SEXUALLY TRANSMITTED INFECTIONS IN OBSTETRICS AND GYNAECOLOGY

Priya Sen

There has been an acute rise in the incidence of sexually transmitted infections (STIs) in women in Singapore over the past 6 years. From 1, 426 cases notified in the year 2000, this has more than doubled to 3, 784 cases notified in 2006. The majority of STIs in these women have occurred in women of child-bearing age. This has a significant impact on pregnancy outcome and fertility rates as well as maternal and infant morbidity and mortality. STIs in women can present as discharges, growths and ulcers; however the majority of women with STIs tend to have no symptoms at all. If this remains undetected during pregnancy, this can result in spontaneous abortion, low birth weight, prematurity and various deleterious sequelae in surviving neonates. Screening for HIV and Syphilis is already carried out routinely in Singapore at the antenatal visit. Screening for other STIs such as Chlamydia, Gonorrhoea, Trichomoniasis and Bacterial Vaginosis; especially in pregnancy where the neonate is also at risk is recommended as a routine in Obstetric and Gynaecological practice.

GROUP B STREPTOCOCCUS INFECTION IN PREGNANCY

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Group B streptococcus (GBS, Streptococcus agalactiae) has been known as a human pathogen since 1930s and has emerged as the leading infectious cause of neonatal morbidity and mortality in the 1970s. Much attention has been given to the prevention of neonatal GBS disease. Guidelines to prevent neonatal GBS disease were developed in the 1990s. After the implementation of these preventive guidelines, the incidence of early-onset disease decreased markedly. However, despite the decrease in the incidence, GBS remains the number one cause of infectious neonatal morbidity and mortality in developed world. The majority of cases of early-onset GBS disease occur in infants whose mothers screened negative for GBS colonization.

GBS has also been recognized as an important maternal pathogen. A variety of maternal GBS infections may occur in the course of pregnancy and the postpartum period. Apart from cervicovaginal colonization, which is usually asymptomatic, GBS can cause urinary tract infections, vulvovaginitis, intra-amniotic infection, mastitis, bacteremia, sepsis, meningitis, endometritis, and wound infections.

Studies on GBS transmission in colonized mothers during delivery report incidences between 16 and 53% and neonatal disease develops with a frequency of 1% to 22% in colonized neonates. Only 1 to2% of infants of colonized women develop early-onset GBS disease in the first week of life.

During labor there are different strategies to prevent neonatal GBS disease. What the screening procedures and optimal treatment regimen should be is still under debate. Some guidelines from CDC and Canadian guidelines recommend universal screening for rectovaginal GBS colonization in pregnant women at 35 to37 weeks of gestation and administration of prophylactic antibiotics during labor to all GBS-positive women. Some have a risk-based strategy making only women with a risk factor receive antibiotics during labor. Risk factors for neonatal GBS disease are prematurity, ruptured membranes for more than 18 hours, fever, GBS-bacteriuria in current pregnancy, or a previous neonate with GBS disease.

The presence of GBS influences the choice of management in patients with PPROM, because subclinical GBS intrauterine infection has been implicated as a major factor in the pathogenesis and consequential maternal and neonatal morbidity. Preterm birth and prolonged membrane rupture are both risk factors for neonatal group B streptococcus sepsis. In KKH, the patient with preterm PROM receive intrapartum group B streptococcus prophylaxis unless there is an available recent negative anovaginal culture. Known group B streptococcus carriers receive intrapartum group B streptococcus prophylaxis regardless of prior treatment. Treatment consists of intravenous penicillin as a 5 million unit initial bolus followed by 2.5 million units every 4 hours, or intravenous ampicillin, 2 g then 1 g every 4 hours.

RECURRENT URINARY TRACT INFECTIONS

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Each year, approximately 1 in 5 women between the age 20-55 years will suffer from a urinary tract infection (UTI). Up to 50% of women will suffer at least 1 UTI in their lifetime, and of these, about a quarter will develop a recurrence. Most recurrences occur within 3 months of the initial infection.

Definitions
Recurrent UTI is the occurrence of a 3 or more symptomatic UTI over 12 months, after resolution of a previous infection. Re-infection is a new infection (negative MSU 2 weeks after treatment) but a relapse is an infection caused by the same bacterial strain from a focus inside the urinary tract within 2 weeks of treatment. It is often impossible to differentiate between relapses and re-infections.

Risk factors
In healthy young women, sexual activity is strongly associated with recurrent UTI. It is likely that there is a mechanical effect with introduction of pathogens during intercourse and minor trauma may also have an effect. Other risk factors in this group is the use of certain types of contraception especially spermicides and diaphragm; genetic link (more common if female relative with recurrent UTI), pregnancy and anatomical or functional abnormality.

In post menopausal women, common factors include oestrogen deficiency, high residual urinary volumes, pelvic floor surgery, urinary incontinence, renal tract stones, and co-existing medical conditions such as diabetes mellitus.

Management
An infection requires confirmation. Other conditions that may present with similar symptoms include detrusor overactivity and painful bladder / interstitial cystitis. Imaging is useful to assess for stones and assess upper tract complications. Cystourethroscopy may be used to diagnosis foreign body, in particular, the woman with previous pelvic floor surgery. Urodynamics may be used to diagnosis detrusor overactivity and to assess post-void residual volumes

When recurrent UTI is confirmed, reversible factors must be addressed. This include changing contraception if spemicide/diaphragm are used, oestrogen therapy, perineal hygiene, anal incontinence, fluid intake and treat causes of voiding difficulty eg anterior vaginal prolapse.

Ongoing management involves treatment of current UTI with antibiotics and long-term antibiotic prophylaxis. Other useful options include methamine hippurate, oestrogen therapy and cranberry juice / tablet.

THE INFERTILE COUPLE'S SEXUAL FUNCTION & RELATIONSHIP: IMPACT & MANAGEMENT

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Two main areas of sexual function often impact the trying- to-conceive (TTC) couple in their journey to conception. Primary reproductive medical care providers are uniquely poised to offer pragmatic solutions for couples to strengthen their interpersonal relationships, while optimizing fecundity.

1) Dyspareunia due to vaginal dryness is common in TTC women, with 75% reporting an increased incidence during intercourse targeted to conception. Unfortunately, common lubricants & even saliva kill sperm. Only 20% of couples discuss dryness with medical providers, and 25% of TTC couples are always using lubricants (such as KY(r)) that are contraindicated while TTC. Pre~Seed(r) Lubricant's formula has been shown in clinical studies not to harm sperm, and has been recently cleared by the FDA as the first ever lubricant intended for use during fertility procedures.

2) Male performance issues, including ejaculation failure or delay, are much more common than often thought. This can manifest as avoidance of timed intercourse, performance "burn-out" during consecutive days of intercourse; or failure to be able to provide samples for diagnostic or therapeutic interventions. Helping couples to appropriately time intercourse and periods of abstinence; appropriate use of pharmaceuticals; and use of a semen collection condom to enhance sample quality, all offer pathways for success.

SINGAPORE FEMALE SEXUAL HEALTH AND CONTRACEPTION SURVEY 2006

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Objectives

Unwanted pregnancy and sexually transmitted infections are pertinent health concerns for women in reproductive age. We decided to look into their sexual health.

Methods

We conducted a cross-sectional longitudinal study on women who attended our public forum. The survey included sexual habits, contraception usage and knowledge on sexually transmitted infection.

Results

655 women were invited to participate in the study. 255 women (38.9%) responded. Mean age group was 41.6 years old (range 14-70 years). 68% were married while 27% were single. 77% were Chinese, 17% Malays and 2% Indians.

Mean age of sexual debut was 24.8(4.2 years. 75% of women had sexual debut between 21-30 years old. 2.5% had sexual debut during their teens. 86.1% had 1 sexual partner. 10.3% had 2 to 3 partners while 1% had 5 or more partners.

88% of women had sex up to thrice a week. Only 7% had previous one night encounter. 26% reported difficulty in sex. Dyspareunia and erectile dysfunction were commonest causes.

Half of women surveyed (53.4%) did not practice any contraception. Fear of side effects was the commonest reason for not using contraception. Barrier method (47%) was most popular while hormonal methods (13%) and IUCD (7%) were less popular. 21% used natural method of contraception. 16.0% perceived natural methods as most reliable contraception.

8.5% had not heard of HIV and sexually transmitted infections. Some women (18.6%) reported not using barrier protection or having less sexual partners despite knowing HIV infection.

Conclusion

This landmark survey shows that Singaporean women are more sexually engaged than thought, but still conservative in their sexual habits. Sexual dysfunction is a significant problem amongst the couples. Reliable methods of contraception are not widely used. More public education needs to be conducted in these areas.

SHOULD ELECTIVE CAESAREAN SECTION BE OFFERED TO PREVENT STRESS URINARY INCONTINENCE AND GENITAL PROLAPSE

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Introduction
There has been much debate in many developing countries regarding the rates of cesarean sections. Advocates for 'natural childbirth' have lobbied hard and in many centres around Australia, 'Childbirth Centres' with solely midwifery care are offered as alternatives to appropriately selected women. Many women, however, request for an elective cesarean section and a survey of female Obstetricians and Gynaecologists were in favour of elective cesarean section for themselves.

What is the Data?
Childbirth and in particular, vaginal delivery has been postulated to be a risk factor for pelvic organ / floor dysfunction. This may be due to injury from mechanical rupture, neuropathy and ischaemia. Unlike the pressure necrosis causing fistulae in prolonged obstructed labours, there are usually long latencies between childbirth and significant symptoms. This complicates research in this field, as do the many potential confounders in childbirth and delivery.

Vaginal deliveries appear to be a risk factor for pelvic organ prolapse. Although DeLancey has demonstrated levator injuries in up to 15% of primaparous women, its actual significance is still being determined. The Oxford Family Planning Association study indicated the first 2 vaginal deliveries confer the greatest relative risk to pelvic organ prolapse.

In terms of pelvic organ function, epidemiological studies have shown that cesarean section may offer women some short to medium-term protection from urinary incontinence. However, as the woman becomes older, age-related changes become more significant risk factors.

Conclusion
At present, there is evidence to demonstrate that levator injury occurs during vaginal delivery. The exact long-term effects of this are yet to be determined. Women who delivery vaginally are at a higher risk of pelvic organ prolapse. However, the risk of cesarean sections require careful consideration.

TREATMENT OF LATE-ONSET HYPOGONADISM IN THE AGING MALE

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Testosterone supplementation should be given, and should be reserved, for those males who are androgen deficient. This statement is evidently so general that (almost) everyone can and will agree with it. The next question is how to arrive at workable guidelines so that this principle can be meaningfully implemented in the everyday medical care of the aging male. A number of as yet unresolved questions arise here. Should the decision to provide androgen treatment be mainly guided by clinical symptomatology of androgen deficiency or should laboratory measurements of plasma levels of testosterone be decisive, or should it be a combination of the two? The clinical symptoms of androgen deficiency in elderly males are rather vague and unspecific, and overlap with symptoms of aging. A substantial number of elderly men with clinical manifestations suggestive of androgen deficiency, appear to have plasma testosterone levels within the range of young adults. So the decision to provide androgen supplementation should be substantiated by laboratory evidence of androgen deficiency.

The above has outlined the many unresolved questions as to the verification of deficiencies in the biological action of androgens in old age and what plasma testosterone levels conclusively represent androgen deficiency. Consequently, a pragmatic approach to this issue must be taken in order to let aging men with a true androgen deficiency benefit from replacement therapy. The question has been authoritatively reviewed by Vermeulen(Vermeulen, 2001) and is also part of guidelines that have been developed over recent years(Nieschlag, Swerdloff, Behre, Gooren, Kaufman, Legros, Lunenfeld, Morley, Schulman, Wang, Weidner, and Wu, 2005a). It is argued that there is no generally accepted cut off value of plasma testosterone for defining androgen deficiency, and in the absence of convincing evidence for an altered androgen requirement in elderly men, Vermeulen arbitrarily considers the normal range of free testosterone (fT) levels in young males also valid for elderly men. Then the normal levels of total testosterone are between 12-35 nmol/l. It is of note that the determination of reference values of laboratory parameters is based on statistical analysis of a population of subjects. In the study of Vermeulen of a healthy male, non obese, population age 20-40 yrs (N = 150), the mean of log transformed early morning T levels was 21.8 nMol/l (627 ng/dl); the mean minus 2 S.D. was 12.5 nMol/l (365 ng/dl) and minus 2.5 S.D. 11 nMol/l (319 ng/dl). For fT, measured by equilibrium dialysis or calculated from T and SHBG levels. The mean was 0.5 nMol/l (14 ng/dl), minus 2 S.D. 0.26 nMol/l (7.4 ng/dl) and minus 2.5 S.D. 0.225 nMol/l or 6.5 ng/dl. If one takes as lower normal limit and threshold of partial androgen deficiency, a conservative value of 11 nMol/l for T and 0.225 nMol/l for fT, which represent the lower 1 % value of healthy young males, then it appears that more than 30 % of men over 75 yrs old have subnormal fT levels. Most authors report rather similar values (Matsumoto, 2002; Muller, den Tonkelaar, Thijssen, Grobbee, and van der Schouw, 2003). For the clinician workable criteria are: the lower limit of normal of total testosterone is 12 nmol/L and of fT 250 pmol/L. It must be clear that values may vary somewhat from laboratory to laboratory, and that the outcome of a laboratory test must be viewed in the context of a diagnostic procedure where it constitutes one element in the diagnostic process in conjunction with the patient's history, physical examination, possibly aided by other diagnostic techniques. So, while laboratory criteria are needed in medicine, it is the skill of the clinician to attribute a meaningful place to them.

Most authors agree that plasma testosterone levels should be measured in early morning samples in view of the circadian rhythm of plasma testosterone, with shows its lowest values in the late afternoon. (Late) afternoon samples might present unduly low values and not be representative of a man's androgen status. (Kaufman and Vermeulen, 2005; Nieschlag, Swerdloff, Behre, Gooren, Kaufman, Legros, Lunenfeld, Morley, Schulman, Wang, Weidner, and Wu, 2005b). The recommendation also agree that a single measurement providing a low testosterone value is to be repeated, certain when that value would be enough reason to start testosterone administration. Small ailments, like a cold or other minor stressors, may temporarily suppress circulating testosterone.

It will not be rare to find rather ambiguous, borderline normal/abnormal levels of plasma total testosterone in

elderly men, even in those men with clinical symptoms of androgen deficiency. In these cases assessment of bioavailable or free testosterone might be an asset. Bioavailable testosterone can be measured in the laboratory using the ammoniumsulphate precipitation technique. The gold standard for free testosterone measurement still is the dialysis method although a mass spectrometry based assessment of free testosterone in ultrafiltrates was recently proposed as a candidate reference method (for review: (Kaufman and Vermeulen, 2005). However, both ammoniumsulphate precipitation and the dialysis technique are non-automated, time consuming and expensive techniques and therefore not routinely available in the vast majority of laboratories. There has been a direct radioimmunoassay claiming to measure free testosterone but this assay has been universally criticized because of lack of accuracy and should not be used (Kaufman and Vermeulen, 2005)

The two most widely used equations for calculating bioavailable or free testosterone are those described by Vermeulen et al(Vermeulen, Verdonck, and Kaufman, 1999) and Sodergard et al.(Sodergard, Backstrom, Shanbhag, and Carstensen, 1982). The equations are largely identical apart from the association constants for the binding of testosterone to albumin and SHBG.

At least two algorithms have been placed on the internet as so-called bioavailable testosterone calculators (www.issam.ch and www.get-back-on-track.com/en/tools/kalkulator.php and www.him-link.com) making these algorithms readily available for distant users. It is redundant to measure /calculate biovailable / free testosterone if plasma total testosterone appeared to in the truly hypogonadal (< 6nmol/L)or in the truly eugonadal range (>15 nmol/L).

As already mentioned, in the absence of a reliable, clinically useful biological parameter of androgen action, these criteria of hypogonadism of the aging men are somewhat arbitrary but for the time being the best to provide guidance. If the laboratory outcome is ambiguous but the clinical symptomatology is convincing, a 3-6 months trial of testosterone treatment may be provide the answer whether a man will benefit from restoring his testosterone levels to normal.(Black, Day, and Morales, 2004)

SUITABLE TESTOSTERONE PREPARATIONS

If it turns out that some men benefit from androgen supplements, are there suitable testosterone preparations available to treat them? The androgen deficiency of the aging male is only partial and consequently only partial substitution will be required

High doses of exogenous testosterone will suppress the gonadotropin output ; of the hypothalamo-pituitary unit, but ideally testosterone administration should leave the residual testicular androgen production intact.

PARENTERAL TESTOSTERONE PREPARATIONS

Conventional parenteral testosterone preparations are from far ideal, even for young hypogonadal males. Plasma testosterone (T) levels fluctuate strongly following administration. The most widely used pharmaceutical forms are the intramuscular administratered hydrophobic long chain T-esters in oily depot, enanthate and the cypionate, at a dose of 200-250 mg/2weeks. They yield transient supraphysiological levels the first 2-3 days after injection, followed by a steady decline to subphysiological levels just prior to the next injection. These fluctuations in T levels are experienced by some of the patients as unpleasant and accompanied by changes in energy, libido and mood. The transient supraphysiological levels might increase the frequency of side-effects. Parenteral testosterone undecanoate (TU) is a new treatment modality for androgen replacement therapy. Several studies have documented its use in hypogonadal men (Behre, Abshagen, Oettel, Hubler, and Nieschlag, 1999; Nieschlag, Buchter, Von Eckardstein, Abshagen, Simoni, and Behre, 1999; Schubert, Minnemann, Hubler, Rouskova, Christoph, Oettel, Ernst, Mellinger, Krone, and Jockenhovel, 2004; von Eckardstein and Nieschlag, 2002). In short: after two loading doses of 1000 mg TU at 0 and 6 weeks, repeated injections at 12 week intervals are sufficient to maintain testosterone levels in the reference range of eugonadal men(Harle, Basaria, and Dobs, 2005; Nieschlag, Behre, Bouchard, Corrales, Jones, Stalla, Webb, and Wu, 2004; Schubert et al., 2004; von Eckardstein and Nieschlag, 2002).It has been argued that this preparation is less suitable for initiation of testosterone treatment of aging men (Nieschlag et al., 2005a). It is thought that the long duration of action might constitute a problem in case a prostate malignancy will be diagnosed, but many urologists

reason that the delay between diagnosing prostate cancer and its treatment is usually much longer than 12 weeks, without an adverse effect on the outcome (Graefen, Walz, Chun, Schlomm, Haese, and Huland, 2005; Nam, Jewett, Krahn, Robinette, Tsihlias, Toi, Ho, Evans, Sweet, and Trachtenberg, 2003). So, certainly after the first uneventful year of androgen administration, it seems reasonable to administer long acting testosterone preparations to elderly men.

ORAL TESTOSTERONE UNDECANOATE

Testosterone undecanoate (TU) is testosterone esterified in the 17(-position with a long aliphatic sidechain, undecanoic acid, dissolved in oil and encapsulated in soft gelatin. Of the 40 mg capsules 63% (25 mg) is testosterone. After ingestion its route of absorption from the gastro-intestinal tract is shifted from the portal vein to the thoracic duct. For its adequate absorption from the gastro-intestinal tract it is essential that oral TU is taken with a meal that contains dietary fat. Without dietary fat the resorption and the resulting serum levels of testosterone are minimal. Maximum serum levels are reached 2 to 6 hours after ingestion. To increase shelf-life the preparation was recently reformulated and the oil in the capsule is now castor oil. Recent studies show that there is dose proportionality between serum testosterone levels and the dose range of 20-80 mg. With a dose of 120-240 mg per day over 80% of hypogonadal men showed plasma testosterone levels in the normal range over 24 hours.
TU, also on the basis of its flexible dosing, is probably best suited to supplement the reduced, but still present, endogenous testicular testosterone production in the ageing male with lower than normal, but not deeply hypogonadal levels, of testosterone. Long-term use has been proven to be safe as demonstrated in a 10 year observation.

TRANSBUCCAL TESTOSTERONE ADMINISTRATION

Transbuccal administration of testosterone provides a means of oral administration of testosterone. The resorption of testosterone through the oral mucosa avoids intestinal absorption and subsequent hepatic inactivation of testosterone. Two studies have assessed the efficacy of transbuccal administration of testosterone. Both studies found that administration of 30 mg of testosterone formulated as a bioadhesive buccal tablet twice daily generated plasma testosterone and DHT levels in the normal range in hypogonadal men (Korbonits, Kipnes, and Grossman, 2004). Gum irritation was noted in approximately 3% of men.

TRANSDERMAL DELIVERY

Testosterone can be delivered to the circulation through the intact skin, both genital and non-genital. Transdermal administration delivers testosterone at a controlled rate into the systemic circulation avoiding hepatic first pass and reproducing the diurnal rhythm of testosterone secretion, without the peak and through levels observed in long-acting testosterone injections

Transdermal patches

Scrotal patches were first designed to deliver testosterone through the scrotal skin, where the permeability is 5 times greater than for other skin sites. It required weekly scrotal shaving, and was difficult for some patients to apply and maintain in position for 24 hours. Transdermal scrotal testosterone administration is associated with high levels of DHT as a result of high concentrations of 5(-reductase in the scrotal skin. The patch may be irritating and the use is not feasible if the scrotal surface is not adequate. To overcome these limitations, non-scrotal skin patches have been developed. These patches have a reservoir containing testosterone with a permeation-enhancing vehicle and gelling agents. Improvements have been reported in sexual function, libido, energy level and mood.
The most common adverse effects are local skin reactions. Fifty percent of men participating in a clinical trial reported transient, mild to moderate erythema at sometime during therapy. However, most of these reactions

were associated with application of patch over a bony prominence or on parts of the body that could have been subject to prolonged pressure during sleep or sitting

TESTOSTERONE GEL

Testosterone gel is also used for replacement therapy. Testosterone gel is hydro-alcoholic, 1% (10 mg testosterone per gram gel) and administered between 5 and 10 g of gel a day, amounting to 50 and 100 mg testosterone. The pharmacokinetics of testosterone gel has been extensively studied. Serum testosterone levels rose 2-3 fold two hours after application and rose further to 4-5 fold after 24 hours. Thereafter serum testosterone remained steadily in the upper range of normal and returned to baseline within 4 days after termination of application of testosterone gel. Mean DHT levels followed the same pattern as testosterone and were at or above the normal adult male range. Serum E2 levels rose and followed the same patterns as testosterone. The application of the testosterone gel at one site or four sites did not have a substantial impact on the pharmacokinetic profile. Later studies showed that 9-14% of the testosterone administered is bioavailable. Steady state testosterone levels are achieved 48-72 hours after the first application. Serum testosterone and free testosterone are similar on days 30, 90 and 180 after start of the administration. The formulation of the testosterone gel allows easy dose adjustments (50-75-100mg testosterone gel).
The clinical efficacy of transdermal testosterone gel on various androgen dependent target organ systems has been very well documented. (Ebert, Jockenhovel, Morales, and Shabsigh, 2005)The safety profile showed that PSA levels rose in proportion to the increase of testosterone levels but did not exceed normal values. Skin irritation was noted in 5.5% of patients in the study. Later studies with a 2.5% testosterone gel showed that 5 g of this gel achieved physiogical serum testosterone levels in men whose endogenous testosterone production was pharmacologically suppressed. These levels were reached after approximately 10 days. Serum DHT and E2 did not exceed normal levels. Remarkably, washing of the site of application 10 minutes after application of the gel did not affect pharmacokinetic profiles. Transfer from one person to another was found to be insignificant. No increase of serum testosterone was found after intense rubbing of skins with persons whose endogenous testosterone levels had been suppressed.

