

Human fertility is defined by the probability of conception, which in fertile couples amounts to 5% or more during a 6-day period preceding the ovulation. However, within this window of fertility the probability of conception rises to 39% on the day of the most fertile-type cervical mucus. It is clear that in current clinical practice human fertility tends to be underestimated with the consequence couples are subjected to excessive medicalization of their natural fertility. Today there is strong evidence that IVF and ICSI carry a significantly higher risk of neonatal and maternal morbidity even in the absence of multiple pregnancy than after natural conception, while even the long-term effects of various assisted reproductive techniques are largely unknown. For these two major reasons we propose an active and minimally invasive, but rational approach in the management of couples when they worry about a delay of conception.

Before referral of the couple to IVF or ICSI we propose the couple a three-step programme.

1. Minimal medicalization using fertility awareness methods. Whenever there is no sterility and corrected grade A factors of reduced fertility we explain to the couple to use fertility awareness based on the Billings method to determine the top-fertile day during the cycle. For assisting the couple during the learning period we have developed a scoring and recording system that is monthly transmitted by telephone to the centre.

2. Minimal invasive exploration. After the medical intake with clinical examination, biochemical testing, transvaginal ultrasound and hysteroscopy the couple is offered the minimally invasive needle transvaginal hydrolaparoscopy. In addition to the fertility awareness the couple now has accurate information on the spermogram and the female internal reproductive organs.

3. Individualized patient strategy. Depending on the results the couple is advised further active expectant management, medical treatments such as COH, IUI, reconstructive surgery or IVF.

This modern approach can only be offered when the reproductive physicians have in addition to their knowledge of assisted reproductive technologies (ART) the necessary skills in basic imaging techniques like ultrasound and hysteroscopy. We demonstrated recently with grade A evidence that by reducing the hysteroscope diameter and by using a standardized minimal invasive technique the examination becomes accessible to every gynecologist with basic endoscopic skills.

Reproductive surgery, including transvaginal laparoscopy, on the contrary needs specific skills, which are subject of intensive training and a specific philosophy with respect for the anatomy and awareness of post-operative adhesion formation. A scientific project of the European Academy for Gynaecological Endoscopy in which they try to prove the construct validity and to define the cut-off levels for a new structured and comprehensive pre-clinical training programme in laparoscopic surgery shows that the endoscopic skills of the routine gynaecological surgeons do not differ significantly from a non-trained population and are significantly inferior to expert surgeons. This scoring system could be an important first step towards correct identification and differentiation of the gynaecological surgeons.

In the hands of expert surgeons there is evidence that reconstructive interventions can achieve higher pregnancy rates than IVF. Moreover, surgery is often needed to improve the implantation rates at IVF. It is clear that such a comprehensive programme aiming the highest quality for the patient cannot be offered when training in reproductive surgical techniques is lacking. When the knowledge is limited to ART only, liberal referral to IVF is obvious but not in favour of the patient.

INVITED SESSION

Session 53 – ESC Exchange Session— Contraception only by Progestogens

Wednesday 21 June 2006

08:30–09:30

O-198 Contraception only by progestogens—oral preparations

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Introduction: Progesterone only contraception is coming of an age. It has a major world-wide role as emergency contraception owing to its exceptional safety and proven effectiveness as a post-coital method. The barrel to its availability continues to fall, as more and more countries and states allow its supply by pharmacists or over the counter. Unfortunately emergency contraception alone will not prevent unintended pregnancy and this session, sponsored by the European Society of Contraception, will focus on progesterone only preparations as routine contraception.

Progestogen only implants and intra-uterine systems have excellent efficacy and a low incidence of adverse events. The National Institute of Clinical Excellence (NICE) (long-acting reversible contraception: the effective and appropriate use of long-acting reversible contraception, October 2005, Nice Guidance see www.nice.org.uk) in England has also recently proven them to be cost-effective for a National Health Service in preventing unintended pregnancy. Scotland will shortly set a Health Service target to improve the proportion of women choosing contraception who opt for a long-acting reversible method. All long-acting reversible contraceptives are currently based on progestogens with the exception of the copper intra-uterine device and combined injectables. The first talk of this session will however focus on progesterone only pills and asks the question 'in 2006 is the progesterone only pill a method only for women who cannot or will not use anything else or should it be offered to all women?'

