), which is the most common cause of fertility problems in women, is frequently associated with obesity, particularly the abdominal phenotype. Although hyperandrogenism is the key feature of PCOS, other inconsistent features are insulin resistance and associated hyperinsulinemia and lipid abnormalities, both included in the so-called Metabolic Syndrome (MS). Although controversial, there are arguments to support the concept that obesity may play an independent pathogenetic role in the development of hyperandrogenism and related clinical features, including menses abnormalities and anovulation. Hyperinsulinemia and alterations of the GH/IGF system are potential key factors explaining this cause-effect relationship. Peripheral mechanisms by which insulin alters ovarian steroidogenesis involve activation of the stromal cell P450c17 enzyme system. These effects may be complementary to that dependent on increased LH signalling at the ovarian level. In fact altered LH regulation and secretion from the pituitary may coexist in the same women. Another mechanism dependent on insulin action is represented by inhibition of the sex hormone-binding protein synthesis in the liver, which in turn may lead to inappropriate free androgen delivery to target tissues. Components of the insulin-related ovarian regulatory system are the Insulin Growth Factors (IGFs). In fact, IGFs stimulate ovarian androgen synthesis, granulosa cell proliferation and oestrogen formation in the granulosa.

Intervention studies by both weight loss and insulin-lowering drugs have substantially indicated that, whatever the therapeutic route chosen, the reduction of insulin concentrations and the improvement of insulin resistance represent the key factors to improve hyperandrogenism and fertility in most women with obesity and PCOS. In addition, there are data indicating that the combination of hypocaloric diet with metformin, a widely used insulin sensitizer, may amplify this effect and selectively reduce visceral fat and normalize leptin concentrations. Available data indicate that weight loss per se may improve fertility rate and favour pregnancy in approximately 20–25 per cent of affected women without any other therapeutic support. In addition, there are data indicating that insulin sensitizers can improve the clomiphene-induced ovulation rate in otherwise clomiphene-resistant obese PCOS women. Correction of hyperinsulinemia also seems to improve the outcome of in vitro fertilization techniques, although this requires more detailed investigation. Last but not least, correction of obesity and hyperinsulinemia appears to be important in the prevention of late-onset metabolic and cardiovascular diseases, towards which women with obesity and PCOS appear to be predisposed.

Gonadal Mosaicism

Tuesday 3 July 2001
Lausanne

O-089. Gonadal mosaicism in the female
McDonough, P.G.

Address not given

Gonadal mosaicism may be the result of acquired chromosomal abnormalities, single gene mutations, or possibly the incorporation of extrachromosomal DNA into a germ line cell (retrotransposons). The risk of pathologic germ line alterations in phenotypically normal individuals is a pervasive problem that almost certainly affects all large multicellular organisms. If