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PIT-FALLS IN THE DIAGNOSIS OF FETAL MACROSOMIA AND PREDICTION OF SHOULDER DYSTOCIA

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Extensive publications on the diagnosis of fetal macrosomia involving the use of ultrasonically-derived fetal weight formulae in the last 15 years have provided data to suggest that ultrasonic EFW can detect up to 75% of fetuses with fetal macrosomia. The use of 2-parameter, 3-parameter, 4-parameter and customised formulae will be discussed. Contingent to the accurate prediction of shoulder dystocia is the accurate prediction of birthweight, the single greatest determinant of risk of shoulder dystocia. In the absence of gestational diabetes mellitus, ultrasonic EFW appears to be of limited value in influencing the mode of delivery. The false positive rate of ultrasonic EFW will also be discussed, as this will impact on the LSCS rate as well as the number of LSCS necessary to avoid a single case of brachial plexus injury due to shoulder dystocia. Separate data on GDM will be presented to show that birthweight determination is vital in the presence of GDM to reduce perinatal morbidity and mortality due to birth injuries.

VACCINES FOR WOMEN

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There are several vaccines which are useful and important for the female population. In this talk, we will highlight some of these vaccines, which are used to prevent diseases like measles, mumps, rubella, chickenpox, influenza, pertussis, hepatitis B and human papillomavirus (HPV) which causes cervical cancer.

The risk of congenital malformations exists if a pregnant mother is infected with infectious diseases like chickenpox1 and rubella2, and thus females should consider vaccination against these diseases prior to their planned pregnancy if they do not have immunity against them. Pertussis vaccination is important because there is a risk of adult caregivers (e.g. mothers) transmitting the disease to the newborns who are susceptible. This is because the infants would only normally receive the first dose of pertussis vaccination in the childhood immunization programme at around 3 months old 3.

The main cause of cervical cancer is due to HPV infections. Cervical cancer is among the top five female cancers in Singapore4. Vaccination against HPV infection will be an option to prevent cervical cancer, in addition to routine cervical smear screening. An effective Virus-Like Particles (VLPs) based prophylactic cervical cancer vaccine designed to provide long-term protection against persistent infection with HPV types 16 and 18 and subsequent lesions will need to induce strong immune responses that persist over many years. The GlaxoSmithKline HPV candidate vaccine, using the novel adjuvant system of ASO4 is able to induce this strong and sustained immune response 5.

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THE AGING MALE - WHY SHOULD WE BE CONCERNED

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The notion of an andropause or male menopause is not rarely viewed with some skepticism by the medical profession. This is a concept that all too readily lends itself to opportunistic exploitation by anti-aging entrepreneurs, usually working outside the public health sector, who tout "rejuvenation cures". It is feared that those who peddle the indiscriminate use of androgens, melatonin and DHEA will perpetuate this even further. Only well-designed studies into the endocrinology of aging, with clear clinical objectives and proper terminology, can ensure that history does not repeat itself and that the baby is not thrown out with the bathwater. Asking who should receive testosterone treatment, and for what purpose, are therefore timely and important questions.

The important questions

The pivotal questions are 1) do aging men show an age related decline of testosterone levels? 2) is this decline inherent to the aging process itself, and occurs also in healthy men, or is the observed decline merely the consequence of intercurrent disease, obesity, stress, relative physical inactivity, drug treatment etc? 3) is the decline of androgens quantitatively significant, in other words does it have clinical significance, does it present itself with the signs and symptoms of hypogonadism as observed in other age groups? 4) further proof of the clinical significance of the age-related decline of androgens is to be gathered from intervention studies of androgen supplementation in elderly men with androgen levels below reference values for aging men. If these studies indeed show that androgen supplementation restores (partially) the signs and symptoms ascribed to androgen deficiency, such studies are a validation of the significance of the age related decline of androgens in men.

QUANTITATIVE ASPECTS OF THE DECLINE OF ANDROGEN LEVELS IN AGING

Several studies document that androgen levels decline with aging (for review reference. Initially, cross-sectional studies but later also longitudinal studies have documented a statistical decline of plasma testosterone by approximately 30% in healthy men between the ages of 25-75 years. Since plasma levels of sex hormone-binding globulin (SHBG) increase with aging plasma testosterone not bound to SHBG decreases even by about 50% over that period. Twin studies have shown that genetic factors account for 63% of the variability of plasma testosterone levels and for 30% of the variability of SHBG levels. Also systemic diseases, increasing with age, are a cause of declining plasma levels of testosterone. While it now has been shown that plasma testosterone, and in particular free testosterone, decline with aging, it remains uncertain what percentage of men becomes actually testosterone deficient with aging. Stringent criteria for testosterone deficiency have not been formulated. In a study of 300 healthy men between the ages of 20-100 years, Vermeulen et al defining their reference range of testosterone between 11 and 40 nmol/l, found one man with subnormal testosterone in the age group between 20-40 years, but more than 20% above the age of 60 years while 15% of men above the age of 80 years still had testosterone values above 20 nmol/l. The implication is that only a certain proportion of men has lower-than-normal testosterone values in old age. It is a group that is difficult to identify in routine clinical practice. Another difficulty is that it is not clear whether for aging men other criteria for testosterone deficiency should be established than for younger men. In other words: are the physiological functions of testosterone in the male maintained by identical amounts of circulating testosterone. In adulthood testosterone is responsible for maintenance reproductive capacity and of secondary sex characteristics, it has positive effects on mood and libido, anabolic effects on bone and muscle, it affects fat distribution and the cardiovascular system. Threshold plasma values of testosterone for each of these functions have not been firmly established neither whether these threshold values change over the life cycle. Theoretically it is possible that in old age androgen levels suffice for some but not for all androgen-related functions. Male sexual

functioning in adulthood, for instance, can be maintained with lower-than-normal values. But there are indications that that the threshold required for behavioural effects of testosterone increases with aging.
The laboratory reference values of testosterone and free testosterone show a wider range than those for most other hormones (for instance thyroid hormones), which makes it difficult to establish whether measured values of testosterone in patients are normal or abnormal. Is a patient whose plasma levels of testosterone fall from the upper to the lower range of the reference values of testosterone, which may constitute a drop of as much as 50%, testosterone deficient? Levels may well remain within the reference range, but that person could be testosterone deficient by his own standard. It is uncertain whether plasma LH is a reliable indicator of male hypogonadism, since there are age-related changes in LH regulation. With aging there are reductions in LH pulse frequency and amplitude. Several studies have found that LH levels are elevated in response to the decline of testosterone levels with aging, but less so than is observed in younger men with similarly decreased testosterone levels. This may be due to a shift in the setpoint of the negative feedback of testosterone on the hypothalamic pituitary unit resulting in an enhanced negative feedback action which leads to a relatively lower LH output.
Another variable that might be significant to assess the androgen status in old age is plasma levels of SHBG. It has been suggested that SHBG capacity might be an informative additional parameter to assess androgen deficiency in old age but a single basal SHBG value is difficult to interpret, the level being determined by several hormonal and non hormonal factors, such as growth hormone, insulin, thyroid hormones, obesity, medications. Nevertheless, the free testosterone value calculated by total testosterone / SHBG (according to a second degree equation following the mass action law) as determined by immunoassay appears to be a rapid, simple and reliable indicator of bioavailable testosterone, comparable to testosterone values obtained by equilibrium dialysis which is the 'golden standard'. So, without much of solid criteria for testosterone deficiency, determination of values of testosterone together with LH and SHBG might provide for the time being a reasonable index of the androgen status of an aging person.

DATA ON THE CORRELATION BETWEEN ANDROGEN LEVELS AND SIGNS AND SYMPTOMS OF ANDROGEN DEFICIENCY

- **Bone mineral density**

With aging there is an exponential increase in bone fracture rate which carries a clear association with the age related decrease of bone mineral density (BMD). In view of the significance of sex steroids in the maintenance of BMD at all ages, the question whether the partial androgen deficiency in aging males plays an important role in the decrease of BMD is pertinent. A pivotal role for androgens for the decrease of BMD has, however, been difficult to establish. Not all scientific findings point to the same direction. Indeed, some studies find a significant, though weak, correlation between androgen levels and bone mineral density at some but not all bone sites others are unable to establish a correlation. There are some recent large scale studies of several hundreds of elderly men, and they demonstrated that bone density at radius, spine and hip are correlated with levels of bioavailable testosterone. Interestingly, the correlation with levels of bioavailable estradiol was much more prominent, probably pointing to the significance of oestrogens in men, also in old age. The suggestion presents itself that the effects of androgen, of which the levels decline in elderly males, are at least partially, mediated via their aromatisation to oestrogens. In line with the latter observation Barett-Connor et al observed a significant negative and graded association between levels of total and bio-available estradiol but not of bio-available testosterone and fracture prevalence in males (median age 67 yrs, range 56-87 yrs) independently of age, body mass index or exercise. While the evidence for a significant role of oestrogens in bone health is growing, the effects of testosterone should not be dismissed. Levels of bio-available testosterone correlated with all regions of proximal femur BMD and total body BMD, after adjustment for age. It is to be remembered that oestrogens are largely (>80%) products of peripheral aromatisation of androgens. In sum, the relevance of androgens (both in their own right and as precursors for the formation of oestrogens) in the age associated osteopenia seems clear on the basis of these recent large scale studies.

- **Body composition**

Body composition is seriously affected by the aging process. Aging is almost universally accompanied by an increase in abdominal fat mass and a decrease of muscle mass. Androgens have a substantial impact on muscle mass and on fat distributions, and therefore the relationship between these signs of aging and testosterone levels have been researched. Several studies have convincingly documented an inverse correlation between abdominal fat mass and free testosterone levels. This correlation appeared independent of age. This finding has clinical relevance: the amount of visceral fat is highly significantly associated with an increased risk of cardiovascular disease, impaired glucose tolerance and non insulin dependent diabetes mellitus (the so-called syndrome X). Whether the abdominal, and more specifically visceral obesity is the consequence of the low T levels or vice versa, visceral obesity induces low plasma levels of testosterone, is not yet clear. It is clear, however, that visceral obesity leads to a decrease of T levels, mainly via a decrease in SHBG levels; hyperinsulinemia associated with visceral obesity suppresses SHBG levels, leading in the first instance to higher quantities of free testosterone which are subsequently rapidly metabolised since the half life of free testosterone in the circulation is short (15-20 minutes). In morbid obesity (BMI > 35) there is also a decrease of free testosterone.
There is an impressive age associated decline in muscle mass (12 kg between age 20 and 70 yrs), which is most pronounced for the fast twitch type II fibres. This loss of muscle mass is a major contributor to the age associated decline in muscle strength and of fatigue. Maximal muscle strength shows a correlation with muscle mass, independently of age. This is again related to the occurrence of falls, fractures and the consequent limitations of independent living. The correlation between testosterone levels and muscle mass and appears stronger than the correlation with muscle strength. In a study of men aged 73-97 yrs, serum T levels were, independently of age, positively related to isometric grip strength and leg extension strength. In institutionalized men, who have lower testosterone concentrations than healthy elderly men, a correlation between testosterone levels and severity of loss of muscle function could be established. By contast, two other studies failed to establish correlations between testosterone and strength. In one in elderly men (65-97 yrs old) a significant correlation was found between free testosterone and muscle mass, but not grip strength. The other, equally, did not find any correlation between T levels and muscle strength.
It must be concluded that the correlation between testosterone levels and muscle mass is readily demonstrable whereas the relation with muscle strength is apparently less firm and could not be demonstrated in all studies. Factors other than androgens, such as growth hormone, probably play a significant role.

Cardiovascular disease

Premenopausal women suffer significantly less from cardiovascular disease than men, and traditionally it is thought that the relationship between sex steroids and cardiovascular disease is predominantly determined by the relatively beneficial effects of oestrogens and by the relatively detrimental effects of androgens on lipid profiles. Nevertheless, the vast majority of cross sectional studies in men are not in agreement with this assumption; they show a positive correlation between FT levels and HDL-C and a negative correlation, with fibrinogen, plasminogen activator inhibitor -1 and insulin levels as well as with coronary heart disease but not with cardiovascular mortality. Recent research shows that the effects of sex steroids on biological systems other than lipids, such as fat distribution, endocrine/paracrine factors produced by the vascular wall (such as endothelins, nitric oxide), blood platelets and coagulation, must also be considered in the analysis of the relationship between sex steroids and cardiovascular disease.
Premenopausal women, in comparison to men, are protected against cardiovascular disease which is ascribed to the cardioprotective effects of oestrogens. It is then paradoxical that in cross-sectional studies of men, elevated levels of oestrogens and relaiively low levels of testosterone appear to be associated with coronary disease and myocardial infarction. Some studies in aging men have shown results that seem to contradict the overall notion that androgens, by their action on lipid profiles, increase the risk for coronary artery disease. In a study of geriatric male patients who had suffered a myocardial infarction, it was found that these patients had low testosterone levels in a threshold manner. These studies suggest the intriguing possibility that, in spite of the overall negative effects of androgens on lipid profiles, a lower-than-normal androgen level in aging

men is associated with an increase of atherosclerotic disease. The explanation may lie in the fact that a complex of risk factors for cardiovascular disease, termed syndrome X or the metabolic syndrome (comprising hypertension, insulin resistance, hypertriglyceridaemia and visceral obesity), is associated with low testosterone levels.
The assumption that the effects of androgens on lipid profiles are only one factor in the relationship between androgens and cardiovascular disease, is supported by Tchernof et al who could demonstate that, upon multivariate analysis, adjusting for visceral obesity, the correlation between androgen levels and lipid parameters loses its significance. Given the fact that cardiovascular disease is associated with low plasma testosterone levels the question whether testosterone supplementation in aging men can reverse these cardiovascular risks is very interesting (for review reference).
The first results of studies wherein testosterone was actually administered to mildly hypogonadal aging men did not indicate negative effects on lipid profiles. In a double-blind, placebo-controlled, crossover study Tenover found that administering testosterone enanthate (100 mg per week) for 3 months to 13 healthy elderly men (with low serum total and non-sex hormone-binding globulin bound testosterone levels) decreased total and low density lipoprotein (LDL) cholesterol without affecting levels of high density lipoprotein (HDL) cholesterol. Results of a study by Morley et al are in agreement with these findings; administration of 200 mg of testosterone enanthate every 2 weeks for 3 months decreased total cholesterol without affecting HDL cholesterol levels

- **Age-related changes in sexuality**

Reliable studies on the relationships between androgens and psychological functions are of rather recent date. There is now solid evidence that androgens stimulate sexual appetite. With regard to erectile function the situation is somewhat less clear. It has become clear that in males between 20 and 50 years approximately 60-80% of the normal physiological levels suffice to maintain sexual functions and that increasing testosterone levels above that threshold adds little to sexual functioning. Whether this holds true for aging men, remains to be established. Both Schiavi et al as well as Bancroft have suggested that circulating androgen levels in elderly men might be insufficient to sustain nocturnal penile tumescence and adequate sexual function.

It is evident that a multitude of factors impact on sexual functioning, at all ages but certainly in old age. Testosterone is one of these factors. Aging is generally associated with a decline in sexual desire, arousal and activity and age. The studies on the relationship between testosterone levels and sexual functioning in old age are certainly not unanimous. Men who desired intercourse with a greater frequency than once a week, had higher T levels than men with lower frequency Schiavi. and (men with the primary diagnosis of hypoactive sexual desire had significantly lower T levels than controls. It has also been reported that men with a greater sexual activity had higher bio-available T levels than men with a lower frequency. In an epidemiological study of 500 men, over 51 years old low levels of bio T were associated with low sexual activity. So, from these studies it would seem that the age-related decrease of androgens may be a factor in the decline in male sexuality. By contrast, other studies, failed to observe any correlation between plasma T levels, as long as they were within the normal range, and sexual activity.
The relationship between erectile dysfunction and androgens is more difficult to establish. Erectile dysfunction increases dramatically with age. Physiologically, testosterone acts primarily on the brain, increasing sexual appetite but animal experimentation shows that androgens stimulate nitric oxide synthesis in the corpora cavernosa. Erectile dysdunction, particularly when associated with a normal libido is only rarely explained by androgen deficiency.

- **Androgens and cognitive performance**

There is some evidence to suggest that testosterone may influence performance on cognitive tasks, which is supported by the finding that testosterone administration to older men enhance performance on measures of spatial cognition. The correlation between T levels and cognitive performance such as spatial abilities or mathematical reasoning, has been confirmed in western and non-western cohorts of healthy males.
Testosterone has also been associated with general mood elevating effects. And some studies have found

associations between lowered testosterone levels and depressive symptoms. Depression is not rare in aging men and impairs their quality of life so the effects that declining levels of androgens may have on mood and on specific aspects of cognitive functioning in aging are well worth to be researched.

CLINICAL MANIFESTATIONS OF ANDROGEN DEFICIENCY

The clinical manifestations of androgen deficiency in elderly men that lend themselves to an objective assessment are a decrease of muscle mass and strength, decrease of bone mass to the degree of osteopenia or osteoporosis, and increase in central body fat. Other signs, such as a decrease in libido and sexual desire, forgetfulness, loss of memory, difficulty in concentration, insomnia and a decreased sense of well being or depression might well be manifestations of androgen deficiency but they might as well be due cerebral (vascular) pathology. Their assessment is more subjective and more difficult to measure objectively. These symptoms should not be overlooked or dismissed for this reason but alternative explanations might apply. If present in combination with the more objective signs of androgen deficiency they corroborate the clinical diagnosis of androgen deficiency.

ADEQUACY OF ANDROGEN REPLACEMENT / CLINICAL ENDPOINTS

Once it has been decided that androgen supplementation should be given to an aging man, what are the guidelines for monitoring, what are the criteria of adequacy. In comparison to the replacement of other hormones, the adequacy of testosterone supplementation is unfortunately difficult to judge. The adequacy of thyroid replacement treatment is nowadays largely monitored by biochemical criteria. The plasma level of TSH is a reliable telltale of undersubstitution or oversubstitution, with an acceptable correlation with clinical symptomatology. The situation with corticosteroid replacement therapy is somewhat more complex; the compounds used are usually not exact copies of natural cortisol but synthetically modified molecules, and plasma ACTH is not commonly used to establish dosage adequacy. Nevertheless, blood pressure, serum potassium, sodium and glucose provide reasonable on the spot guidance as to the adequacy of corticosteroid replacement.

It is common clinical practice to judge the adequacy of androgen replacement by the effects on general well-being, mood, sexual interest and sexual activity. Hemoglobin and hematocrit levels might provide another index in the sense that anemia, for which no other explanation can be found, might point to undersubstition. Bone mineral density, though determined by multiple factors, can be regarded as an indicator of adequacy of sex steroid replacement but changes in bone mineral density are slow and a higher frequency of measurement than every two years is usually not informative. These parameters do not provide quick reference whether androgen is adequate.

A general principle in hormone replacement therapy is that plasma levels to be achieved over the 24 hours of the day must come close to normal references values, and ideally follow the normal diurnal pattern. So, an impression of adequate levels might be gained by determining plasma testosterone before administration of the next dose of the androgen preparation, but this measurement does not reveal deviations from reference values between two administrations. These fluctuations are strong with injectable testosterone esters but much less so with transdermal or oral testosterone preparations.

SUMMARY AND CONCLUSIONS

There is now solid evidence that in aging men statistically a decline of (free) testosterone levels occurs; yet many men will continue to have normal reference values of testosterone, so androgen deficiency in old age is by no means the rule. But, while a large number of men continue to have normal testosterone levels well into high age, a smaller proportion is androgen deficient and their quality of life might be improved with androgen supplementation. The identification of aging men with androgen deficiency remains a difficult problem in routine clinical practice. Aging men often show clinical signs of hypogonadism (loss of muscle mass/strength, reduction in bone mass and an increase in visceral fat). These manifestations might indicate androgen deficiency but often normal plasma testosterone levels are found. A theoretical question is whether there is an impairment

of the biological action of androgens in target organs in old age explaining the discrepancy between signs and symptoms of androgen deficiency in old age on the one hand and the laboratory findings on the other. In order to let aging testosterone deficient men benefit from androgen supplementation, their identification should be guided by clinical signs of androgen deficiency: loss of lean body mass and bone mass, increase in (visceral) fat mass, and a decline in psychological and sexual functioning. Arbitrarily, presently There is now solid evidence that in aging men statistically a decline of (free) testosterone levels occurs; yet many men will continue to have normal reference values of testosterone. This might point to not only a fall but (also) an impairment of the biological action of androgens in target organs. Meanwhile a role for oestrogens in men has become clear. Positive effects of oestrogens have been noted on bone and the cardiovascular system, and possibly adverse effects on prostate stromal hyperplasia.
The first small scale studies of androgen supplement administration in aging men were not disappointing. Risks of prostate and cardiovascular disease are probably lower than anticipated. For the treatment of postmenopausal women 'designer oestrogens' are being developed; similarly, 'designer androgens' retaining beneficial anabolic effects with elimination of potentially harmful effects on the prostate and cardiovascular system, could be devised. Important research questions are: 1) Is the decline of production or bioactivity of androgens in aging men causally related to signs of aging such as loss of lean body mass? 2) Is androgen replacement a remedy? 3) How can we identify aging men who are clinically androgen deficient and who might benefit from androgen replacement? 4) Do we have suitable androgen preparations for this purpose? 5) Will selective androgen receptor modulators be an advantage? 6) What will be the risks of interventions with drugs?