Method: The advantage and disadvantage of the progestogen only pill based on different progestogens will be debated and compared to that of the combined oral contraceptive pill.

Results: The development of desogestrel progestogen only pill which appears to prevent ovulation in a much greater proportion of women than the progestogen only pills containing norethisterone or levonorgestrel has increased the range of women who may wish to choose the progestogen only pill as their preferred option.

Conclusions: Women seeking contraception should be informed of all methods. Individual women need to understand in detail the advantages and disadvantages of methods which are safe in their particular case. These methods should include the progestogen only pill.

The progestogen only pill has an important role to play as a method of contraception in breast feeding women and women with various medical conditions in whom oestrogen is contra-indicated. However, it should not be ignored as an option for healthy women. If the progestogen only pill is chosen by a woman under 40 years of age, the progestogen (desogestrel) which has greatest efficacy in preventing ovulation should be prescribed.

O-199 Contraception only by progestogens: injectables and implants

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The consequence of poor access to family planning services, as well as the lack of availability of effective contraceptive methods results in a high number of unwanted pregnancies. There is also an unmet need for contraceptives with long-term action. Injectables and implants eliminate the need to take daily contraceptives such as pills or coitally dependent contraceptives such as condoms and other barrier methods.

Several subdermal implants for female contraception have been developed by using different progestins. These implants are inserted subdermally, under local anesthesia. The preferred site is the inner part of the non-dominant arm.

Immediately following insertion, they begin to release the progestin continuously. The amount of steroid released per day drops slowly and progressively throughout the months or years of use. The first-generation implant is Norplant, which consists of six capsules releasing levonorgestrel and effective for 7 years. Jadelle with two rods, which also contains levonorgestrel is effective for 5 years. Implanon is a one rod implant that delivers etonogestrel and is effective for 3 years. The implant method is used by many women for spacing pregnancies or for long-term contraception. The main advantage of implant systems are the high efficacy rate and the long duration of action without compliance issues. For insertion and withdrawal, skilled and trained health provider is important.

Progestogen-only injectables are highly effective, long-acting and reversible hormonal methods of contraception. Depo-Provera which contains 150 mg depot medroxyprogesterone acetate (DMPA) is administered by deep intramuscular injection every 12 weeks. The other progestogen-only injectable contraceptive, Noristerat which contains 200 mg norethindrone oenanthate is administered every 8 weeks.

All the delivery systems are based on the use of steroidal hormones delivered continuously at very low doses, which suppress ovulation. Ideally, progestogen-only injectable contraceptives and contraceptive implants are started within 7 days of the onset of menstrual bleeding, because ovulation is unlikely to occur when these contraceptive methods are initiated during this period. Side effects are an important contributor to poor compliance and discontinuation of contraceptive methods. Frequent bleeding problems are the main drawbacks of implants and injectables containing only progestogens. With most progestogen methods, menstrual disturbances are likely with a pattern of irregular vaginal bleeding in the first instance and amenorrhoea in the long term.

These methods are highly effective and relatively acceptable. Careful patient selection with prior counselling and supportive follow-up care can significantly decrease discontinuation rates owing to bleeding changes.

O-200 Intrauterine systems

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FREE COMMUNICATION

Session 54 – ART—Single Embryo Transfer

Wednesday 21 June 2006

10:00–11:45

O-201 Monozygotic twinning with blastocyst culture and single blastocyst transfer: increasing incidence predates zona manipulation and blastocyst culture

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Introduction: The incidence of multiple pregnancies has escalated dramatically in every country in which IVF is practised, putting disproportionate pressure on population growth and on neonatal nursery facilities, while potentially also compromising the chance that an infertile couple will have a healthy baby. Although polyzygotic multiple pregnancy can be overcome to a major degree by elective single embryo transfer, especially with blastocyst culture (1,2) monozygotic (MZ) twinning is not prevented. A rising prevalence of MZ twinning with IVF has been observed by many authors, but the cause remains unclear. Using robust data, we have examined the changing secular frequency of MZ twinning in the community generally and the extent to which this frequency has been influenced by modern IVF practices and culture techniques.