OVERACTIVE BLADDER : THE CONDITION & ITS AFFECT ON SEXUAL ACTIVITY OF WOMEN

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The overactive bladder (OAB) is a condition characterized by urinary urgency, frequency and urge incontinence. It is widely prevalent; more than 55 million people in the developed countries suffer from OAB, of which 55% are women. In 1998, the Asia Pacific Continence Advisory Board did a cross-sectional survey within 11 Asian countries and found an overall prevalence of urinary incontinence to be 12.2%, of which 50.6% had an overactive bladder. Yet, an estimated 80 percent of patients do not seek help or treatment for this condition. OAB significantly affects the quality of life; its effects range from incontinence to the inability to enjoy sexual activity. In a study done in the University of Pittsburgh where 78 women diagnosed with overactive bladder completed two questionnaires: one that evaluated the presence and degree of bother caused by their symptoms of overactive bladder; and one that evaluated the patient's sexual function. By comparing answers on both questionnaires, the researchers found that women who expressed a higher degree of bother as a result of urge urinary incontinence were less likely to enjoy sexual activity and became less sexually active.

The mainstay treatment for OAB is pharmacotherapy. The drugs most often used worldwide are oxybutynin and tolterodine. In an open-label, prospective study done at Northwestern University, Illinois, on 2878 women suffering form OAB, 52.1% of women admitted to having reduced interest in sex because of their bladder condition. After treatment with transdermal oxybutynin, coital incontinence was reduced in 19.3%, whilst 19.1% reported that their sex lives improved.
The main side-effects are related to its anti-cholinergic affect on the saliva glands, digestive system and skin, which in turn, reduces compliance with the medication. Newer drugs are darifenacin and solifenacin and have a lower incidence of side-effects.
For those who cannot tolerate oral medication, intravesical botox injection is another treatment option.

BOTULINIM TOXIN - AN ALTERNATIVE TREATMENT FOR VAGINISMUS

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Vaginismus is the instantaneous involuntary tightening in anticipation of vaginal penetration. In other words "a vagina in panic." Hence in my mind, a way to relax the pelvic muscles besides counseling, psychotherapy, and relaxation techniques, would be to paralyse the muscles. Secondly, to identify sensitive or painful spots which could trigger muscle spasm by "mapping" out the hot spots in the vaginal opening with a cotton bud. Hence, my management plan is focused on relaxation or paralysis of the pelvic muscles and treating the sensitive area.

Fenton's operation in my personal view is a phantom procedure which is radical and potentially destructive to the puborectalis and the perineal body. The scar tissue upon healing may worsen the condition. Hence, failure rate is high anecdotally.

The technique which I have devised, uses botulinum toxin to paralyse the pubococcygeus and puborectalis muscles with division of the frenulum of the labia minora when required.

Five patients underwent the procedure from 2005 to 2006 and four became pregnant.

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RECENT ADVANCES IN AETIOLOGY, GENETIC IMPLICATIONS AND TREATMENT OF MALE INFERTILITY

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The spermatozoon is a unique cell, designed to deliver its genetic material to the egg, and in that process contribute to the first mitotic spindle and the ability of the embryo to continue its development. There has been a better understanding of spermatogenesis and its biology, including the role of gene mutations that result in abnormal spermatogenesis. Specific genetic causes especially micro-deletions of the Y-chromosome and mutations in the androgen receptor gene can result in idiopathic OATS. Future treatment options may include the use of embryonic stem cells to generate spermatozoa, as well as testicular transplantation.

SPERM DNA DAMAGE: IS IT IMPORTANT IN MALE INFERTILITY & WHAT CAN WE DO ABOUT IT?

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Damage to the sperm DNA (chromatin) has been associated with poor semen quality, low fertilization rates, impaired embryo development, increased miscarriage rates, and elevated diseases in offspring (including birth defects and cancers). The causes of sperm DNA damage are thought to be oxidative stress and aberrant apoptosis in the sperm. Smoking, medications (anti-depressants), chemical exposure (dioxin, organic solvents) and environmental toxins (air pollution) have all been associated with higher levels of chromatin damage. Couples with histories of early embryonic loss and repeated miscarriages should in particular be evaluated. The Sperm Chromatin Structure Assay (SCSA Diagnostics, Brookings, SD, USA) is the most robust test of sperm DNA integrity. Frozen samples can be pooled and shipped for processing, to rule out high levels of DNA damage as a cause for fertility failures. Studies suggest that men with high sperm DNA damage may benefit from taking antioxidant supplements and treatment of subclinical infections resulting in leukospermia. The use of ART to overcome high levels of DNA damage remains controversial.

ROLE OF SALPINGOSCOPY IN INFERTILITY

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Study Objective:
To report the role of salpingoscopy for evaluation of tubal factors in infertility.

Setting:
Tertiary referral center for advanced gynaec endoscopic surgery in India.

Design:
Retrospective study of 3462 cases between years 1996-2005 where salpingoscopy was carried out during endoscopy as a part of infertility investigation.

Measurements and Main Results:
Total 3462 cases underwent endoscopic evaluation for infertility. Tubal factor was assessed primarily with choromopertubation followed by Salpingoscopy. Visual inspection of tubal endothelium was graded according to Brossen's classification. In hydrosalpinx after fimbrioplasty, salpingoscopic evaluation of tubal mucosa was carried out. Patients with findings worse than Grade 2 changes were subjected for salpingectomy considering the high probability of ectopic pregnancy. We observed that in grade I & II the pregnancy rate is around 71% & 44% with very less ectopic pregnancy rate of 4 & 7% respectively. In grade III case patients treated with IUI, pregnancy rate was 31% & ectopic pregnancy rate was 18%. Where as in grade IV & V, patients were not subjected for IVF ET and the ectopic pregnancy rate was ~92% which was significantly high.

Conclusions:
Salpingoscopy seems to be a very useful tool in assessment of tubal factor for infertility. It has good prognostic and predictive value. In cases of grade 3 or higher salpingoscopic findings ectopic pregnancy rates are considerably high & therefore IVF ET is a better & preferable option.

ENDOMETRIOSIS : UNUSUAL CASES

Sanjay Patel, Dr. Yogendra Jhala &Dr. Rujul Patel

Introduction

Endometriosis is one of the most complex and least understood diseases in our field .

The incidence of endometriosis has risen dramatically in the last few
Decades.

In this video we will discuss some of the unusual cases that we have managed in the last few years in our unit.

This video shows multiple **yellow vesicles** scattered all over in the pelvis, giving it a dramatic appearance. A biopsy of the lesion does document the presence of endometrial tissue. What is unusual about it is, that they are on the anterior surface of the uterus, which is not usual finding.

Endometriosis may cause significant distortion of the pelvic anatomy, especially in the posterior compartment.

Here you can see pouch of Douglas is completely obliterated due to adhesions of recto-sigmoid with left adnexa & posterior wall of the uterus.

Some times there is axis rotation of the uterus due to adhesions & Adenomyosis often co-exists with endometriosis.

Here you can see a prominent band in the posterior compartment which looks like utero-sacral ligament, but when it was traced up, it was actually the medially displaced ureter. Displacement of ureter is found in about 25% of cases of endometriosis. This puts the ureter at an increased risk if it is not identified. If you can't identify the ureter, it is be a good idea to insert a ureteric stent or preferably a fibreoptic ureteric catheter.

Endometriosis more commonly affects posterior compartment, however, it can affect **anterior compartment** as well, as it is seen in this case. There are endometriotic lesions in the utero-vesical pouch causing adhesions between omentum, round ligament, fallopian tube & uterus. It is important to remember to do cystoscopy in such cases just to rule out bladder endometriosis.
Endometriosis is also more commonly found in women with **congenital mullerian** anomalies . This is the hysteroscopy of a patient with unicornuate uterus.
This is the laparoscopy view of the same patient. You can see on the left side there is a non-communicating horn with haematometra & the haematosalpinx. There is also endometriosis on the left side affecting ovary, fallopian tube, recto-sigmoid colon & the pelvic side wall. We prefer to use suction irrigation cannula & other blunt instruments rather than scissor or any other energy devices for lysis of adhesions due to endometriosis. In this case we carried out salpingo-oophorectomy with excision of the non-communicating horn.
This was quite an interesting case of **ruptured endometriotic cyst.**
She actually presented with symptoms & signs of acute Abdomen.
The inflammatory response causes adhesions of appendix & omentum with anterior abdominal wall. After carrying out adhesiolysis, cystectomy was performed.

This 37 yrs old lady had undergone 6 months ago an apparently straightforward **vaginal hysterectomy** for severe dysmenorrhoea & menorrhagia .
She continued to suffer from cyclical pelvic pain & ultrasound showed bilateral ovarian cysts.
When we performed laparoscopy they turned out to be bilateral endometriomas & bilateral oophorectomy was performed after a long & difficult adhesiolysis. In such cases, risk of injury to ureter, bladder & recto-sigmoid colon is quite high.

This case just highlights one of the few disadvantages of the vaginal hysterectomy that you don't have an opportunity to inspect & treat adnexal pathology.

This 22 yrs old young lady had undergone laparoscopic ovarian bilateral endometrioma cyst aspiration & fulguration of cyst lining 5 months ago.
Folowing the surgery, she was suffering from persistent fever & loss of weight for which she was given several courses of antibiotics & even empirical anti-tuberculosis treatment.
Ultrasound was showing recurrence of ovarian cysts.
When we performed laparoscopy & adhesiolysis, they turnd out to be bilateral **ovarian abscesses**. They were drained & cysts were excised & this resulted in dramatic symptomatic improvement.

Adhesions are an inevitable consequence of any abdominal surgery especially endometrisis surgery & preliminary studies of use of Adept, which contains 4% icodextrin solution, are quite promising.
It is also not very uncommon to find endometriosis in **previous surgery scars**.

This patient had developed it in the caesarean section scar & she got better only after it was completely excised.
In this particular case, we had removed the cyst lining directly thro' the **umbilical port** & 6 months later, she had developed the scar endometriosis.
We learnt a lesson from that & since then we always use either an endobag technique or pull it thro' the cannula so that the cyst lining doesn't come in contact with the abdominal wall at all.

Conclusion
In conclusion I would like to say that treatment of endometriosis remains challenging.

Management of advanced stages of endometriosis require a higher level of endoscopy surgery skills & this sort of surgeries should be reserved for specialized centres.
Severe cases often require multiple surgeries and sometimes hysterectomies to remove the uterus and both ovaries even in very young pre-menopausal women.

LAPAROSCOPIC MANAGEMENT OF BROAD LIGAMENT MYOMA

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Study Objective:
To demonstrate the standardized technique of laparoscopic broad ligament myomectomy.

Design:
Few case reports of broad ligament myoma in video format.

Setting:
Tertiary referral center for Gynaec endoscopic surgery in India.

Patients:
From January 1996 to January 2007, 68 patients with moderate to large size symptomatic (true & false) broad ligamentary myomas (age group 22-36) underwent laparoscopic myomectomy. 60 cases had false broad ligament myomas & 8 cases were true broad ligament myomas.
Delayed childbearing age and symptomatology will determine the indications for conservative surgery. Laparoscopic myomectomy has provided minimal invasive alternative to laparotomy for subserosal and intramural myomas & hysteroscopic access for sub mucous myomas. It is associated with faster recovery and less postoperative adhesions. Main concerns are post-operative adhesions, subsequent fertility, reproductive outcome and long-term recurrence.
Pre-op GnRHa associated with hypo-estrogenic side effects & an increased tumor recurrence and loss of cleavage planes due to hydropic degeneration. This may make dissection difficult. About 10% do not respond to GnRHa. We did not use GnRHa pre-operatively. Preoperative ultrasonography is invaluable in planning the approach.
The standard approach is an oblique incision over the broad ligament parallel to the vascular structures. Injection Pitressin was not infilterated I any case. We prefer to use harmonic scalpel for this as it not only controls the bleeding but also creates a demarcation of tissue plane by its unique cavitational effect.
Ureters are main concern with this type of myomas, as it alters the normal course of the ureters. Fiber-optic ureteric catheterization is an excellent measure for primary prevention of ureteric injury. We perform ureteric catheterization as a routine in all cases.

Results:
Employing the above technique all 51 cases were performed without any major complications. However 10% cases suffered few minor post-operative complications; including febrile episodes, blood transfusions & prolonged catherterisation. The average blood loss was 60 cc with highest amount up to 250 ml requiring intra-op transfusions. The average duration of surgery was 90 min with maximum of 250 mins. The average hospital stay was 48/60 hours.

Conclusion:
Broad ligamentary leiomyomas are the most difficult to tackle at laparoscopy, however adherence to all microsurgical principles & prevention of ureteric injury makes them most rewarding. As compare to open surgery the recovery period & blood loss is far less. Selection of proper instruments & fiber optic ureteric catheter in some cases makes the approach much easier & safer. In a way, it's superior to the open myomectomy procedure.

APPEARANCES OF GENITAL TUBERCULOSIS

Dr Sanjay Patel MD
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The global prevalence of genital tuberculosis (TB) is estimated to be 8-10 million cases, with a rising incidence in the industrialized and developing countries partly as a result of its association with HIV virus infection. A diagnosis of genital tract tuberculosis has profound implications for the asymptomatic women seeking fertility. The diagnostic dilemma arises because of varied clinical presentations, diverse results on imaging and laproscopy, and a mixed bag of bacteriological and serological tests. Hence genital tuberculosis is a diagnosis based on the collective evidence from imaging technics, direct visualization by endoscopy, histopathology of genital tract material, and serology.
Pelvic ultrasound, a useful initial screening test, was able to identify ascites/loculated fluid (100%), adnexal mass (93%), peritoneal thickening (69%), Omental thickening (61%), and endometrial involment (83%) in cases of genital TB.
Chauhan et al reported suspicion of patient having genital TB on hysterosalpingo-graphies performed for infertility in about 7-20% in their series.
Endoscopy has the dual advantage of pelvic organ visualization and sample collection from inaccessible sites for laboratory diagnosis. The fallopian tubes are almost universally affected, as evidenced by complete tubal block in 80%, adhesions and calcifications in 43%, adherent mass in 35.8%, nodular sclerosis in 11.7%, and miliary tubercles and ascites in 9.4% cases of genital TB. Diagnostic hysteroscopy allows visualization of tubercles, microcaseation, distorted ostium, synechiae, and out-pouching in the endometrial cavity. Biopsy may also be taken from suspicious sites.
Material for laboratory diagnosis should be collected with two objectives, histology and culture, and the tissue should be divided into two equal parts.
Culture methods are still the gold standard in the detection of genital TB.Culture is traditionally performed Lovenstein Jenson (LJ) or Middlebrook THIO media, growth may be detected after 4-5 weeks. However improvements in media such as BACTEC 460 have allowed colonies to grow even when the count less with added advantage of reduced culture time to 2 weeks. The radiometric culture BACTEC has a sensitivity of 80-90%.
The polymerase chain reaction is a technique that shows rapid detection and quantification of few DNA copies with high sensitivity and specificity. Its sensitivity is so high that it requires only <10 bacteria/ml. It can also be applied to peritoneal fluid where the culture is difficult due to a low bacterial load. However the PCR test has its own share of false negative results which are largely due to contamination of the sample with heparin which is a known PCR inhibitor, absence of even a single AFB in the sample collected, and high salt concentration of a specimen which interferes with the PCR results. PCR cannot distinguish between live and hiked bacilli and there is a small risk of false positive results.
Detection by microsurgery needs 10,000 bacilli/mL,by LJ culture 1000 bacilli/mL,by BACTEC 10-100 bacilli/mL,and by PCR < 10 bacilli/mL.
However when the culture and PCR results don't tally, it leads to further confusion.

Conclusion
Tuberculosis, an age old disease, is making a comeback with the HIV pandemic. There is an urgent need for developing definitive diagnostic methods and criteria to be applied to make a conclusive diagnosis of genital

TB. Endoscopy has the dual advantage of pelvic organ visualization and sample collection from inaccessible sites for laboratory diagnosis.

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"VAGISITE(TM) TECHNOLOGY IN WOMEN'S HEALTH: TREATMENT OF RECALCITRANT MONILIAL VULVOVAGINITIS"

Program Overview
In Singapore, it is estimated that approximately 77 percent of general practitioners see up to 5 patients with vulvovaginal candidiasis (VVC) per week, while 33 percent of OB/GYNs see up to 10 patients with this condition. Due to this high prevalence rate, this presentation will inform participants regarding the management of VVC, with a brief overview of bacterial vaginosis, and a novel vaginal drug delivery system for the treatment of these vaginal infections.

Vulvovaginal Candidiasis (VVC)
Approximately 75% of all women will experience at least one episode of VVC with 50% experiencing multiple episodes of VVC. Candida albicans accounts for ~85% of all cases of VVC. However, an increasing number of yeast infections can be contributed to non-albicans infections, namely C. glabrata, which may be the cause of many cases of recurrent, drug-resistant VVC. It should be understood that no single factor is the sole cause for the onset of VVC; instead, various factors increase the likelihood of VVC. Therefore, this presentation reviews the etiology and prevalence of VVC while spending a majority of the time focusing on the therapeutic management of VVC.

Bacterial Vaginosis (BV)
BV is a polymicrobial clinical syndrome which left untreated can have deleterious consequences. BV has been linked to premature membrane rupture, premature delivery, low birthweight delivery, and increased risk of STD transmission. Due to the deleterious nature of this untreated infection, this presentation reviews the antibiotics covering all important pathogens involved.

SITE RELEASE(tm) Technology
An advance in vaginal drug delivery technology has been available in the United States since 1999. This technology has allowed for novel therapeutic options for the treatment of VVC and BV. This presentation reviews this new technology, its applicability in BV and VVC treatment, and its advantages.

Program Faculty
Daniel J. Thompson, JD, MS
Vice President, Medical Information and Business Development
KV Pharmaceutical

Dan Thompson has more than 20 years of experience in the health care field and is currently the Vice President of Medical Information and Business Development at KV Pharmaceutical. Mr. Thompson received his Bachelor of Science in Professional/Science Studies from the University of Notre Dame and continued his Masters program from the University of Missouri. Thereafter, he received his Doctorate of Jurisprudence from the Saint Louis University School of Law where he earned a specialized certification in Health Law. Mr. Thompson is an accomplished leader within the pharmaceutical industry and a recognized expert within the area of women's health focusing on vaginal infections and enhancement of drug delivery technology.

PULMONARY EMBOLISM AND AMNIOTIC FLUID EMBOLISM - INITIAL MANAGEMENT OF OBSTETRIC COLLAPSE

Tracey A Johnston
Consultant in Fetal Maternal Medicine,
Birmingham Women's Hospital, Birmingham, UK

Pulmonary embolism remains the commonest cause of maternal mortality in the UK, and amniotic fluid embolism carries with it an extremely high risk of mortality. Both these conditions can result in sudden obstetric collapse, and will often prove fatal if prompt effective resuscitation is not employed. This lecture will briefly summarise the aetiology, incidence and outcome of these two conditions, as well as their clinical presentation. The acute management of obstetric collapse will be discussed, as will advanced management of these two specific causes. This will form the basis of the practical session on Saturday.

THE URGENT AND DIFFICULT CAESAREAN SECTION

Tracey A Johnston
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Accurate classification of caesarean section is extremely important to allow effective communication between the members of the intrapartum team, as well as comparison and audit against predetermined standards. The term 'emergency' caesarean section is widely used, with an accepted 30 minute decision to delivery interval. There is good evidence that this is not always achieved. In difficult cases, there is often pressure to achieve delivery rapidly, but this may compromise the mother and possibly the fetus in certain circumstances. Classification of caesarean section will be discussed, along with a range of difficult conditions and situations, and strategies to minimise risk will be presented.

EVIDENCE BASED APPROACH TO AN INFERTILE COUPLE

C.V.Kannaki Uthraraj
India

The pattern of investigating and treating an infertile couple is undergoing a metamorphosis as new data arrive on fecundity, conception window, molecular basis of infertility .Though In vitro and genetic techniques are advancing, data on fertilization, implantation ,early embryo development and reproductive genetics is still primitive for clinical application.Endocrine and ultrasound measurements in the female cannot determine oocyte quality while semen analysis in the male is a limited predictor of fertilizing ability. Also, more studies would help in understanding the conditions in the Fallopian tube and endometrium that support fertilization and early embryogenesis.
However as diagnostic tools are improving in efficacy and surgical and assisted reproductive techniques are becoming more effective, the algorithm of investigating and treating an infertile couple is now being tailored on evidence. Investigations in current use will be weighed on the basis of evidence so that the decision of steering treatment with, cost and safety and improvement in pregnancy rates will be analysed.

UPDATE ON THE PHYSIOLOGY & FUNCTION OF THE FALLOPIAN TUBE - WHY IT MATTERS IN THE AGE OF IVF

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Critical events of early reproduction occur within the Fallopian tube including: gamete transportation; sperm storage, capacitation and selection; final oocyte maturation; fertilization; and early embryonic development. Novel research over the past decade has shown the dynamic microenvironments in the tube that change in response to gamete and embryo presence; as well as the role of disease in limiting normal reproduction. It is important to remember that over 98% of all babies born are conceived in the tube. Medicine & research should be directed to optimizing fecundity in proportion to actual demographic patterns. Improving reproductive outcomes for a majority of patients requires optimizing tubal health, this should include diagnosis and treatment of subclinical infections (e.g. Chlamydia or bacterial vaginosis), as well as endometriosis. The potentially deleterious effects of some medications (e.g. clomiphene) on tubal function should also be considered. Systematic data reviews suggest improved pregnancy outcomes for some groups following tubal flushing and after the use of tubal sperm perfusion for insemination. Taken together, recent reports suggest the Fallopian tube continues to deserve medical respect and management.

SUCCESS RATES OF INFERTILITY TREATMENTS-WHAT TO TELL YOUR PATIENTS?

SF Loh
Senior Consultant, KKIVF

Patients today are getting more knowledgeable and sophiscated. They frequently demand to know the various treatment options available to them, the costs and success rates of various treatments as well as the possible complications. Fertility specialists need to present these information to their patients in a clear and unbiased way to allow the patients to choose a treatment option which best suits their needs.

Success rates of various infertility treatments, including the simple clomiphene induction of ovulation, laparoscopic tubal surgery, laparoscopic treatment of endometriosis, treatment for male infertility, Intra-uterine insemination (with or without ovarian stimulation), IVF/ICSI will be discussed.

While it is important to inform the patients the age specific success rates of ART treatment, it is also important to educate them about complications like Ovarian hyperstimulation and higher order multiple pregnancies. It is important to present to the patients the pregnancy rate of single, versus double versus triple embryo transfer to allow them to make an informed decision about their treatment.

LETROZOLE AND ITS USE IN OVULATION INDUCTION

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Aromatase is a member of the cytochrome P450 hemoprotein containing enzyme complex super family. It catalyzes the rate-limiting final step in estrogen (E) production, the hydroxylation of androstenedione to estrone and of Testosterone to Estrogen. Aromatase is a good target for selective inhibition because estrogen production is a terminal step in the biosynthetic sequence. A large number of aromatase inhibitors have been available and utilized in the clinical studies over the last 20 years. The third generation antiaromatase agents include two nonsteroidal drugs namely letrozole and anastrozole. Aromatase inhibitors are completely absorbed after oral administration with mean terminal half life of 45 h(range 30-60). They are cleared from the systemic circulation mainly by the liver. Gastrointestinal disturbances account for most of the adverse events, although these have seldom limited therapy. Other adverse effects are asthenia, hot flushes, headache, and back pain. Advantages off the them are-extremely potent in inhibiting the aromatase enzyme, very specific in inhibiting the aromatase enzyme without significant inhibition of the other steriodogenesis, administered,100%bioavailability after oral administration, rapid clearance from the body (short half life of 45 h),no accumulation of the medications or their metabolites, very safe without significant contraindications. Clearly, treatment with aromatase inhibitors in this group of patients is associated with a good ovulation rate, thick endometrium, and a considerable number of pregnancies. Patients treated with a combined regimen required less gonadotropin. The ideal dose of letrozole is unknown; however, it seems that the dose of 2.5 mg to 5 mg daily for 5 days is the most effective. Aromatase inhibitors are promising new drugs for the induction of ovulation and superovulation.

LETROZOLE AND OVULATION INDUCTION- A REVIEW

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Introduction

Letrozole (LTRZ) is a third-generation aromatase inhibitor. Blocking the estrogen production by inhibiting aromatization would release the Hypothalamic/ pituitary axis from estrogen negative feedback which increases FSH which stimulates development of ovarian follicles. Popularity was gained for Letrozole because of the observation of mono-ovulation, and absence of negative effect on endometrium and cervical mucous. Aromatase is a member of the cytochrome P450 hemoprotein containing enzyme complex super family. It catalyzes the rate-limiting final step in estrogen (E) production, the hydroxylation of androstenedione to estrone and of T to E. For many years, aromatase inhibitors have been used as an adjunct treatment for breast cancer. Letrozole and anastrazole the two aromatase inhibitors are completely absorbed after oral administration, with a mean half-life of approximately 45 hours (range, 30-60 hours). Aromatase activity is present in many tissues, such as the ovaries, the brain, adipose tissue, liver, breast, and in malignant breast tumors. The main sources of circulating estrogens are the ovaries in premenopausal women and adipose tissue in postmenopausal women.

Review of Literature

It was first postulated1 that blocking E production by inhibiting aromatization would release the hypothalamic-pituitary axis from estrogenic negative feedback. As a result, FSH secretion increases, stimulating the development of ovarian follicles . Because aromatase inhibitors block high levels of E from androgen conversion, the effects in women with polycystic ovary syndrome (PCOS) are more prominent1. In addition, androgens that are normally converted to estrogens accumulate in the ovary, and these androgens increase follicular sensitivity to FSH1.. Unlike CC, aromatase inhibitor does not deplete E receptors or produce a negative effect on the endometrium. The half life of Letrozole is 45 hours. Clomiphene citrate (CC), on the other hand, has a longer half-life (2 weeks) that results in prolonged central E receptor depletion2. A study showed3 treated women with CC-resistant PCOS with 2.5 mg of letrozole (22 patients) or 1 mg of anastrazole daily from day 3 to day 7 of the cycle (18patients). Endometrial thickness was greater in the letrozole group (8.2 mm) than in the anastrazole group (6.5 mm). The ovulation rate in the letrozole group was 84.4% and in the anastrazole group was 60%. The pregnancy rates were also statistically higher in the letrozole than in the anastrazole group (18.8% vs. 9.7% per cycle, respectively). The mean number of leading follicles was 1.7 in both groups. There were no cases of multiple gestations. Although the ideal dose of anastrazole is still unknown, it seems that the dose of 1 mg daily is much too low. Clearly, treatment with aromatase inhibitors in this group of patients is associated with a good ovulation rate, thick endometrium, and a considerable number of pregnancies

Aromatase inhibitors as an adjunct treatment with gonadotropins:

In a prospective, nonrandomized study involving women with unexplained infertility or mild male factor 4, 36 women were treated with letrozole and Follicle stimulating hormone (FSH), 18 women with CC and FSH, and 56 women with FSH only. Follicle stimulating hormone was administered on days 3-7, until the day of hCG administration. Compared with the FSH-only group, the required amount of FSH was significantly lower in the letrozole and FSH and in the CC and FSH groups. There was no difference in the number of follicles of 18 mm among the three groups. The pregnancy rate per cycle in the CC and FSH group (10.5%) was significantly lower than in the letrozole and FSH group (19.1%) and the FSH-only group (18.7%). Another study5 evaluated women who were superovulated with gonadotropin or a combined regimen of gonadotropin and letrozole (5 mg daily on days 3-7). Gonadotropin was started on day 3 of the cycle as well ("overlapping approach").

There were 145 cycles in the gonadotropin only group and 60 cycles in the letrozole and gonadotropin group. Patients treated with a combined regimen required less gonadotropin and developed more follicles but had thinner endometrium. However, there was no significant difference in the pregnancy rates between the two groups (gonadotropin 20.9%, gonadotropin and letrozole 21.6%). It seems that, compared with a 2.5-mg daily dose, a 5-mg dose yields more follicles 6. A study compared these two doses and found that 5 mg of letrozole daily was associated with a higher number of follicles and a higher pregnancy rate7. Recently, another study8 demonstrating the use of AIs in combination with recombinant FSH and GnRH antagonists, showed good clinical results in comparison to the use of recombinant FSH plus GnRH antagonist in assisted reproductive technology (ART) for poor responders. The stimulation protocol consisted of administering combination oral contraceptives (OCs) for 14-21 days, 5 mg/d letrozole was started orally, 4 days after discontinuing OCs, for a total of 5 days. On the last day of LTRZ administration, hMG containing 75 IU of LH and 75 IU of FSH per ampule, was added to the protocol daily, at a dose of 150 IU/d IM until the day before hCG administration. A GnRh antagonist was initiated at 0.25 mg/d SC after finding either an E2 level 250 pg/mL or a leading follicle at 13-14 mm in diameter. None of the patients had to be cancelled due to a lack of ovarian response and they all made it to oocyte aspiration. Human chorionic gonadotropin, 10,000 IU IM was administered once the leading follicle reached 18-20 mm in diameter. All mature oocytes obtained were microinjected with a single sperm (intracytoplasmic sperm injection) within 6 hours. Serum E2 on hCG day (pg/mL) 401.2 ± 205.5,Number of amp0ules of hMG 150 IU administered per patient (total dose) 6.4 ± 1.6 (960 ± 225 UI), Number of oocytes/patient 5.3 ± 2.7, Fertilization rate (%) 70.3%, Number of embryos transferred/patient 2.4± 0.8,Implantation rate 15%, Clinical pregnancy rate 31%,Miscarriage rate 14%,Ongoing pregnancy rate 27%. This data show that despite a low number of oocytes aspirated per patient (average 5.3± 2.7), the quality was satisfactory and led to the presence of good quality embryos available for transfer. The ongoing PR of 27% per initiated cycle was quite satisfactory, considering the overall number of oocytes initially available for ICSI per patient. The number of units of hMG (960± 225 UI) per patient was well below the usual dose of gonadotropins in standard protocols with GnRH antagonists in normal responders 9 where most patients used between 1,800 and 2,500 IU per cycle. The average endometrial thickness of 8.7 ± 2.3 mm on the day of hCG administration with a nice triple layer pattern, reflects the lack of competition for estrogen receptors at the endometrial level by the AI. The low number of oocytes retrieved, certainly can be taken as a disadvantage, as there were no frozen embryos for future transfer to add to the cumulative PR. The dose of LTRZ used, 5 mg/d for 5 days, seems appropriate based on previous studies in non-ART patients 10 .

Action and effects of letrozole:

It is an extremely potent in inhibiting the aromatase enzyme

- Very specific in inhibiting the aromatase enzyme without significant inhibition of the other steriodogenesis
- Orally administered
- 100%bioavailability after oral administration
- Rapid clearance from the body (short half life of 45 h)
- No accumulation of the medications or their metabolites
- No significant active metabolites

Aromatase inhibitors are completely absorbed after oral administration with mean terminal half life of 45 h(range 30-60). They are cleared from the systemic circulation mainly by the liver. Gastrointestinal disturbances account for most of the adverse events, although these have seldom limited therapy. Other adverse effects are asthenia, hot flushes, headache, and back pain11. The blocking of estrogen production would be release of the hypothalamic/pituitary axis from estrogenic negative feedback, thereby increasing gonadotropin secretion and resulting in stimulation of ovarian follicles. Because of short half life compared to CC, this would be ideal for this purpose since it is eliminated from the body rapidly. This was referred to as Central hypothesis. There is evidence that both circulating estrogen and locally produced estrogen exert negative feedback on the release of gonadotropins. In women with PCOS , relative over suppression of FSH may be the result of excessive androgen produced from the ovary being converted to estrogen by aromatisation in the brain. The aromatase inhibitors suppress estrogen production in both the ovaries and the brain. In the case of PCOS, therefore,

aromatase inhibitors should result in a robust increase in FSH release and subsequent follicle stimulation and ovulation. In order to explain another mechanism of action of aromatase inhibitor, a second hypothesis, called peripheral hypothesis is explained. They act locally in the ovary to increase follicular sensitivity to FSH. This may result from accumulation of intraovarian androgens, since conversion of androgen substrate to estrogen is blocked by aromatase inhibition.

The short half life of the aromatase inhibitors and limited administration to the early part of the follicular phase allow the rapid clearance of the medications, before the important stage of fertilization and embryogenesis. This , in addition to the absence of accumulation of the aromatase inhibitors or any of their metabolites, would make them safe for the ovarian stimulation. Clomiphene citrate is the most commonly prescribed agent for ovulation induction. Unfortunately, despite high rates of ovulation, pregnancy rates per cycle remain relatively low. An antiestrogenic effect of clomiphene on the endometrium is postulated. Despite normal ovulation, 15-50% of women on clomiphene will develop a thin endometrium (<8mm) with a tendency toward a non-trilaminar pattern of the endometrium at the mid-cycle. This has been shown to be a repetitive phenomenon in subsequent cycles and is not improved by addition of supplemental estrogen, suggesting that it is a result of estrogen receptor depletion. Both thin endometrium and non-trilaminar pattern of the endometrium at mid-cycle have been associated with low pregnancy rates and early pregnancy loss. For women who experience this adverse effect of clomiphene, the next step is induction of ovulation with gonadotropins, which significantly increases both the cost of and risk associated with treatment, particularly for women with polycystic ovarian syndrome, who are at increased risk of ovarian hyperstimulation.

Letrozole is a potent reverisible aromatase inhibitor that has been used to prevent peripheral aromatisation of androgens in the treatment of postmenopausal women with metastatic breast cancer. The excellent oral bioavailability and relatively short half life (45 hours) make letrozole a viable alternative to clomiphene for ovulation induction

There are concerns about the side effects of letrozole , which include risk of osteoporosis, hepatic dysfunction and teratogenic effect on the fetus if the patient conceives in the treatment cycle. But such apprehensions may not be scientific as the duration of therapy of letrozole for induction of ovulation is only for 5 days and half life is only 45 hours.

Lastly and not the least, the drug is yet to be approved by FDA for induction of ovulation, though this drug has been approved for carcinoma breast. This fact has found extensive publicity in the media which has generated serious public concern further information about the efficacy of aromatase inhibitor for ovulation induction will not be available unless FDA approves large number of clinical trials. Reports already available indicate encouraging results with satisfactory outcome in terms of achieving pregnancies following induction of ovulation with letrozole with no adverse effects

Conclusion:
letrozole appears to be safe, effective and inexpensive drug for induction of ovulation especially in Clomiphene resistant women. Though the Low-cost COH protocol combining Letrozole and hMG at low doses yields a low number of oocytes in ART, it gives a satisfactory ongoing PR in the group of normal responder patients with limited economic means. Popularity was gained for Letrozole because of the observation of mono-ovulation, and absence of negative effect on endometrium and cervical mucous. Though FDA approval is not present for Infertility use large series of observation is needed to popularize the drug.

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THE USE OF GNRH ANTAGONISTS IN SUPEROVULATION AND IUI PROTOCOLS

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Unlike the GnRH agonists, which have been routinely used in ovarian stimulation protocols for almost 20 years, the GnRH-antagonist acts via a dose-dependent competitive blockade of the pituitary GnRH-receptors. This results in an immediate suppression of gonadotrophin secretion (in particular LH) from the anterior pituitary. As, iDespite n spite of the obvious advantages of this new class of substances the controversial discussion about the influence of the antagonists on implantation and embryo quality has been ongoing for the last few years.and follicular maturation??? New data from a recent meta analysis (1) has demonstrated that the live birth rate per cycle is equivalent between antagonist and agonist protocols, however there is a significant reduction in the amount of FSH used and lower probability of OHSS associated with hospitalisation.

Recently, flexible protocols where the GnRH antagonist is applied according to leading follicle size rather than a fixed day of stimulation have been developed in order to prevent a premature LH surge. A recent (2) meta-analysis of four randomised trials comparing a fixed vs flexible starting day for the GnRH antagonist concluded there was no statistically significant difference in pregnancy rates, but a significant reduction in the amount of FSH utilised in favour of the flexible protocol.

A series of studies have however raised concern about late administration of the GnRH antagonist, as used in a flexible protocol. In three studies (3,4,5), the implantation and pregnancy rates were higher when the antagonist was initiated on a fixed day (stimulation day 6) compared to administration in a flexible protocol according to follicle size ((15 mm).

Whilst Kolibianakis et al. (3) reported no difference in overall pregnancy rate in flexible over fixed day antagonist administration, the implantation rate was lower in the flexible protocol, when there were no follicles of (15 mm on stimulation day 6. In this group, higher concentrations of LH and oestradiol were observed prior to antagonist administration. In a second study Kolibianakis et al (6) reported that profound suppression of LH after GnRH antagonist suppression was associated with a significantly higher ongoing pregnancy rate. They argued that exposure of the genital tract/oocyte to LH may adversely affect the implantation rate, mainly by altering endometrial receptivity. One issue here that may have complicated the interpretation of the results is the very late administration of the GnRH antagonist ((15 mm). It is generally recommended that the antagonist should be administered when the leading follicle is 14mm at the very latest.

Co-treatment with oral contraceptive pill (OCP) programming can also be utilised with GnRH antagonists in order to facilitate scheduling the start of FSH therapy, rather than waiting for the patient to have a spontaneous menses. There are now a number of studies reporting the use of OCP pill programming with either daily 0.25mg (7) or single dose 3mg Cetrotide in routine ART (8,9) and also poor responder (10,11) patients. Recently there have been a number of studies published on the use of GnRH antagonists in IUI cycles (12,13). Future studies in this area are still required to elucidate the optimal protocol in IUI cycles.

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POLYCYTSIC OVARY SYNDROME (PCOS): THE SOUTH ASIAN PERSPECTIVE

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The polycystic ovary syndrome (PCOS) continues to challenge the clinician despite an exponential rise in research and development on this subject in the past two decades. PCOS has evolved from being a mere gynaecological curiosity to be recognised as a complex endocrine problem with multifactor causes and as a marker of serious long-term consequences. It is the commonest cause of anovular infertility in women, while its clinical features are heterogeneous and may change throughout the lifespan of an affected individual, from adolescence to postmenopausal age (1, 2). This leads to an affected woman seeking health care from differing disciplines and care givers The manifestations of PCOS are largely influenced by obesity and related metabolic alterations viz. insulin resistance and the metabolic syndrome. Hyperinsulinaemia and obesity do in fact have profound effects on both the pathophysiology and the clinical problems of PCOS (3). Compared to lean women with PCOS, those with increased body mass index are characterised by a worsened hyperandrogenism and metabolic dysfunction that correlates closely with oligomenorrhoea, ovulatory failure and poorer pregnancy outcome (4). The increasing prevalence of obesity among young women with PCOS may be explained by the worldwide increase in obesity, particularly in South Asia, which is the epicentre of the current pandemic of insulin resistance and type 2 diabetes mellitus (T2DM) (5). Hence, a pathophysiology-based approach to management of PCOS is of much relevance for both preventive and curative medical practice in South Asia, and will also offer a better understanding of the complex aetiology of this syndrome.

The importance of obesity as a contributor to the pathogenesis of PCOS is highlighted by the efficacy of lifestyle intervention and weight loss, not only on metabolic alterations but also on hyperandrogenism, menstruation and fertility (6). Lifestyle interventions to reduce central obesity will improve the quality of life of affected women and correct the insulin resistance and help achieve fertility, metabolic and androgen profiles in the short-term, as well as impact on reducing possible long-term complications of the syndrome such as T2DM, hypertension and coronary artery disease. Pharmacological treatments are for specific problems of PCOS, such as: infertility with clomiphene citrate or gonadotropins and metformin, followed by ovarian diathermy; hirsutism with cyproterone acetate (alone or in combination with ethinylestradiol) and spironolactone, irregular menses with cyclical cyproterone acetate combined with ethinylestradiol. Women with PCOS also require regular surveillance to detect glucose intolerance, hyperlipidaemia, endometrial hyperplasia and consequent complications. This chapter will address issues on the diagnosis, epidemiology and management of co-morbid features of this common endocrine disorder and outline a symptom oriented approach with short- and long-term goals of management.

Case definition and diagnosis of PCOS

The identification of an affected woman was plagued by controversy across the Atlantic due to the lack of a

unique phenotype. This has been largely resolved by the recent revision of the diagnostic criteria by consensus at Rotterdam in 2003, which defines an affected case by the presence of any two of the following: oligomenorrhoea or amenorrhoea, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries on ultrasound scanning, having excluded disorders such as Cushing's syndrome, congenital adrenal hyperplasia or androgen secreting tumour that can mimic PCOS (7). The polycystic ovary (PCO) was redefined as an ovary with 12 or more follicles that measure 2-9 mm in diameter and/or an ovarian volume exceeding 10 cm3, which is distinct from the multicystic ovary that could occur during puberty. The attending doctor must be well aware of the need for this sonographic distinction since the picture of PCOS also emerges around puberty due to its increased insulin resistance unmasking the manifestation of PCOS. The new diagnostic criteria for PCOS suggest three possible phenotypes: classic well characterized PCOS (hyperandrogenism and anovulation), ovulatory hyperandrogenism and normoandrogenic oligo/anovulation, where the latter presentation may elude diagnosis for sometime (8). Overall, 6% to 9% of reproductive-aged women suffer from PCOS, making this disorder one of the most common endocrine abnormalities of women of reproductive age (9). The prevalence of PCO is 20-33%, while its mere presence does not equate with the diagnosis of the syndrome. However, controversy yet exists as to what proportion of women with PCO alone would convert into the syndrome with time, while community based diagnosis of PCO has revealed that approximately 80% are symptomatic at the time of identification (10). It is interesting that the threshold for diagnosis of PCOS based on the above criteria differ between gynaecologists and endocrinologists, where gynaecologists place greater reliance on ultrasound diagnosis and elevated luteinizing hormone (LH) while endocrinologists rely more on oligomenorrhoea and hyperandrogenism (11). It is interesting, that despite insulin resistance and the resulting hyperinsulinaemia being central to the pathophysiology of PCOS, it is not a key diagnostic criterion. There is paucity of data on problems encountered in the diagnosis and the prevalence of PCOS in South Asia, possibly due to limitation of resources. A community survey being currently conducted in Sri Lanka suggests that the prevalence of PCOS is similar to reports from the West (personal communication), which highlights the importance of arriving at a regional consensus for case definition that is practical and cost effective, that will also take into consideration socio-cultural influences on the health seeking behaviour of affected South Asian women. Furthermore, laboratory support being not uniformly available, a more practical approach to carrying out the very essential and appropriate investigations to evaluate the woman with suspected PCOS and its metabolic problems must be encouraged (Figure 1). The primary health care workers also require to be appropriately trained to recognise affected women at grass root level in the rural settings, in order to refer appropriately for specialised management and also provide support for those affected.

Ethnic differences in clinical manifestations of PCOS and its relevance to South Asia

Geographic variations and ethnic differences in the prevalence of PCOS have not been well explored in the South Asian region. Dunaif and co-workers reported an increased rate of PCOS among an insulin resistant ethnic group, the Caribbean Hispanics (12), while Knochenhauer et al found in a US based study that the prevalence of PCOS among black women was comparable with that of whites (13). The study carried out by Rodin et al on South Asian immigrants living in London revealed a very high prevalence of PCO (52%). They also demonstrated that the insulin resistance of South Asians with PCO without type 2 diabetes was comparable to that of South Asian women with type 2 diabetes and without PCOS (14). This led the first author and co-workers in England to study in detail the clinical manifestations and the degree of insulin resistance of PCOS among British Asian women living in the North of England and who belonged to the 2nd and 3rd generations of migrant populations and compare them with affected white Europeans. This revealed that South Asians living in England had clinical problems significantly different from affected white European women in that the South Asians presented with symptoms at a younger age, developed menstrual irregularity in their teens, had greater degree of hirsutism and significantly greater fasting insulin and insulin resistance than BMI matched European counterparts (15). An extension of this study on a cohort of indigenous Sri Lankan women with PCOS mirrored a similar clinical picture that manifests at an even earlier age and who had greater central obesity in relation to their BMI. The latter study also revealed that fasting insulin concentrations among the indigenous Sri Lankans was 3-fold greater than that observed among affected migrant Asians. Similarly, fasting plasma homocysteine, a biochemical marker of premature atherosclerosis, was significantly greater

among Sri Lankan PCOS women that correlated very closely with their high degree of insulin resistance (16). These observations in young South Asian women with PCOS bear major implications on their long term risks of coronary artery disease and call for a multidisciplinary effort towards early screening and primary prevention of metabolic complications. In the light of these findings and Sri Lankan women having a high rate of literacy and urbanization in the South Asian region, it is reasonable to hypothesize that a change in lifestyle in a high-risk ethnic group influences their degree of manifestation of the metabolic problems of PCOS.