Materials and methods: Australian national annual birth statistics were reviewed from 1920 to 2003 to determine the sex of babies at birth among multiple gestations. The relative frequency of dizygotic (DZ) and MZ pregnancies was estimated using Weinberg's rule (which states that the number of DZ twins = the number of opposite-sex twins, and that the excess of same-sex twins represents the number of MZ twins). Data for IVF conceptions (since

1979) was provided by Australia's National Perinatal Statistics Unit and examined in 5-year cohorts.

Results: DZ twinning was relatively constant from 1920 until the 1960s, at a rate per 1000 confinements of 7.5, falling to ~6.0 before a dramatic increase with the advent of ovulation induction, reaching 300/1000 IVF conceptions by 2000. Among natural conceptions, MZ twinning has been increasing steadily, from 3.1 in 1920 to 5.0 in 2000. For IVF conceptions, MZ occurred in only 2 per 1000 confinements in the 1980s, when culture conditions were probably sub-standard, rising to 2.5 in the early 1990s, to 7 in the late 1990s and to 14/1000 or more since 2000. The MZ twinning rate in Australia 2003 was the same for day 3 (cleavage-stage) and for days 5–6 (blastocyst-stage) transfers, at ~17/1000 confinements.

Discussion: As IVF techniques have improved there has been a steady and substantial increase in MZ twinning. This study shows for the first time that the increase coincides with improving culture conditions and started before manipulations of the zona, whether for ICSI, assisted hatching and embryo biopsy, and before extended culture. Transfer of just one embryo can therefore still lead to twins, and sometimes to triplets. We show that MZ twinning has increased also among natural conceptions in Australia over the past 80 years (as it has in the UK), to now rival non-IVF DZ twinning in prevalence in the community. Reasons remain speculative, but include improving maternal nutrition and thus improved oocyte metabolism. This finding is consistent with our observations that twinning is more likely with good quality embryos (unpublished). If this increasing rate of MZ twinning turns out to be a natural, opportunistic adaptation to improved nutrition or culture conditions, it could prove difficult to reverse as IVF embryo quality continues to improve. Because two implanting embryos have twice the chance of MZ twins resulting than a single implanting embryo, the best way of minimizing MZ twinning is to transfer blastocysts one at a time, irrespective of maternal age.

References

1. Henman et al. (2005) *Fertil. Steril.*, **84**:1620–1627.
2. McArthur et al. (2005) *Fertil. Steril.*, **84**:1627–1636.

O-202 What do the infertile couples prefer: single or double embryo transfer—a single child or twins—and why? Results of a survey

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Introduction: The purpose of the present study was to evaluate infertile couples' attitudes towards the choice between transfer of one or two embryos, to twinning and their acceptance of the associated neonatal risk, and to elucidate which factors have an impact on their choices including the influence of perception of risk.

Materials and methods: All IVF/ICSI couples referred to the Fertility Clinic at Aarhus University Hospital, Skejby Sygehus, September 2004 were approached by a 56-item mailed anonymous questionnaire. The questionnaire ascertained demographic data, the desire for twin pregnancy, treatment-related stress, physical pain side effects and importance of number of reimbursed IVF treatments. Finally, the respondents were presented with three scenarios describing potential pregnancy complications. The respondents were asked to indicate their wish for a twin pregnancy under the conditions described in the scenarios. The χ^2 -test, *t*-test, ANOVA, Mann–Whitney *U*-test, Kruskal–Wallis test and logistic regression models were used as appropriate. SPSS (Statistical Package for Social Sciences), and Stata were used for data analyses.

Results: Of 588 couples approached, a total of 414 women (70.4%) and 404 men (68.7%) returned the questionnaire. The majority of the patients and their partners preferred having twins (58.7%) to having one child at a time (37.9%), while only 3.5% claimed to be indifferent. A large majority of 78.5% expressed wish to have two embryos transferred in a future treatments, while only 6.2% wanted SET. Among the 229 respondents who preferred one child at a time, 81.2% planned to have DET in their next treatment. In comparison, 98.6% of the respondents who preferred twins would opt for DET in their next treatment. Reasons for wanting twins were a positive attitude towards having twins, wish for siblings and age, while reasons for wanting one child at a time were risk for the fetuses, risk for the mother and risk of complications in twin