Symptom oriented management of PCOS

In view of the heterogeneity of clinical problems that can affect an individual patient the management of PCOS has to be tailored to the needs of the affected woman at any given time. There are five broad categories of women with PCOS that require appropriate specific medical care: the obese adolescent with irregular periods, the young career oriented women who is greatly perturbed by her skin problems of hirsutism, acne, acanthosis and androgenic alopecia (Figures 2,3), the infertile woman with irregular periods seeking a pregnancy, the pregnant woman with PCOS anxious to have a healthy newborn, and the obese woman with irregular heavy periods who has completed her family and is at risk of long term metabolic problems.

The common factor to all these clinical scenarios that requires adequate attention by all groups of carers alike is the problem of tackling excess body fat that is chiefly central in distribution and correlates with visceral adiposity (4). The measurement and recording of the anthropometry of affected women as an essential routine in clinical practice cannot be overemphasized and is of great relevance when caring for the affected South Asian woman, for whom the cut off value for Class I obesity is a BMI exceeding 24 kg/m2 and the waist circumference (when measured at the level of the upper right iliac crest in mid respiration using a non-stretchable plastic tape) is 80 cm (17). However, the cut off value for waist circumference based on the 95th centile of each ethnic group's age and gender matched control group value should be determined, where the local results for urban Sri Lankan women at 5 years post partum revealed this to be 83.5cm (personal communication). The attending clinician must bear in mind the possibility of a fatty liver in the centrally obese woman with PCOS that requires in her basic assessment the testing of liver enzymes and where possible hepatic imaging, which has implication on the need to encourage weight reduction as well as being cautious when selecting medication that can have hepatic side effects.

Weight reduction

Tackling the problem of obesity is the most difficult; where one needs to explain to the affected woman and her family, from the first assessment itself, that weight reduction and subsequent weight maintenance would help ameliorate much of the symptoms of PCOS, which requires the maximum cooperation by the patient herself. Encouraging her towards an appropriate diet and physical exercise are the important aspects of behavioural modification that should be ideally implemented and monitored at primary care level where optimum patient co-operation and compliance will be ensured. Awareness by the patient and her carer that there is a gradual fall in energy expenditure (basal metabolic rate) with weight gain of approximately 1kg per year in a woman beyond the age of 30 years, that those at risk of obesity from PCOS in particular should adhere to a healthy diet and regular physical exercise of at least 30 minutes per day on five days of the week from an early age. A nutritionist's regular educational inputs and encouragement to limit the intake of simple sugars and fast foods with the consumption of high fibre containing carbohydrates in moderate quantities with practical food alternatives that are socio-culturally acceptable is of vital importance in the management of all clinical categories of women with PCOS. Norman and co-workers who compared the effects of short term meal replacements with long term advice on moderate fat or carbohydrate restriction on women with PCOS found both to be equally effective in maintaining weight reduction and in improving reproductive and metabolic variables of PCOS (18). Therefore, the attending clinician in a busy outpatient specialist setting in South Asia must be sensitive to the issue of imposing long term restrictions on young woman with PCOS who feel otherwise healthy, and must approach this problem with adequate sensitivity and through shared care with a multidisciplinary team who can regularly educate, counsel and monitor the therapeutic effects of their lifestyle modification.

In the short term, weight reduction improves both metabolic and endocrine aspects of PCOS as well as clinical markers such as ovulation. However extreme weight loss is rarely achieved with a constant risk of a weight regain following initial weight loss. Hence, a modest weight loss goal of 5-10% would be a practical approach that would be equally effective in restoring spontaneous menstruation in the adolescent and fertility in those seeking motherhood, which is also compatible with better long-term success in managing the metabolic problems of affected women (4, 6). The patient must also be educated that a lower maternal BMI at conception can yield a better pregnancy outcome with fewer PCOS related pregnancy complications such as miscarriage, diabetes mellitus, hypertension, and fetal growth retardation. One must be also be sensitive to the fact that such women are liable to have problems with body image and a greater tendency to depression that has potential to affect their quality of life and stability of marital relationships when the clinician may have to take on the role of a counsellor and confidante (19). A health related quality of life survey among PCOS subjects carried out in Sri Lanka confirmed that the affected women have a significantly lower sense of well being and poorer health related quality of life score than ethnically matched controls which has significant bearing when caring for these women in our local setting (20).

The role of metformin in PCOS

The rationale for using insulin sensitizers, particularly the biguanide metformin, in selected subjects with PCOS has been extensively addressed in the past few years. Metformin is preferred to the glitazones (rosiglitazone and pioglitazone) as the first choice of an insulin sensitizer. Its place in the treatment of infertility has been extensively studied; where a meta-analysis and systematic review concludes that it is effective for anovulation of PCOS and justifies its use as a first line agent with additional benefit on parameters of the metabolic syndrome. Ovulation rates are higher when metformin is combined with clomiphene (76% versus 46% when used alone), but there is no conclusive evidence as yet to indicate whether there is an increased multiple pregnancy rate with this combination (21). Few studies have studied the use of metformin with gonadotrophins for ovulation induction and for in vitro fertilization with no clear evidence of a significant benefit.

However, there is no data as yet regarding safety in its long-term use in young women seeking help for hirsutism and menstrual irregularity alone. Hence it is recommended only as a short-term adjuvant to general lifestyle improvements, and not as a replacement for increased exercise and improved diet (21). We need to bear in mind that a randomized, placebo-controlled, double-blind multicentre study in U.K which studied the effect of metformin 850 mg twice daily compared with placebo over 6 months revealed that metformin does not improve weight loss in obese anovular women with PCOS (22), which has been supported by subsequent workers who recommend that metformin should not be used as a weight loss drug but only as an adjunct to lifestyle modification in women with PCOS (23). Insulin resistance has also been linked with recurrent miscarriages in pregnancy where metformin use in the first trimester has shown significant improvement in pregnancy outcome. So far, evidence for safety of continued therapy throughout gestation is insufficient, and randomized placebo-controlled double-blind clinical trials are awaited prior to a recommendation of sustained metformin therapy throughout pregnancy (24). Nevertheless, a recent meta-analysis of the use of metformin in the first trimester was associated with a statistically significant 57% protective effect and lower fetal malformation rate than the untreated PCOS controls (25).

The safety of metformin with altered liver function caused by a fatty liver complicating insulin resistance of PCOS needs specialist evaluation prior to commencing short-term therapy. There is potential for metformin to reverse the hepatic pathology, but such patients need careful monitoring in the light of currently available data suggesting metformin being beneficial in overcoming hepatic steatosis pending results of on-going randomised control studies (26). Therefore it is recommended that monitoring liver function of all PCOS women on metformin is imperative prior to and during treatment. The place of metformin in reducing long-term cardiovascular risks of insulin resistance alone remains unresolved, although diabetes prevention trials have yielded promising results. Prevention of metabolic consequences of obesity and insulin resistance of PCOS has been studied in affected women randomized to 6-month treatment with metformin versus ethinyl estradiol-cyproterone acetate oral contraceptive pills, which revealed that metformin was beneficial on the lipid profile and blood pressure (27).

In summary, the available data indicate that metformin, either as monotherapy or in combination with clomiphene in clomiphene-resistant patients, is an effective treatment for anovulation in PCOS and has a role in preventing early pregnancy loss with a reassuring safety profile. Ameliorating the metabolic syndrome associated with insulin resistance of PCOS with metformin may also prevent long-term cardiovascular and diabetes complications, pending further evidence. Based on these data, metformin should be considered as a first-line short-term therapy for most women with PCOS (28).

Management of cutaneous manifestations of PCOS

Hirsutism and acne are common and cause great distress for women, particularly the younger pre-marital group, with PCOS. Acanthosis nigricans, a cutaneous marker of insulin resistance, is another manifestation of the South Asian with PCOS who has a greater propensity to insulin resistance. Drugs for cosmetic effects although available are only partially effective on terminal hairs and require at least six months therapy for the affected woman to appreciate its benefit. Therefore physical therapy such as hair removal or bleaching must be encouraged, particularly until drug treatment takes effect. However, bleaching of dark hair can prove to be disadvantageous since the hair tends to change its colour to an orange-red tint. Electrolysis and laser photothermolysis are considered the most effective cosmetic procedures, although the benefits of these methods should not be considered permanent and may cause temporary scarring. Therefore, management of hirsutism is generally based upon a dual approach: a pharmacological therapy to reduce androgen secretion and/or androgen action, and removal of terminal hair already present (29). Ovarian suppression of androgen secretion with oral contraceptives is widely used in these women, which also ensures regular menses and reduces the risk of endometrial hyperplasia, although its efficacy on improving skin problems can be somewhat limited. The most effective medical therapy for hirsutism is the use of anti-androgen drugs such as cyproterone acetate (which can be given cyclically in combination with ethiny oestradiol) and spironolactone. Acne may be treated with different tools, according to the severity of the condition and other characteristics of the patient, which include topical and systemic retinoids and antibiotics, topical antibacterial agents, androgen suppression by oral contraceptives, and anti-androgen drugs. Hence, the management of cutaneous manifestations require a multidisciplinary approach between dermatologist, endocrinologist and the gynaecologist.

Although a few trials have studied the short-term effect of adding metformin to the drug regimen used for skin problems of PCOS, a recent study on the long-term effects of metformin and flutamide (an anti-androgen) in PCOS showed that combining the two drugs maintained the specific effect of each of the compounds, without any additive or synergistic effect. This finding adds relevance to the usefulness of metformin combined with anti-androgens for the overweight-obese young PCOS woman and provides a rationale for targeting different long-term therapeutic options of the individual patient (30). Overall the effects of multiple treatment options on the subjective and objective measures of hirsutism have displayed varying results. The outcomes reported to date have shown a positive trend toward using spironolactone and cyproterone acetate in women with PCOS and hirsutism. Meanwhile a comparison made between flutamide versus spironolactone and cyclical Diane 35" over a period of 9 months for idiopathic hirsutism revealed comparable outcomes and no major side effects observed in either group (31). Hence the individual specialist should utilise the regime that he/she is most familiar with and drugs that are most cost effective for the patient for an average period of 9-12 months, at which point the patient could make her choice to stop the medication and review progress with lifestyle modification alone. Meanwhile cyclical drospirenone (a derivative of 17(spironolactone) and ethinyl oestradiol combination exerts significant antiandrogenic activity and is effective in improving facial hirsutism, where the beneficial effect is reported to be most obvious after six cycles and continues thereafter at a slower rate (32).

Gestational diabetes, PCOS and long term type 2 diabetes mellitus

The hormonal changes of pregnancy being diabetogenic, women with insulin resistance of PCOS are at particular risk of developing gestational diabetes (GDM) with its attendant problems of perinatal morbidity and mortality, and the development of pregnancy induced hypertension. Therefore it is imperative that all women with PCOS undergo a 75g oral glucose tolerance test pre-conception and if there is impaired glucose tolerance to achieve normoglycaemia with diet, exercise and if necessary metformin from the time of being managed for ovulatory problems. For those with normal glucose tolerance pre-conception, a risk factor based

approach at antenatal booking is mandatory with regular testing to exclude GDM, particularly between 24 to 28 weeks of gestation. A greater awareness of the strong association between GDM and PCOS, particularly among South Asians, would lead to a significant lowering of pregnancy losses and improve the perinatal outcome of these high-risk pregnancies. A recent study of a cohort of Sri Lankan women with previous GDM reviewed at 3 years post partum demonstrated a close correlation between insulin resistance and the metabolic syndrome with PCOS (33). Hence, women with PCOS require special attention from pre-pregnancy to long-term follow after partus of their risk of T2DM and cardiovascular disease.

In the last few decades South Asia has experienced rapid urbanization, a change from traditional to fast foods and sedentary life style that adversely affect health, which has brought a new set of problems in the form of chronic non-communicable diseases, chiefly diabetes mellitus and cardiovascular disease. GDM is most common in populations with a high prevalence of T2DM. Global diabetes prevalence estimates for 2025 predicted by King et al, estimated that adults aged >20 years with diabetes in the world would increase by 122% when compared to that of 1995 (34). The increase was predicted to be 42% in developed countries and 170% in developing countries; with over 75% of diabetics in the world being from developing countries. The greatest increase in this pandemic was projected to occur in the Indian subcontinent, which is indeed the emerging pattern (35, 36). This undoubtedly will increase the burden of GDM in South Asia. A study conducted in 2003 in a defined rural population in Sri Lanka revealed an age-standardized prevalence of 10.3% for GDM (37) that reflects a threefold rise from its previous prevalence determined in 1987 (38). We also reported that non pregnant South Asian women (including indigenous Sri Lankans) with PCOS, and in the 3rd decade of life, had a far greater degree of insulin resistance and fasting hyperinsulinaemia than their white European counterparts (15, 16). Thus the emerging problem of T2DM in women suffering from PCOS in South Asia needs our timely attention to ensure their optimal management utlizing available health care resources.

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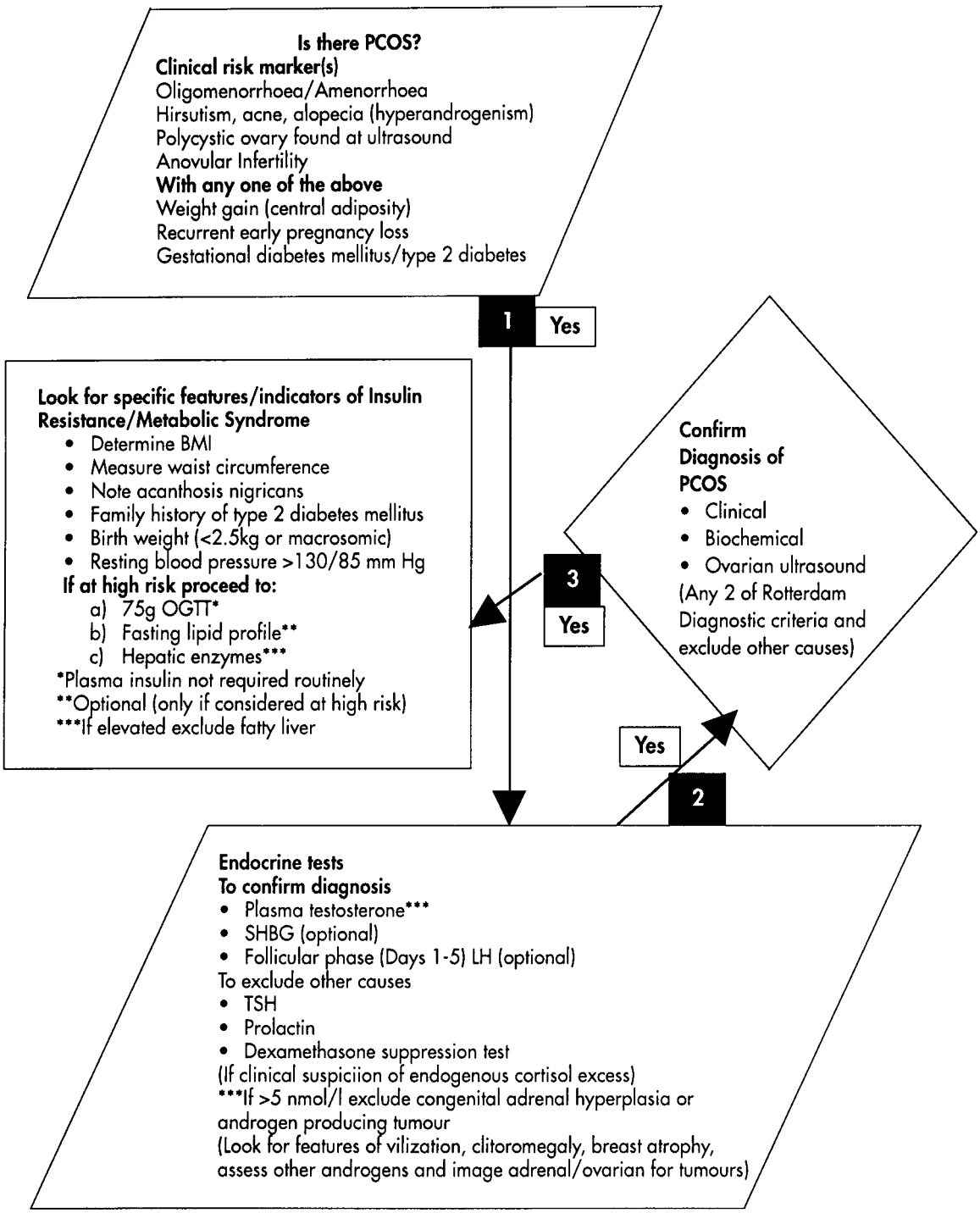
Figure 1
Proposed algorithm for the evaluation of polycystic ovary syndrome (PCOS) in South Asian women



LAPAROSCOPIC MYOMECTOMY - WHEN IS LAPAROTOMY NEEDED?

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The use and effectiveness of Laparoscopic Myomectomy has been evaluated by several studies. The improved laparoscopic techniques, suturing ability and effective morcellation have meant that more and more laparoscopic procedures are being done. Yet there are limits when a laparotomy will have to be done.
This review will assess the indications for laparotomy at Laparoscopic Myomectomy. The Pre operative decision on Laparotomy / Laparoscopic Myomectomy would be made by the following assessment. The size, number, location, consistency and the involvement of the uterine cavity are limiting factors. The preoperative use of GnRh may require laparotomy. The presence of Adenomyosis or associated pathology or the inability to withstand prolonged Trendelenburg position will necessitate laparotomy. The need for future pregnancy will require greater care at surgery to prevent rupture uterus.
Intraoperatively the decision to convert to laparotomy will be based on operator experience. Deep seated large myomas, severe hemorrhage during surgery and technical problems with equipment would require laparoconversion. The rate of conversion in several studies is low 2- 8% but these were at the hands of well organized centers. How will the infrequent laparoscopic surgeon make a decision and carry out the procedure?

LAPAROSCOPIC MYOMECTOMY - WHEN IS LAPAROTOMY NEEDED?

A Kurian Joseph MD
Chennai - India

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SATURDAY, 24 MARCH 2007

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IMPACT OF OBESITY ON THE OUTCOME OF THE TREATMENT OF POLYCYSTIC OVARY SYNDROME IN ADOLESCENCE

Dramusic V. Annapurna V, Anita Kali, P.C.Wong
NUH- NUS

Few subjects provoked such controversy in the field of reproductive endocrinology as PCOS did. During puberty metabolic cascade occurs creating endocrine changes similar to those seen in PCOS. If obesity is present it can lead to increased androgen stimulation (acne and hirsutism), inadequate feedback (chronic anovulation) and eventually PCOS.
In Adolescent clinics in NUH 700 adolescents with menstrual disorders were screened, treated and followed-up over 10 years. Clinically they presented as Sec. Amenorrhea in 41% (288); Dysfunctional Uterine Bleeding:23,9% (157); Prim. Amenorrhea: 18,6% (128) and Oligomenorrhea :16,8% (117). However, out of all groups 25,6% were confirmed to be PCOS. Data on clinical, hormonal, ultrasound and psychological screening and treatment procedures are explained in detail (cyproterone acetate being main mode of treatment in that age group).
Good outcome of treatment occurred in 62,7% (of these only 13,8 were obese), condition didn't change in 11,3% (obese: 64,2%) and condition worsened in 26% (obese: 64%).In our opinion
complete management of PCOS in adolescence should include: medical correction of hormonal disbalance, body weight correction, psychological intervention: group therapy is a useful vehicle to manage anxiety and depression, raise self-esteem and educate on diet and exercise regime (group or buddy system).
In conclusion obesity in adolescence clearly favours hyperandrogenic conditions and influences the outcome of the treatment. Follow-up of 179 adolescents with PCOS, 73 with PCOS-like syndrome (some but not all PCOS features) and 117 girls with Oligomenorrhea indicated poor response to treatment and high recurrences among obese girls.

PRETERM LABOUR: MODERN MANAGEMENT

Teoh Tiong Ghee
UK

The incidence of preterm birth is increasing and continues to be a significant cause of neonatal morbidity and mortality. Techniques exist to predict early birth. Prevention can therefore be targeted so that effective measures can be adopted in an attempt to improve outcome.

Predictors of preterm labour include previous obstetric history, cervical length, fetal fibronectin.
Interventions to prevent delivery and improve neonatal outcome remain unsatisfactory. These include progesterone, tocolysis and cerclage. Women who would benefit from these interventions are still difficult to identify.

An improved understanding of the mechanisms underlying the pathological process in preterm birth will allow screening and interventions to be appropriately be targeted.

TRAINING STAFF TO DEAL WITH EMERGENCIES: SCENARIOS AND DRILLS

Tracey A Johnston
Consultant in Fetal Maternal Medicine,
Birmingham Women's Hospital, Birmingham, UK

This session will provide a very practical approach to setting up and providing this type of training locally. The four stages of scenario training will be outlined - environment, set, dialogue and closure. The type of equipment required will be listed, and techniques for feedback discussed. The different types of learners will be highlighted to demonstrate that different approaches and techniques suit different people. How to deal with difficult learners will be addressed briefly. The role of fire drills in testing systems will be discussed.

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ASSESSING OVARIAN RESERVE: HOW, WHO & WHEN?

Lisa Webber

The concept of ovarian reserve is a very useful one, particularly in the context of otherwise unexplained infertility and if selecting women for in vitro fertilization. Various methods have been proposed for assessing ovarian reserve including anti-Mullerian hormone, inhibin B, antral follicle counts, ovarian volume, ovarian stimulation tests and assorted combinations of these parameters. Whilst some of these tests may have a direct clinical application in helping to plan a couple's treatment, their roles as "screening tests" for women wishing to delay childbearing may be less certain. According to accepted criteria for a screening test (WHO and Council for Europe) any condition suitable for screening should have adequate treatment or other intervention available. When the condition is poor ovarian reserve, that intervention may be to stop contraception. However, the impact of this information for a woman not in a position to start actively trying to conceive could be disastrous.

UPDATE ON HORMONAL SUPPLEMENTATION IN ART PROTOCOLS

Colin M Howles
Vice President Scientific Affairs Reproductive Health and Metabolic Endocrinology, Merck Serono International SA, Geneva, Switzerland

In a spontaneous menstrual cycle, only one follicle out of a cohort of 10-20 usually completes maturation and ovulates to release a mature oocyte. The aim of FSH stimulation in ART protocols is to overcome the selection of a dominant follicle and to allow the growth of multiple follicles. However, the number and quality of oocytes, which are recruited, is known to decline in women of advanced maternal age, and hence successful treatment for these patients continues to be a major challenge in ART programs.

The associated reduction in oocyte quality as manifested by the increase in aneuploid embryos is most likely due to suboptimal cytoplasmic maturation (including reduced capacity of oocyte mitochondria to generate sufficient quantities of energy required for fertilisation and cell division). This review will examine the available evidence for the use of various supplementary agents as a means of augmenting follicular recruitment and cytoplasmic integrity, so as to improve the prognosis for these women. Recent studies indicate that androgen supplementation may be one area to explore further. The availability of r-hLH has made it possible to investigate the role of LH in the endocrinology of follicular recruitment. It appears that a defect in the balance of LH/FSH might be involved in the subtle age-related decline in follicular recruitment, and slected patients of older reproductive age undergoing ART might benefit from the addition of LH and/or hGH. Further studies are required to investigate the physiological mechanisms behind this observation, and to assess the possible effect of androgen, LH, hGH supplementation on the age-related decline in pregnancy rate.

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TREATMENT OF OSTEOPOROSIS - WHY, WHOM, WHEN AND WHAT DRUG

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Why treat? (i) fractures increase morbidity and mortality; 30-50% of women, and 15-30% of men suffer a fracture related to osteoporosis in their lifetime. Spine and hip fractures increase morbidity, mortality and impose a financial burden on the community. The burden of other fractures (time off work, doctor visits, investigations) also contributes to the high human and financial cost of fractures, (ii) the burden of fractures is increasing because longevity is increasing, (iii) bone loss does not slow in old age, it accelerates, (iv) effective and safe treatments are available.

Whom and when? The most important factor determining whom and when to treat is an individual's absolute risk for fracture (ARF). If the ARF is 2/1000 persons/yr and a drug halves fracture risk, then one event is averted, one women will sustain a fracture despite treatment and 998 who were not going to fracture had treatment. Thus, one fracture is prevented but 999 women/yr are treated without benefit. If the ARF is ten times higher, i.e., 2/100 women/yr and the still drug halves the risk, one fracture is prevented again but only 99 women are treated. Knowledge of an individual's absolute risk is central to making decisions.

The need to intervene increases with advancing age, lower BMD, and prior fracture; each of these contributes independently to fracture risk. About 85% of fractures occur in women over 60 years of age. An important signal for the need to treat is a prior vertebral or non-vertebral fracture. The risk for further fractures increases 3 to 5 fold as the number or severity of prevalent vertebral deformities is increased. In a person with osteoporosis, an incident fracture (with or without a prevalent fracture at baseline), increases the absolute risk of a further incident fracture to 30-40% within three years. Thus, the evidence of anti-fracture efficacy is strongest in patients with a baseline vertebral or non-vertebral fracture. It is optimal to treat fewer older persons (> 60 years) at high risk rather than many younger persons at low risk. This ensures that those likely to respond to treatment receive it, and those at low absolute risk and thus unlikely to benefit remain untreated.

What drug? Anti-resorptive agents reduce the intensity of remodelling allowing more complete secondary mineralization of bone tissue restoring bone material stiffness. These drugs reduce the progression of trabecular and cortical thinning, and loss of trabecular connectivity and so maintain or increase bone strength, even though they cannot reverse structural damage. The anabolic agent, PTH, results in partial reconstruction of the skeleton with the deposition of new bone tissue on the periosteal, endocortical and trabecular surfaces thickening the cortex and trabeculae albeit with some increase in cortical porosity adjacent to the endosteum. The overall effect is to increase bone strength and reduce fracture risk. The decision regarding therapy must be evidence based.

Spine fractures The most rigorously studied drugs reported to reduce spine fractures in women with osteoporosis include alendronate, risedronate, raloxifene, PTH and strontium ranelate (SR). These drugs reduce the risk of symptomatic (clinical) and asymptomatic (morphometric) single vertebral fractures by about 40-50% and multiple vertebral fractures by about 80-90%. The benefits have been reported within the first 6-18 months of treatment. HRT and etidronate have also been reported to reduce spine fracture rates but the studies are less rigorous. The level of evidence for anti-vertebral fracture efficacy of calcitonin and vitamin D metabolites is insufficient for inferences to be made with confidence. Evidence for anti-fracture efficacy is less compelling in women with osteopenia with a fracture, osteopenia alone, and for men. Head-to-head comparator studies have not been done. Hence, it is not known whether any one drug is more efficacious than another and this cannot be inferred from meta-analyses.

Non-spine fractures Only the two bisphosphonates, SR and hormone replacement therapy (HRT) have been reported to reduce hip fractures in community dwelling women. PTH has been reported to reduce the risk of

non-vertebral fractures, not hip fractures. Raloxifene has not been reported to reduce the risk of non-vertebral or hip fractures except in a post-hoc sub-analysis. Calcium plus vitamin D and hip protectors have been reported to reduce hip fractures in nursing home residents and institutionalised elderly. PTH use is likely to be limited to severe osteoporosis and will probably need to be followed by an anti-resorptive drug. HRT is not recommended for fracture risk reduction unless postmenopausal symptoms are debilitating. Evidence for anti-fracture efficacy of calcitonin, fluoride, anabolic steroids, or active vitamin D metabolites is insufficient to justify their use.

How long? It remains unclear as to whether anti-fracture efficacy is sustained beyond 3-5 years. There is no evidence for increases in fracture rates in studies in human subjects However, prolonged therapy with bisphosphonates may increase the bone tissue mineral content and brittleness. High doses in animals resulted in micro-damage, a decline in toughness of bone (the ability to absorb energy without cracking) but no decrease in overall bone strength. The relevance of these animal studies to humans is uncertain. There is disagreement as to whether short periods of 1-2 years off therapy are appropriate after every 3-5 years on treatment. Stopping treatment is followed by increased remodelling, bone loss and further structural damage. Recurrence of bone loss is likely to occur sooner with cessation of HRT or raloxifene than with bisphosphonates. The FLEX trial suggests that there is a sustained effect of alendronate after stopping treatment but methodological issues make interpretation of the data difficult. There is no evidence that combining bisphosphonates with either raloxifene or HRT reduces fractures more than either drug alone (although combined therapy may produce greater increases in BMD). Women and men with fragility fractures should be treated with agents that have been thoroughly investigated.

MATERNAL CARDIAC DISEASE

Teoh Tiong Ghee
UK

Cardiac disease is the second commonest cause of maternal mortality in the United Kingdom. 80% of these deaths are due to acquired heart disease. The commonest conditions are cardiomyopathy, ischaemic and valvular heart disease. The management of women with Cardiac Disease before, during and after pregnancy at St Mary's Hospital will be discussed.

SCREENING FOR THROMBOPHILIA IN PREGNANCY

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Tan Tock Seng Hospital

The term thrombophilia describes disorders of the haemostatic mechanisms which predispose an individual to thromboembolism. Thrombophilic abnormalities can be inherited, acquired or complex (acquired factors interacting with a genetic background). Significant haemostatic changes such as increased concentrations of most clotting factors and decreased concentrations of some of the natural anticoagulants occur in normal pregnancy resulting in a hypercoagulable state. It is becoming increasingly evident that this interaction between thrombophilia and pregnancy results in increased risk of venous thromboembolism and may be associated with other vascular complications such as fetal loss, pre-eclampsia, placental abruption and intrauterine growth restriction. Although the relative risk for these complications is increased, meta-analysis suggests that the absolute risk of venous thromboembolism and adverse pregnancy outcomes remains low. Apart from recurrent pregnancy loss in the antiphospholipid syndrome and the prevention of venous thromboembolism, there is inadequate evidence on the benefit of antithrombotic therapy to guide treatment in other pregnancy complications. Further randomised controlled trials are needed to assess the harm-benefit ratio. Until then, testing for thrombophilia should be performed only on a selective basis.

THE ENDOCRINOLOGY OF OBESITY

Kevin TAN Eng Kiat
MBBS, MRCP, FRCP, FAMS

Obesity rates have increased over the past 20 years and with this, the prevalence of obesity-related medical conditions like diabetes and heart disease. At the same time, the concept of adipose tissues as an inert storage compartment of triglycerides has changed to one of an active endocrine organ responsible for insulin resistance and a source of enzymes and proteins like leptin, adiponectin and resistin.

Obesity is more than body mass index limits. The increased risk of cardiovascular disease seems to be related more to visceral adiposity than gluteofemoral adiposity. The pro-inflammatory adipokines produced by visceral fat promote the development of insulin resistance and subsequent cardiovascular disease.

Current and future therapies directed at obesity aim at addressing the above mechanisms.

THE IMPORTANCE OF NUTRITION IN GESTATIONAL DIABETES

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The reported prevalence of Gestational Diabetes (GD) is 1 - 14% of all pregnancies depending on the population studied and the diagnostic tests utilized (1). In Singapore, approximately 8.6% of all pregnancies are complicated by GD (2).

It is well established that diabetes mellitus in pregnancy may have acute as well as long term complications for mother and the fetus. Medical Nutrition Therapy (MNT) is important in managing existing diabetes, and preventing or at least slowing, the rate of development of diabetes complications during pregnancy.

A recent large clinical trial reported that treatment of GD with MNT, blood glucose monitoring and insulin therapy as required for glycemic control improved maternal health-related quality of life and reduced serious perinatal complications, without increasing the rate of cesarean delivery, as compared with routine care (3).

The goals of MNT in gestational diabetes are to: 1) provide adequate energy for appropriate weight gain; 2) achieve and maintain blood glucose levels in the normal range; 3) prevent ketonemia; 4) address individual nutrition needs of the pregnant mother, taking into account personal and cultural preferences and willingness to change; and 5) maintain the pleasure of eating.

MNT for GD primarily involves a carbohydrate-controlled meal plan that promotes optimal nutrition for maternal and fetal health. Recent guidelines state that a minimum of 175 g of carbohydrate / day should be provided to gestational diabetics through 3 small - moderate meals and 2 - 4 snacks.

Translating MNT guidelines into practical and realistic food choices, including details as portions and meal and snack timings, that can be applied in the daily lives taking into consideration the eating preferences of the pregnant mother is best left in the hands of a qualified dietitian and success in achieving the goals will require the active participation of the diabetic mother in the decision-making process. Case studies will be used to illustrate meal solutions for Singaporean mothers.

Recent guidelines on MNT in GD from the Ministry of Health, Singapore; the Joslin Diabetes Centre and Joslin Clinic as well as the American Diabetes Association will be reviewed - compared and contrasted - to help identify best practices for use in treating and managing GD (4, 5 and 6).

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MANAGING OBESE INFERTILE WOMEN PRECONCEPTION

Lisa Webber

If a woman's obesity comes to medical attention preconception it is usually in the context of delayed conception. The challenging part of her management is to convince her that her weight has anything to do with her presenting problem - and then to help her correct it. Currently there is much debate surrounding setting BMI limits for fertility treatment and in most parts of the UK NHS-funded in vitro fertilization is denied to women with a BMI above 30. If losing weight is a requirement of entry onto any form of assisted conception programme, then it must follow that effective support for achieving this is provided. A pilot multi-disciplinary weight management programme that was set up at a London teaching hospital for obese women wishing to conceive is presented.

OBESITY IN PREGNANCY

Teoh Tiong Ghee
UK

Overweight and obesity are common findings in women of reproductive age in the UK; as 32% of 35-64-year old women are overweight and 21% obese. Obesity causes major changes in many features of maternal intermediary metabolism. Insulin resistance appears to be central to these changes and may also be involved in increased energy accumulation by the fetus. Maternal obesity is associated with many risks to the pregnancy, with increased risk of miscarriage (three-fold) and operative delivery (20.7 versus 33.8% in the obese and 48.4% in the morbidly obese group). Other risks to the mother include an increased risk of pre-eclampsia (3/9 versus 13.5% in the obese group) and thromboembolism (0.05 versus 0.12% in the obese group). There are risks to the fetus with increased perinatal mortality (1.4 per 1000 versus 5.7 per 1000 in the obese group) and macrosomia (>90th centile; versus 17.5% in the obese group). Maternal obesity is associated with an increased risk of obesity in the long term. Obese women should try to lose weight before pregnancy but probably not during pregnancy. There is no real evidence base for the management of maternal obesity but some practical suggestions are made.

CORD BLOOD STEM CELLS AND THEIR CLINICAL UTILITY

David Roberts

Dr David Evan Roberts is a practising paediatrician, specialising in neonatology at Joondalup Health Campus, Glengarry Hospital and St John of God Hospital, Subiaco, Perth, Western Australia.

Abstract
The development of Dolly the Sheep (1997) and the isolation of the Human Embryonic Stem Cell (1998) heralded the enormous potential of Stem Cells as a platform for regenerative medicine and other therapies. But the immunological problems associated with using allogeneic (another person's) stem cells have prompted researchers to look for sources of autologous (self) stem cells. Embryonic stem cells are clouded in ethical controversy. Therapeutic cloning (somatic cell nuclear transfer) as a solution to the immunological problem, but is equally controversial. The answer is cord blood stem cells.

We have known for 25 years that cord blood is enormously rich in stem cells of varying types. As well, cord blood stem cells are still young. We now understand that stem cells age; indeed that is what the process of aging is - the aging of stem cells. Just why cord blood contains so many stem cells is an extraordinary story.

In oncology today, cord blood is an alternative to bone marrow in the transplant setting. But the future uses of stem cells are likely to go well beyond this. In the future, we will use our cord blood stem cells several times in our lives. The routine medical history of the future will read, "Do you take any medications?"; "Are you allergic to anything?"; "Do you have your cord blood stored?"

ROLE OF INDEPENDENT LACTATION CONSULTANT

Betty Lee
Free-lance Lactation Consultant

An independent lactation consultant or one in private practice is an integral member of the breastfeeding mother's healthcare team. This role carries tremendous responsibilities and is important to ensure that optimal care is delivered. Our focus is on helping breastfeeding mothers and their families in achieving their own breastfeeding goals.

The importance of formal lactation education and extensive clinical experience is essential to help and equip us with the knowledge in our work.

We have to maintain certain standards of practice and to ensure that level of care facilitates continued health and wellness particularly as it relates to breastfeeding management and early parenting issues. Practising as an independent lactation consultant means providing quality care to the public and accepting responsibility for that care.

Maintaining a referral system is integral to the delivery of assistance to breastfeeding women. Working in private practice usually permits minimal contact with staff at various hospitals. Networking with doctors, colleagues from all hospitals and participation in professional association form an essential part of our support system.

However, private practice lactation consultants enjoy the autonomy of being your own boss. You are able to set your own hours and work around family functions.

IS THERE A PLACE FOR DOULAS IN SINGAPORE?

Ginny Phang
Certified Doula
Childbirth Educator
Hypnotherapist
Hypnofertility
Hypnobirthing

Ever wondered why modern parents-to-be engage Professional Labor Support Providers (Doulas) to support them through their pregnancy, during labor and birth and early postpartum? What do Doulas's actually do and what is their role in the birthing room? How do Obgyns and Nurses feel about Doulas and do Doulas have a role in Nursing?

BABY MASSAGE AND BONDING

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NYP

Bonding is the attachment that forms between an infant and its mother beginning at birth. During the time immediately post -delivery, when the mother is holding her baby for the first time, high levels of endorphins, oxytocin and endogenous opiates are released in the mother's brain (Travaathan1987). This results in intense pleasure of gratification and wanting mothers to be bond with their infants.
In this paper, the art and the advantages of infant massage will be explored and some proven research papers will be discussed. The technique of infant massage will also be taught.

There are many advantages of infant massage. Infant massage will help parents build a bond with their babies - period to get to know each other It reduces stress responses to painful procedures and abdominal colic. A study done by Field T et al (1986) has shown that massaged infant gained 47 percent of weight gain and showed better performance on the Brazelton Scale on orientation; motor activity and regulation of sate behavior. Infant massage improves mother -infant interactions for mothers with postnatal depression (Onozawa et al 2001)
In conclusion, infant massage is not only massaging a baby, - it is about building and nurturing relationships, which enhances parent- baby bonding and attachment.

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COMPUTER-BASED TRAINING (CBT)

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The School of Health Sciences (SHS), Nanyang Polytechnic has been providing Health Sciences education for the past 15 years. It currently offers 6 full-time Diploma Programmes in various fields of healthcare as well as numerous full-time and part-time advanced and specialist programmes. With a team of dedicated lecturers, designers and IT specialists, SHS has been leveraging on technology to continually expand its e-Learning curriculum content by developing multimedia and interactive digital media packages made available for students' on-demand access. Our e-Learning packages are developed for the local context and allow students to learn at their own pace and encourage self-discovery and life-long learning. Currently there are more than 30 web-based integrated e-Learning packages providing learning experiences that lead to students' comprehension and mastery of new skills and knowledge in diverse areas. To familiarise students with the ward setting so as to better prepare them for their first clinical attachments, the Virtual Ward program was developed to simulate a real hospital ward. Besides detailing a hospital ward set-up, actual case scenarios are also included to allow students to apply theory to practice within a clinical setting, in a safe and non-threatening environment. This promotes the development of students' critical thinking, clinical reasoning and problem-solving skills and enhances their confidence during their clinical practice. This paper aims to share the utilization of computer-based training at the School of Health Sciences, Nanyang Polytechnic.

ONCOLOGY NURSING - IMPACT ON SEXUALITY POST RADIOTHERAPY

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A diagnosis of cancer and its treatment can have a significant effect on a person as a whole. With the improvement in survival rates, survivors live longer with the consequences of treatment. Developing an understanding of peoples' experiences in order to maximize their ability to live well after treatment is therefore very important. This cross-sectional study was conducted with the purpose of examining the perceptions of women diagnosed with cervical and uterine cancers in Singapore about the impact of radiotherapy on their sexuality. It also sought to examine womens' information needs regarding sexuality. A questionnaire was designed specifically for the study, consisting of 24 items adapted from Bourgoesis-Law's needs assessment instrument (Bourgoesis-Law & Lotocki, 1999) and the 14-item Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983). This was sent to 267 women recruited from a Gynaecology Cancer Centre in KK Women's and Children's Hospital. An information sheet, consent form and two stamped-addressed return envelopes were included in this mailed survey. Data was analysed using the Statistical Package for Social Sciences 11.5 (SPSS). A disappointingly low response rate (12%) has limited the ability to make firm recommendation. However problems encountered in recruiting participants give rise to important methodological insights for consideration for future studies. Results demonstrated that women who reported sexual function effects (56.3%) after cancer therapy experienced a decrease in sexual activity, more coital pain and decreased interest in sex than women who did not report these effects. Importantly, these effects were found to cause distress in these women. It was also found that 'changes in the body' and 'feelings about yourself as a woman', as well as the 'lack of information' were the most difficult aspects of the effect of illness and treatment on sexuality. Information regarding sexuality was reported to be deficient in this group of women with participants stating that they would like to have received more information through pamphlets with the addition of discussion with a doctor or nurse. In addition, general information about sexuality was found to be important and useful. Recommendations from the study findings are directed towards conducting large-scale research and crucially towards the education of nurses regarding sexuality and cancer, including methods of effectively assessing women's needs for information and specialist referral.

CHALLENGES IN MINIMALLY INVASIVE SURGERY: NURSING ASPECTS

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Perioperative environment is known to be possibly the most hazardous of all clinical environments for both patients and staff. It is the role of the nurse to promote and safeguard the interest and well-being of the patient and ensure that no action in her area of responsibility is detrimental to the patient. It is therefore the responsibility of nurses to keep themselves updated with the current practices so that they are best to manage any situation.

Minimally invasive surgery has developed rapidly over the past few years. The increase use of minimally invasive surgery approaches has impact on the operating room personnel as well as affecting the nursing care of patients. Emerging technology and competition among vendors of equipment and instrumentation is a great challenge for perioperative nurses in supporting minimally invasive surgery. An understanding of the current applications of technology and perioperative nursing responsibilities is therefore needed to assure quality patient care in the operating theatre especially in current situation now whereby patients know and expected more.

SUNDAY, 25 MARCH 2007

IPL(INTENSE PULSED LIGHT)

Geun-Soo Lee, M.D., Ph.D.
Woo & Hann's Skin & Laser Clinic, Seoul, Korea

When IPL(Intense pulsed light) was introduced In early 1990s, it was regarded cumbersome machine. But, since several years ago IPL sources have been successfully used for coagulation of blood vessels, telangiectasia, poikiloderma of Civatte, rosacea, port-wine stains, facial wrinkles, skin laxity, hair removal, and superficial pigmented lesions, such as freckles, lentigenes. And also, there are numerous IPL indications can be listed in clinical practice. It is obvious that not all IPL machines are the same. In fact, very low power ones are used in salons and spas in some countries. Until now, hundreds and thousands of IPL manufactures showing their product in the market annually. Most systems produced today use a xenon arc lamp as a light source. By the optical filtering technique, filtered spectrum of light reacts on the three main chromophores with high intensity. They are hemoglobin, melanin, and water. IPL can cover all these three different chromophores in one pulse of light. IPL is a noncoherent light usually in a broad wavelength spectrum of 515-1200 nm. The emitted light from the light source is gentle, non-invasive, and long lasting.

The advanced IPL model are not a dangerous machine that provokes unwanted side effects. On the contrary, they have a lot of advantages compare to the laser systems. For instance, relatively lower cost the exposure area is much larger, no specific social downtime, and can save times for perform procedures.

StarluxTM (Palomar, Burlington,MA)is not only a model of IPL system, but also a multi functional skin rejuvenation system. This system acts as a multifunctional device for treating vascular and pigmented lesions(LuxG, LuxY), inflammatory acne(LuxV), hair removal(LuxRs), photofacial/photorejuvenation(LuxG, LuxY, Lux1540 Fractional), leg vein treatment(LuxG, Lux1064:Nd YAG), and as a noninvasive facial lifting(LuxIR Fractional). Due to the strong cooling effect the pain is very much decreased, and the panel control system is designed user-friendly. The skin is cooled throughout treatment, permitting the operator to deliver high-energy pulses while providing maximum comfort and safety to the patient. The flashed light passes absorption and dichromatic filtration in its system, which eventually provides more protection to the skin. The StarLux™ delivers pulsed light in one smooth pulse, rather than the train of multiple power spikes. Its smooth pulse technology prevents a rapid rise in skin temperature for far more comfortable treatments. StarLux™ is able to deliver high energy to the target pigment and oxyhemoglobin due to its active contact cooling feature, which chills the handpiece's sapphire tip to as low as 4°C. A variety of handpieces in Starlux™ system tailored for specific indications makes treatment easy. Actually, we need pay attention more to the evolution of IPL, because of the progress of IPL is quite remarkable,

THE Q-SWITCHED LASERS

Tay Yong Kwang
Head and Senior Consultant Dermatologist
Changi General Hospital, Singapore

The Q-switched lasers including the Q-switched ruby (694nm), Q-switched Alexandrite (755nm), Q-switched Nd:YAG (1064/532nm) are effective in removing pigmented lesions, by selectively targeting melanosomes. Regardless of what system is used, pigment laser treatment should be initiated at the threshold fluence, which causes an immediate tissue-whitening effect that signals appropriate energy deposition in the melanosome. For darker skin tones, like in the Asian population, the Q-switched Nd:YAG has the lowest incidence of side effects (e.g. hypopigmentation) since its wavelength is more weakly absorbed by melanin than the other laser systems.

The following conditions can be treated with the Q-switched lasers: lentigines, nevus of Hori, labial melanosis, tattoos and certain birthmarks e.g. café-au-lait macules, nevus of Ota and nevus of Ito. There is conflicting evidence on the use of Q-switched lasers for melasma.

In Asian patients with dermal melasma and where associated Hori nevus is present, the Q-switched Nd: YAG laser may be useful. The use of the Q-switched Nd: YAG laser for non-ablative skin resurfacing will be briefly discussed.

In conclusion, the Q-switched lasers have become a common tool in the treatment of a wide variety of benign pigmented lesions and we look forward to even more powerful and effective systems that will lead to improved clinical outcomes.

FRACTIONATED LASERS

Geun-Soo Lee, M.D., Ph.D.
Woo & Hann's Skin & Laser Clinic, Seoul, Korea

For the purpose of skin rejuvenation or acne scar, laser resurfacing has been regarded one of the best method. Due to ablative resurfacing lasers like pulsed carbon dioxide and erbium YAG lasers, more precise skin surface remodeling could be achieved. Because they have been provided the predictable results, they played a key role for laser resurfacing until the beginning of this century. But, when we think about the drawbacks like prolonged recovery time, considerable social downtime, or significant side effects, such as postinflammatory hyper or hypopigmentations, ablative resurfacing lasers is not always preferred by patients and doctors. Cooling system installed nonablative lasers can transfer thermal damage only to the targeting areas like upper dermis or the appendegeal organs in upper dermis. The epidermal protection and downtimeless procedure were possible by these lasers, but efficacy is less and unpredictable compared with ablative lasers. And, the treatment depth does not reach deep inside to dermis without downtime.

To get over the drawbacks of both ablative and non-ablative devices, the new concept of fractional photothermolysis was developed for skin remodeling in 2004. Actually fractional photothermolysis is based on the concept of creating focal or partial thermal damages. It is designed to create microscopic thermal wounds to achieve skin rejuvenation without significant side effects. The Fraxel(tm) SR750 laser(Reliant Technologies, Palo Alto, CA), which employs 1550 nm, is the first true fractional laser. It has been cleared FDA approval for the treatment of pigmented lesions, periorbital rhytides, skin resurfacing, soft tissue coagulation, and recently for acne and surgical scars. The effect of the Fraxel(tm) SR750 laser demonstrated by a great number of peer group review. The next generation the Fraxel(tm) SR1500 laser was released on the market in 2006 and the new version can deliver higher fluences, wider microthermal zones, and save treatment time. The Fraxel(tm) SR1500 laser has an optical spot size that is adjusted at each pulse energy level for optimizing depth of thermal damage.

It is difficult to be called true fractional resurfacing laser without some essential factors, those are microscopic thermal wounding, mid infrared wavelength for optimal water absorption, and sufficient capacity of power to reach up to 1000 _m. Since 2006, some devices employed fractional concept. But, without histologic studies that support the clinical result, we may classify them in another group, "quasi" nonablative fractional resurfacing. To be called true fractional laser, sufficient epidermal and dermal changes should be revealed clinically and histologically.

THERMAGE CRF - APPLICATIONS FOR NON-INVASIVE ABDOMINAL TISSUE TIGHTENING

Nantapat Supapannachart
Thailand

The Thermage capacitive radio frequency (CRF) device, widely acknowledged to be the gold standard in tissue tightening technology, has greatly extended its range of applications to treat loose and sagging skin and renew facial and body contours. New treatment tips and improved generator technology make treatments faster and more versatile. Thermage is fully FDA cleared and clinically proven to deliver superior results in skin tightening and contouring on all areas of the body.

Thermage has recently introduced new treatment tips specifically designed for the treatment of larger body areas, such as abdomen, thighs and legs. The latest Thermage applications and treatment outcomes are being discussed.

VAGINAL REJUVENATION - HYPE OR HEAL?

Lee Keen Whye
Consultant Obstetrician & Gynaecologist
Gleneagles Medical Centre,Singapore

Vaginal rejuvenation is a surgical art to enhance the vagina functionally and aesthetically. Rejuvenation is a catchy term in anti-aging and aesthetic medicine. It embodies reconstruction, giving the organ a fresh breath and a lease of new life. Hence, in vaginal reconstruction surgery, there is a functional aspect and an aesthetic aspect to be attained. In gynaecology, the focus is on operating on diseased organs and correcting anatomical defects e.g. vulva cancer and uterovagina prolapse. In vaginal rejuvenation, an added focus is on the patient's expectations. This is the essence of aesthetic gynaecology.

It has been said that the most powerful sex organ is the brain. But, this power is not harnessed by mere thinking or dreaming. It requires an interaction of all our senses, sight, touch, sound and so on. I will showcase my personal selection of cases in vaginal rejuvenation like hymen repair, labiaplasty and vaginoplasty. At the same time debunk the hypocritical statement of "size does not matter."

Vaginal rejuvenation empowers women with a new lifestyle option. The answer of whether it is hype or heal is a personal order.

FACTORS ASSOCIATED WITH BREASTFEEDING PRACTICES & DURATION: A PROSPECTIVE COHORT STUDY

Cynthia Pang
Senior Lactation Consultant
KK Women's and Children's Hospital

Background
The initiation rate of breastfeeding conducted in 2001 in Singapore (Foo et al, 2005) was high at 94.5%, but the duration of exclusive breastfeeding was extremely low (7% at 4 months and almost zero at 6 months). Other local studies were conducted more than 5 years ago and studies from other countries on factors influencing breastfeeding practices may differ with our local situation.

Methods
Participants from a large maternity hospital were interviewed prior to discharge from the hospital and subsequently follow-up interviews were conducted at six weeks, four months and six months postnatal using questionnaire with a mixture of closed and open-ended questions.

Results
The exclusive breastfeeding at six weeks was 22.6%, and the rate fell to 17.3% at four months and 3.1% at six months, At six weeks postpartum, the most common maternal and infant related reason for cessation of breastfeeding was 'not enough milk' (49.8%) and 'baby unable to latch' (21%). Malay mothers compared with Chinese mothers (OR=0.61, 95% CI=0.41-0.89) were significantly less likely to cease breastfeeding at six weeks postpartum. Mothers with no intention to exclusively breastfeed were found to be 6 times more likely to cease breastfeeding compared with exclusive breastfeeding at six weeks postpartum. Mothers who did not initiate breastfeeding within 1 hour of birth were more likely to cease breastfeeding at six weeks postpartum.

Conclusion
Modifiable factors such as early initiation within one hour after birth and intention to breastfeed exclusively were found to be significantly associated with continuation of breastfeeding and exclusive breastfeeding at six weeks postpartum.

CLOSER TO BREASTMILK: THE "IDEAL" MILK FORMULA?

Dr Steven Ng
Consultant Neonatologist & Paediatrician, Steven's Baby & Child Clinic, Gleneagles Medical Centre, Singapore

Research into the functional constituents of breastmilk has led to a number of recent additives to infant formulas which include nucleotides, prebiotics, probiotics, long chain polyunsaturated fatty acids (LCPUFA) and sialic acid.

Impact of additives on immune responses
There is increasing evidence that LCPUFAs influence the inflammatory immune response. In a recent study, docosahexaenoic acid (DHA) supplementation was associated with a significant reduction in the incidence of bronchitis in the first year of life. Nucleotide-supplemented formulas have been associated with fewer and shorter episodes of diarrhoea, and in one landmark trial, infant formula fortified with nucleotides enhanced Haemophilus influenzae type b and Diphtheria humoral antibody responses in immunized infants. Supplementation of infant formulas with Fructo-oligosaccharides (FOS) has also been associated with decreased severity of diarrhoeal illness and constipation, and reduced symptoms of irritable bowel syndrome. Probiotic Supplementation with probiotics (cultures of bacteria beneficial to a healthy gut microflora) not only results in intestinal immunostimulation, and decreased gastrointestinal infections but also reduces by 50% the incidence of eczema at 2 years.

Neurodevelopment
Supplementation with LCPUFAs increases the early rate of visual maturation in preterm infants, and also confers a beneficial effect on information processing. Several variables can influence the impact of LCPUFA intake, including the quantitiy and the source of DHA and arachidonic acid (ARA) in formulas. There is emerging evidence of the long-term effects of LCPUFA supplementation on not just preterm but also full-term infants.

Long-term impact of infant formula supplements
Infant formulas should also protect from long-term complications such as osteoporosis, obesity and hypertension. Breastfed infants generally have a lower fat mass than formula-fed infants even at 1 year of life, and further follow-up is needed to assess if this difference is sustained and also as to whether there is any impact on maturity-onset chronic diseases.

Breastfeeding and dietary supplementation with LCPUFAs during infancy has been associated with lower blood pressure in later childhood. In a follow-up study of children at age 6 years, those fed LCPUFA supplemented formula in infancy had significantly lower blood pressure than control subjects. The diastolic pressure of breastfed children was significantly lower than that of the non-supplemented formula group, but did not differ from the LCPUFA formula group. Dietary modification ie early exposure to LCPUFAs may thus reduce cardiovascular risk in adulthood.

IMPACT OF INFANT NUTRITION ON OBESITY

Dr Steven Ng
Consultant Neonatologist & Paediatrician, Steven's Baby & Child Clinic, Gleneagles Medical Centre, Singapore

We compared growth, skin-fold measurements and fat mass in breast-fed (BF, n=21) versus formula-fed (FF, n=14) full-term infants from birth until 12 months of age. The BF group was exclusively breastfed up to 2 months of age, while the FF group was predominantly or exclusively formula-fed. Anthropometry, skin-fold measurements at 4 different sites and percentage fat mass as determined by the Deuterium Oxide dilution technique for measuring total body water were performed at 3, 6 and 12 months of age. All 35 babies were full-term at birth ((BF) 39.3±1.2 weeks vs (FF) 39.0±0.8 weeks). Weight, length, head circumference and mid-arm circumference at birth were similar. There were no significant differences between the 2 groups with regards to anthropometry, mid-arm circumference (MAC), skin-fold measurements or percentage fat mass (% Fat) (mean±SD, $p>0.05$):

Age (mth)	Diet	MAC (cm)	Triceps (mm)	Biceps (mm)	Subscapular (mm)	Suprailiac (mm)	% Fat
3	BF	14.5±0.8	8.3±1.8	6.8 ±1.4	8.1±1.4	7.7±1.7	25.3±5.8
	FF	14.3±0.7	7.9±1.1	7.3±1.3	8.3±1.6	7.9±1.6	25.5±6.2
6	BF	15.2±1.4	8.3±1.9	5.7±1.1	7.4±1.5	5.9±1.0	24.0±8.9
	FF	15.5±0.7	8.0±0.8	6.0±1.5	7.5±1.2	7.1±0.9	24.9±8.6
12	BF	16.0±1.0	9.0±3.4	5.6±0.8	9.4±1.9	7.0±2.7	19.8±1.9
	FF	15.5±0.9	7.7±2.5	4.3±0.9	7.5±1.7	6.1±2.5	20.2±1.7

Conclusion: There was a trend towards breastfed infants being leaner when compared to formula fed infants. Early nutrition may have an effect on infant adiposity later on in life.

FREE PAPERS

DEVELOPMENT OF NON-INVASIVE PRENATAL EXCLUSION OF ALPHA THALASSAEMIA USING FETAL DNA FROM MATERNAL PLASMA

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[4]Molecular Diagnosis Center, National University Hospital, Singapore

Objective

Couples with the α-thalassaemia double gene deletions(αα/—SEA, αα/—FIL and αα/—THAI) are at-risk of carrying fetuses with the fatal HbBart\'s hydrops fetalis. We aim to exclude HbBartís hydrops non-invasively using cell-free fetal DNA from the maternal plasma and prevent miscarriages of at-risk mothers with unaffected fetuses from unnecessary invasive procedures.

Material and Method

Detection limit of quantitative fluorescence(QF)-PCR of polymorphic microsatellite markers within the breakpoints of the α-thalassaemia deletions was optimised using spiked(1:50) DNA samples consisting of αα/αα, αα/—SEA, —SEA/—SEA, αα/—FIL and αα/—THAI genotypes. The optimised protocol was performed on 28 families each consisting of maternal plasma, parental(paternal/maternal) and fetal DNA. Presence of fetal paternally-inherited microsatellite markers in maternal plasma DNA would exclude HbBartís hydrops fetalis.

Result

Fetal paternally-inherited microsatellite markers were detected in 10 maternal plasma later confirmed unaffected by HbBartís hydrops. Absence of fetal markers in the remaining 18 samples required further analysis with pure fetal DNA. Of these, 1 fetal sample was confirmed HbBartís hydrops(—SEA/—SEA). Paternally-inherited fetal alleles were detected in 10 of 26 maternal plasma unaffected by HbBartís hydrops.

Conclusion

HbBartís hydrops was excluded non-invasively with 100% accuracy using fetal DNA from maternal plasma. Thirty-eight percent(10/26) of the screened population would have avoided unnecessary invasive prenatal testing. The ability to differentiate between maternally- and paternally-inherited microsatellite markers is useful for the identification of fetal alleles amongst the overriding maternal DNA in the maternal plasma. In conclusion, fetal DNA in maternal plasma can be used to exclude HbBartís hydrops fetalis noninvasively.

QUANTITATIVE FLUORESCENCE-POLYMERASE CHAIN REACTION (QF-PCR) OF UNCULTURED AMNIOCYTES: INCREASED STRINGENCY IN THE PRENATAL DIAGNOSTIC CRITERIA OF CHROMOSOMAL ANEUPLOIDIES

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Objective
Diagnostic results of chromosomal aneuploidies using QF-PCR are considered valid with the presence of two or more informative microsatellite markers per chromosome. Our aim is to evaluate and improve this current diagnostic criterion for increased accuracy of molecular genetics diagnosis.

Material and Method
QF-PCR of 19 microsatellite markers on chromosomes 13 (n=5), 18 (n=5), 21 (n=6), X and Y (n=3) were performed on 812 amniotic fluid samples. Samples with two or less informative microsatellite markers per chromosome were repeated.

Result
The number of informative markers per chromosome increased to 3 in all trisomic samples (n=38) in the repeated run, resulting in distinct biallelic (1:2 or 2:1) or triallelic (1:1:1) ratios which were otherwise, not observed during the first run for 3 samples. Eight out of 25 normal samples with previously uninformative microsatellite markers (<2) showed a distinct biallelic (1:1) ratio with ≥2 markers in the repeated run. Eleven out of 87 samples with two informative markers per chromosome during the first run showed an increase to 3 informative markers in the repeated run.

Conclusion
We have shown that the minimum number of informative markers per chromosome for valid QF-PCR results can be increased from the current 2 to 3. This increase in stringency of diagnostic criterion will increase the confidence of reporting accurate QF-PCR diagnostic results.

RAPID AND COST EFFECTIVE MODEL FOR PRENATAL DIAGNOSIS

LL Su[1], M Choolani, SSY Ho, S Ponnusamy, N Kothandaraman, A Biswas
National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074
Yong Loo Lin School of Medicine, National University of Singapore , 5 Lower Kent Ridge Road, Singapore 119074

Objectives To propose a cost-effective model, which could merge rapid molecular tests (fast Fish) with Karyotyping for prenatal diagnosis.. We aim to test the hypothesis that if we test for trisomy 21 routinely, but for trisomy 13 and 18 only if the ultrasound abnormalities were present, we would rapidly detect more than 90% of these fetal aneuplodies using fast FISH with considerable cost saving.

Methods Modeling study based upon 211 cases of trisomy 13, 18, 21 diagnosed between January 1992 to October 2004 was performed. Presence or absence of structural abnormalities were analyzed. Fast FISH protocol was tested through optimisation of hybridisation time and temperature.

Results 80.3% of trisomy 18 (n=53) and 90% of trisomy 13 (n=18) fetuses had ultrasound abnormalities. However, 42.4% of trisomy 21 fetuses (n=53) had no detectable ultrasound abnormalities. Testing for chromosomes 21, X and Y routinely but for chromosomes 18 and 13 only in the presence of ultrasound abnormalities allow 93% of these aneuploidies to be identified rapidly ($z=3.2$; $p=0.001$). Through optimisation of the hybridisation time and temperature, our modified FISH protocol allows FISH results to be obtained within 2 hours.

Conclusion Fast FISH allows results to be available within two hours. Routine rapid molecular testing for trisomy 21, but targeted testing for trisomy 13 and 18 based upon ultrasound abnormality, allows rapid detection of more than 90% of significant fetal aneuploidies. This novel approach of fast FISH and targeted testing lead to faster speed and lower cost in prenatal diagnosis.

SATURDAY, 24 MARCH 2007

LAPAROSCOPIC MYOMECTOMY - WHEN IS LAPAROTOMY NEEDED?

A Kurian Joseph MD
Chennai - India

The use and effectiveness of Laparoscopic Myomectomy has been evaluated by several studies. The improved laparoscopic techniques, suturing ability and effective morcellation have meant that more and more laparoscopic procedures are being done. Yet there are limits when a laparotomy will have to be done.
This review will assess the indications for laparotomy at Laparoscopic Myomectomy. The Pre operative decision on Laparotomy / Laparoscopic Myomectomy would be made by the following assessment. The size, number, location, consistency and the involvement of the uterine cavity are limiting factors. The preoperative use of GnRh may require laparotomy. The presence of Adenomyosis or associated pathology or the inability to withstand prolonged Trendelenburg position will necessitate laparotomy. The need for future pregnancy will require greater care at surgery to prevent rupture uterus.
Intraoperatively the decision to convert to laparotomy will be based on operator experience. Deep seated large myomas, severe hemorrhage during surgery and technical problems with equipment would require laparoconversion. The rate of conversion in several studies is low 2- 8% but these were at the hands of well organized centers. How will the infrequent laparoscopic surgeon make a decision and carry out the procedure?

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IMPACT OF OBESITY ON THE OUTCOME OF THE TREATMENT OF POLYCYSTIC OVARY SYNDROME IN ADOLESCENCE

Dramusic V. Annapurna V, Anita Kali, P.C.Wong
NUH- NUS

Few subjects provoked such controversy in the field of reproductive endocrinology as PCOS did. During puberty metabolic cascade occurs creating endocrine changes similar to those seen in PCOS. If obesity is present it can lead to increased androgen stimulation (acne and hirsutism), inadequate feedback (chronic anovulation) and eventually PCOS.
In Adolescent clinics in NUH 700 adolescents with menstrual disorders were screened, treated and followed-up over 10 years. Clinically they presented as Sec. Amenorrhea in 41% (288); Dysfunctional Uterine Bleeding:23,9% (157); Prim. Amenorrhea: 18,6% (128) and Oligomenorrhea :16,8% (117). However, out of all groups 25,6% were confirmed to be PCOS. Data on clinical, hormonal, ultrasound and psychological screening and treatment procedures are explained in detail (cyproterone acetate being main mode of treatment in that age group).
Good outcome of treatment occurred in 62,7% (of these only 13,8 were obese), condition didn't change in 11,3% (obese: 64,2%) and condition worsened in 26% (obese: 64%).In our opinion
complete management of PCOS in adolescence should include: medical correction of hormonal disbalance, body weight correction, psychological intervention: group therapy is a useful vehicle to manage anxiety and depression, raise self-esteem and educate on diet and exercise regime (group or buddy system).
In conclusion obesity in adolescence clearly favours hyperandrogenic conditions and influences the outcome of the treatment. Follow-up of 179 adolescents with PCOS, 73 with PCOS-like syndrome (some but not all PCOS features) and 117 girls with Oligomenorrhea indicated poor response to treatment and high recurrences among obese girls.

PRETERM LABOUR: MODERN MANAGEMENT

Teoh Tiong Ghee
UK

The incidence of preterm birth is increasing and continues to be a significant cause of neonatal morbidity and mortality. Techniques exist to predict early birth. Prevention can therefore be targeted so that effective measures can be adopted in an attempt to improve outcome.

Predictors of preterm labour include previous obstetric history, cervical length, fetal fibronectin.
Interventions to prevent delivery and improve neonatal outcome remain unsatisfactory. These include progesterone, tocolysis and cerclage. Women who would benefit from these interventions are still difficult to identify.

An improved understanding of the mechanisms underlying the pathological process in preterm birth will allow screening and interventions to be appropriately be targeted.

TRAINING STAFF TO DEAL WITH EMERGENCIES: SCENARIOS AND DRILLS

Tracey A Johnston
Consultant in Fetal Maternal Medicine,
Birmingham Women's Hospital, Birmingham, UK

This session will provide a very practical approach to setting up and providing this type of training locally. The four stages of scenario training will be outlined - environment, set, dialogue and closure. The type of equipment required will be listed, and techniques for feedback discussed. The different types of learners will be highlighted to demonstrate that different approaches and techniques suit different people. How to deal with difficult learners will be addressed briefly. The role of fire drills in testing systems will be discussed.

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ASSESSING OVARIAN RESERVE: HOW, WHO & WHEN?

Lisa Webber

The concept of ovarian reserve is a very useful one, particularly in the context of otherwise unexplained infertility and if selecting women for in vitro fertilization. Various methods have been proposed for assessing ovarian reserve including anti-Mullerian hormone, inhibin B, antral follicle counts, ovarian volume, ovarian stimulation tests and assorted combinations of these parameters. Whilst some of these tests may have a direct clinical application in helping to plan a couple's treatment, their roles as "screening tests" for women wishing to delay childbearing may be less certain. According to accepted criteria for a screening test (WHO and Council for Europe) any condition suitable for screening should have adequate treatment or other intervention available. When the condition is poor ovarian reserve, that intervention may be to stop contraception. However, the impact of this information for a woman not in a position to start actively trying to conceive could be disastrous.

UPDATE ON HORMONAL SUPPLEMENTATION IN ART PROTOCOLS

Colin M Howles
Vice President Scientific Affairs Reproductive Health and Metabolic Endocrinology, Merck Serono International SA, Geneva, Switzerland

In a spontaneous menstrual cycle, only one follicle out of a cohort of 10-20 usually completes maturation and ovulates to release a mature oocyte. The aim of FSH stimulation in ART protocols is to overcome the selection of a dominant follicle and to allow the growth of multiple follicles. However, the number and quality of oocytes, which are recruited, is known to decline in women of advanced maternal age, and hence successful treatment for these patients continues to be a major challenge in ART programs.

The associated reduction in oocyte quality as manifested by the increase in aneuploid embryos is most likely due to suboptimal cytoplasmic maturation (including reduced capacity of oocyte mitochondria to generate sufficient quantities of energy required for fertilisation and cell division). This review will examine the available evidence for the use of various supplementary agents as a means of augmenting follicular recruitment and cytoplasmic integrity, so as to improve the prognosis for these women. Recent studies indicate that androgen supplementation may be one area to explore further. The availability of r-hLH has made it possible to investigate the role of LH in the endocrinology of follicular recruitment. It appears that a defect in the balance of LH/FSH might be involved in the subtle age-related decline in follicular recruitment, and slected patients of older reproductive age undergoing ART might benefit from the addition of LH and/or hGH. Further studies are required to investigate the physiological mechanisms behind this observation, and to assess the possible effect of androgen, LH, hGH supplementation on the age-related decline in pregnancy rate.

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TREATMENT OF OSTEOPOROSIS - WHY, WHOM, WHEN AND WHAT DRUG

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Why treat? (i) fractures increase morbidity and mortality; 30-50% of women, and 15-30% of men suffer a fracture related to osteoporosis in their lifetime. Spine and hip fractures increase morbidity, mortality and impose a financial burden on the community. The burden of other fractures (time off work, doctor visits, investigations) also contributes to the high human and financial cost of fractures, (ii) the burden of fractures is increasing because longevity is increasing, (iii) bone loss does not slow in old age, it accelerates, (iv) effective and safe treatments are available.

Whom and when? The most important factor determining whom and when to treat is an individual's absolute risk for fracture (ARF). If the ARF is 2/1000 persons/yr and a drug halves fracture risk, then one event is averted, one women will sustain a fracture despite treatment and 998 who were not going to fracture had treatment. Thus, one fracture is prevented but 999 women/yr are treated without benefit. If the ARF is ten times higher, i.e., 2/100 women/yr and the still drug halves the risk, one fracture is prevented again but only 99 women are treated. Knowledge of an individual's absolute risk is central to making decisions.

The need to intervene increases with advancing age, lower BMD, and prior fracture; each of these contributes independently to fracture risk. About 85% of fractures occur in women over 60 years of age. An important signal for the need to treat is a prior vertebral or non-vertebral fracture. The risk for further fractures increases 3 to 5 fold as the number or severity of prevalent vertebral deformities is increased. In a person with osteoporosis, an incident fracture (with or without a prevalent fracture at baseline), increases the absolute risk of a further incident fracture to 30-40% within three years. Thus, the evidence of anti-fracture efficacy is strongest in patients with a baseline vertebral or non-vertebral fracture. It is optimal to treat fewer older persons (> 60 years) at high risk rather than many younger persons at low risk. This ensures that those likely to respond to treatment receive it, and those at low absolute risk and thus unlikely to benefit remain untreated.

What drug? Anti-resorptive agents reduce the intensity of remodelling allowing more complete secondary mineralization of bone tissue restoring bone material stiffness. These drugs reduce the progression of trabecular and cortical thinning, and loss of trabecular connectivity and so maintain or increase bone strength, even though they cannot reverse structural damage. The anabolic agent, PTH, results in partial reconstruction of the skeleton with the deposition of new bone tissue on the periosteal, endocortical and trabecular surfaces thickening the cortex and trabeculae albeit with some increase in cortical porosity adjacent to the endosteum. The overall effect is to increase bone strength and reduce fracture risk. The decision regarding therapy must be evidence based.

Spine fractures The most rigorously studied drugs reported to reduce spine fractures in women with osteoporosis include alendronate, risedronate, raloxifene, PTH and strontium ranelate (SR). These drugs reduce the risk of symptomatic (clinical) and asymptomatic (morphometric) single vertebral fractures by about 40-50% and multiple vertebral fractures by about 80-90%. The benefits have been reported within the first 6-18 months of treatment. HRT and etidronate have also been reported to reduce spine fracture rates but the studies are less rigorous. The level of evidence for anti-vertebral fracture efficacy of calcitonin and vitamin D metabolites is insufficient for inferences to be made with confidence. Evidence for anti-fracture efficacy is less compelling in women with osteopenia with a fracture, osteopenia alone, and for men. Head-to-head comparator studies have not been done. Hence, it is not known whether any one drug is more efficacious than another and this cannot be inferred from meta-analyses.

Non-spine fractures Only the two bisphosphonates, SR and hormone replacement therapy (HRT) have been reported to reduce hip fractures in community dwelling women. PTH has been reported to reduce the risk of

non-vertebral fractures, not hip fractures. Raloxifene has not been reported to reduce the risk of non-vertebral or hip fractures except in a post-hoc sub-analysis. Calcium plus vitamin D and hip protectors have been reported to reduce hip fractures in nursing home residents and institutionalised elderly. PTH use is likely to be limited to severe osteoporosis and will probably need to be followed by an anti-resorptive drug. HRT is not recommended for fracture risk reduction unless postmenopausal symptoms are debilitating. Evidence for anti-fracture efficacy of calcitonin, fluoride, anabolic steroids, or active vitamin D metabolites is insufficient to justify their use.

How long? It remains unclear as to whether anti-fracture efficacy is sustained beyond 3-5 years. There is no evidence for increases in fracture rates in studies in human subjects However, prolonged therapy with bisphosphonates may increase the bone tissue mineral content and brittleness. High doses in animals resulted in micro-damage, a decline in toughness of bone (the ability to absorb energy without cracking) but no decrease in overall bone strength. The relevance of these animal studies to humans is uncertain. There is disagreement as to whether short periods of 1-2 years off therapy are appropriate after every 3-5 years on treatment. Stopping treatment is followed by increased remodelling, bone loss and further structural damage. Recurrence of bone loss is likely to occur sooner with cessation of HRT or raloxifene than with bisphosphonates. The FLEX trial suggests that there is a sustained effect of alendronate after stopping treatment but methodological issues make interpretation of the data difficult. There is no evidence that combining bisphosphonates with either raloxifene or HRT reduces fractures more than either drug alone (although combined therapy may produce greater increases in BMD). Women and men with fragility fractures should be treated with agents that have been thoroughly investigated.

MATERNAL CARDIAC DISEASE

Teoh Tiong Ghee
UK

Cardiac disease is the second commonest cause of maternal mortality in the United Kingdom. 80% of these deaths are due to acquired heart disease. The commonest conditions are cardiomyopathy, ischaemic and valvular heart disease. The management of women with Cardiac Disease before, during and after pregnancy at St Mary's Hospital will be discussed.

SCREENING FOR THROMBOPHILIA IN PREGNANCY

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The term thrombophilia describes disorders of the haemostatic mechanisms which predispose an individual to thromboembolism. Thrombophilic abnormalities can be inherited, acquired or complex (acquired factors interacting with a genetic background). Significant haemostatic changes such as increased concentrations of most clotting factors and decreased concentrations of some of the natural anticoagulants occur in normal pregnancy resulting in a hypercoagulable state. It is becoming increasingly evident that this interaction between thrombophilia and pregnancy results in increased risk of venous thromboembolism and may be associated with other vascular complications such as fetal loss, pre-eclampsia, placental abruption and intrauterine growth restriction. Although the relative risk for these complications is increased, meta-analysis suggests that the absolute risk of venous thromboembolism and adverse pregnancy outcomes remains low. Apart from recurrent pregnancy loss in the antiphospholipid syndrome and the prevention of venous thromboembolism, there is inadequate evidence on the benefit of antithrombotic therapy to guide treatment in other pregnancy complications. Further randomised controlled trials are needed to assess the harm-benefit ratio. Until then, testing for thrombophilia should be performed only on a selective basis.

THE ENDOCRINOLOGY OF OBESITY

Kevin TAN Eng Kiat
MBBS, MRCP, FRCP, FAMS

Obesity rates have increased over the past 20 years and with this, the prevalence of obesity-related medical conditions like diabetes and heart disease. At the same time, the concept of adipose tissues as an inert storage compartment of triglycerides has changed to one of an active endocrine organ responsible for insulin resistance and a source of enzymes and proteins like leptin, adiponectin and resistin.

Obesity is more than body mass index limits. The increased risk of cardiovascular disease seems to be related more to visceral adiposity than gluteofemoral adiposity. The pro-inflammatory adipokines produced by visceral fat promote the development of insulin resistance and subsequent cardiovascular disease.

Current and future therapies directed at obesity aim at addressing the above mechanisms.

THE IMPORTANCE OF NUTRITION IN GESTATIONAL DIABETES

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The reported prevalence of Gestational Diabetes (GD) is 1 - 14% of all pregnancies depending on the population studied and the diagnostic tests utilized (1). In Singapore, approximately 8.6% of all pregnancies are complicated by GD (2).

It is well established that diabetes mellitus in pregnancy may have acute as well as long term complications for mother and the fetus. Medical Nutrition Therapy (MNT) is important in managing existing diabetes, and preventing or at least slowing, the rate of development of diabetes complications during pregnancy.

A recent large clinical trial reported that treatment of GD with MNT, blood glucose monitoring and insulin therapy as required for glycemic control improved maternal health-related quality of life and reduced serious perinatal complications, without increasing the rate of cesarean delivery, as compared with routine care (3).

The goals of MNT in gestational diabetes are to: 1) provide adequate energy for appropriate weight gain; 2) achieve and maintain blood glucose levels in the normal range; 3) prevent ketonemia; 4) address individual nutrition needs of the pregnant mother, taking into account personal and cultural preferences and willingness to change; and 5) maintain the pleasure of eating.

MNT for GD primarily involves a carbohydrate-controlled meal plan that promotes optimal nutrition for maternal and fetal health. Recent guidelines state that a minimum of 175 g of carbohydrate / day should be provided to gestational diabetics through 3 small - moderate meals and 2 - 4 snacks.

Translating MNT guidelines into practical and realistic food choices, including details as portions and meal and snack timings, that can be applied in the daily lives taking into consideration the eating preferences of the pregnant mother is best left in the hands of a qualified dietitian and success in achieving the goals will require the active participation of the diabetic mother in the decision-making process. Case studies will be used to illustrate meal solutions for Singaporean mothers.

Recent guidelines on MNT in GD from the Ministry of Health, Singapore; the Joslin Diabetes Centre and Joslin Clinic as well as the American Diabetes Association will be reviewed - compared and contrasted - to help identify best practices for use in treating and managing GD (4, 5 and 6).

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MANAGING OBESE INFERTILE WOMEN PRECONCEPTION

Lisa Webber

If a woman's obesity comes to medical attention preconception it is usually in the context of delayed conception. The challenging part of her management is to convince her that her weight has anything to do with her presenting problem - and then to help her correct it. Currently there is much debate surrounding setting BMI limits for fertility treatment and in most parts of the UK NHS-funded in vitro fertilization is denied to women with a BMI above 30. If losing weight is a requirement of entry onto any form of assisted conception programme, then it must follow that effective support for achieving this is provided. A pilot multi-disciplinary weight management programme that was set up at a London teaching hospital for obese women wishing to conceive is presented.

OBESITY IN PREGNANCY

Teoh Tiong Ghee
UK

Overweight and obesity are common findings in women of reproductive age in the UK; as 32% of 35-64-year old women are overweight and 21% obese. Obesity causes major changes in many features of maternal intermediary metabolism. Insulin resistance appears to be central to these changes and may also be involved in increased energy accumulation by the fetus. Maternal obesity is associated with many risks to the pregnancy, with increased risk of miscarriage (three-fold) and operative delivery (20.7 versus 33.8% in the obese and 48.4% in the morbidly obese group). Other risks to the mother include an increased risk of pre-eclampsia (3/9 versus 13.5% in the obese group) and thromboembolism (0.05 versus 0.12% in the obese group). There are risks to the fetus with increased perinatal mortality (1.4 per 1000 versus 5.7 per 1000 in the obese group) and macrosomia (>90th centile; versus 17.5% in the obese group). Maternal obesity is associated with an increased risk of obesity in the long term. Obese women should try to lose weight before pregnancy but probably not during pregnancy. There is no real evidence base for the management of maternal obesity but some practical suggestions are made.

CORD BLOOD STEM CELLS AND THEIR CLINICAL UTILITY

David Roberts

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Abstract
The development of Dolly the Sheep (1997) and the isolation of the Human Embryonic Stem Cell (1998) heralded the enormous potential of Stem Cells as a platform for regenerative medicine and other therapies. But the immunological problems associated with using allogeneic (another person's) stem cells have prompted researchers to look for sources of autologous (self) stem cells. Embryonic stem cells are clouded in ethical controversy. Therapeutic cloning (somatic cell nuclear transfer) as a solution to the immunological problem, but is equally controversial. The answer is cord blood stem cells.

We have known for 25 years that cord blood is enormously rich in stem cells of varying types. As well, cord blood stem cells are still young. We now understand that stem cells age; indeed that is what the process of aging is - the aging of stem cells. Just why cord blood contains so many stem cells is an extraordinary story.

In oncology today, cord blood is an alternative to bone marrow in the transplant setting. But the future uses of stem cells are likely to go well beyond this. In the future, we will use our cord blood stem cells several times in our lives. The routine medical history of the future will read, "Do you take any medications?"; "Are you allergic to anything?"; "Do you have your cord blood stored?"

ROLE OF INDEPENDENT LACTATION CONSULTANT

Betty Lee
Free-lance Lactation Consultant

An independent lactation consultant or one in private practice is an integral member of the breastfeeding mother's healthcare team. This role carries tremendous responsibilities and is important to ensure that optimal care is delivered. Our focus is on helping breastfeeding mothers and their families in achieving their own breastfeeding goals.

The importance of formal lactation education and extensive clinical experience is essential to help and equip us with the knowledge in our work.

We have to maintain certain standards of practice and to ensure that level of care facilitates continued health and wellness particularly as it relates to breastfeeding management and early parenting issues. Practising as an independent lactation consultant means providing quality care to the public and accepting responsibility for that care.

Maintaining a referral system is integral to the delivery of assistance to breastfeeding women. Working in private practice usually permits minimal contact with staff at various hospitals. Networking with doctors, colleagues from all hospitals and participation in professional association form an essential part of our support system.

However, private practice lactation consultants enjoy the autonomy of being your own boss. You are able to set your own hours and work around family functions.

IS THERE A PLACE FOR DOULAS IN SINGAPORE?

Ginny Phang
Certified Doula
Childbirth Educator
Hypnotherapist
Hypnofertility
Hypnobirthing

Ever wondered why modern parents-to-be engage Professional Labor Support Providers (Doulas) to support them through their pregnancy, during labor and birth and early postpartum? What do Doulas's actually do and what is their role in the birthing room? How do Obgyns and Nurses feel about Doulas and do Doulas have a role in Nursing?

BABY MASSAGE AND BONDING

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Bonding is the attachment that forms between an infant and its mother beginning at birth. During the time immediately post -delivery, when the mother is holding her baby for the first time, high levels of endorphins, oxytocin and endogenous opiates are released in the mother's brain (Travaathan1987). This results in intense pleasure of gratification and wanting mothers to be bond with their infants.
In this paper, the art and the advantages of infant massage will be explored and some proven research papers will be discussed. The technique of infant massage will also be taught.

There are many advantages of infant massage. Infant massage will help parents build a bond with their babies - period to get to know each other It reduces stress responses to painful procedures and abdominal colic. A study done by Field T et al (1986) has shown that massaged infant gained 47 percent of weight gain and showed better performance on the Brazelton Scale on orientation; motor activity and regulation of sate behavior. Infant massage improves mother -infant interactions for mothers with postnatal depression (Onozawa et al 2001)
In conclusion, infant massage is not only massaging a baby, - it is about building and nurturing relationships, which enhances parent- baby bonding and attachment.

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COMPUTER-BASED TRAINING (CBT)

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The School of Health Sciences (SHS), Nanyang Polytechnic has been providing Health Sciences education for the past 15 years. It currently offers 6 full-time Diploma Programmes in various fields of healthcare as well as numerous full-time and part-time advanced and specialist programmes. With a team of dedicated lecturers, designers and IT specialists, SHS has been leveraging on technology to continually expand its e-Learning curriculum content by developing multimedia and interactive digital media packages made available for students' on-demand access. Our e-Learning packages are developed for the local context and allow students to learn at their own pace and encourage self-discovery and life-long learning. Currently there are more than 30 web-based integrated e-Learning packages providing learning experiences that lead to students' comprehension and mastery of new skills and knowledge in diverse areas. To familiarise students with the ward setting so as to better prepare them for their first clinical attachments, the Virtual Ward program was developed to simulate a real hospital ward. Besides detailing a hospital ward set-up, actual case scenarios are also included to allow students to apply theory to practice within a clinical setting, in a safe and non-threatening environment. This promotes the development of students' critical thinking, clinical reasoning and problem-solving skills and enhances their confidence during their clinical practice. This paper aims to share the utilization of computer-based training at the School of Health Sciences, Nanyang Polytechnic.

ONCOLOGY NURSING - IMPACT ON SEXUALITY POST RADIOTHERAPY

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A diagnosis of cancer and its treatment can have a significant effect on a person as a whole. With the improvement in survival rates, survivors live longer with the consequences of treatment. Developing an understanding of peoples' experiences in order to maximize their ability to live well after treatment is therefore very important. This cross-sectional study was conducted with the purpose of examining the perceptions of women diagnosed with cervical and uterine cancers in Singapore about the impact of radiotherapy on their sexuality. It also sought to examine womens' information needs regarding sexuality. A questionnaire was designed specifically for the study, consisting of 24 items adapted from Bourgoesis-Law's needs assessment instrument (Bourgoesis-Law & Lotocki, 1999) and the 14-item Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983). This was sent to 267 women recruited from a Gynaecology Cancer Centre in KK Women's and Children's Hospital. An information sheet, consent form and two stamped-addressed return envelopes were included in this mailed survey. Data was analysed using the Statistical Package for Social Sciences 11.5 (SPSS). A disappointingly low response rate (12%) has limited the ability to make firm recommendation. However problems encountered in recruiting participants give rise to important methodological insights for consideration for future studies. Results demonstrated that women who reported sexual function effects (56.3%) after cancer therapy experienced a decrease in sexual activity, more coital pain and decreased interest in sex than women who did not report these effects. Importantly, these effects were found to cause distress in these women. It was also found that 'changes in the body' and 'feelings about yourself as a woman', as well as the 'lack of information' were the most difficult aspects of the effect of illness and treatment on sexuality. Information regarding sexuality was reported to be deficient in this group of women with participants stating that they would like to have received more information through pamphlets with the addition of discussion with a doctor or nurse. In addition, general information about sexuality was found to be important and useful. Recommendations from the study findings are directed towards conducting large-scale research and crucially towards the education of nurses regarding sexuality and cancer, including methods of effectively assessing women's needs for information and specialist referral.

CHALLENGES IN MINIMALLY INVASIVE SURGERY: NURSING ASPECTS

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Perioperative environment is known to be possibly the most hazardous of all clinical environments for both patients and staff. It is the role of the nurse to promote and safeguard the interest and well-being of the patient and ensure that no action in her area of responsibility is detrimental to the patient. It is therefore the responsibility of nurses to keep themselves updated with the current practices so that they are best to manage any situation.

Minimally invasive surgery has developed rapidly over the past few years. The increase use of minimally invasive surgery approaches has impact on the operating room personnel as well as affecting the nursing care of patients. Emerging technology and competition among vendors of equipment and instrumentation is a great challenge for perioperative nurses in supporting minimally invasive surgery. An understanding of the current applications of technology and perioperative nursing responsibilities is therefore needed to assure quality patient care in the operating theatre especially in current situation now whereby patients know and expected more.

SUNDAY, 25 MARCH 2007

IPL(INTENSE PULSED LIGHT)

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When IPL(Intense pulsed light) was introduced In early 1990s, it was regarded cumbersome machine. But, since several years ago IPL sources have been successfully used for coagulation of blood vessels, telangiectasia, poikiloderma of Civatte, rosacea, port-wine stains, facial wrinkles, skin laxity, hair removal, and superficial pigmented lesions, such as freckles, lentigenes. And also, there are numerous IPL indications can be listed in clinical practice. It is obvious that not all IPL machines are the same. In fact, very low power ones are used in salons and spas in some countries. Until now, hundreds and thousands of IPL manufactures showing their product in the market annually. Most systems produced today use a xenon arc lamp as a light source. By the optical filtering technique, filtered spectrum of light reacts on the three main chromophores with high intensity. They are hemoglobin, melanin, and water. IPL can cover all these three different chromophores in one pulse of light. IPL is a noncoherent light usually in a broad wavelength spectrum of 515-1200 nm. The emitted light from the light source is gentle, non-invasive, and long lasting.

The advanced IPL model are not a dangerous machine that provokes unwanted side effects. On the contrary, they have a lot of advantages compare to the laser systems. For instance, relatively lower cost the exposure area is much larger, no specific social downtime, and can save times for perform procedures.

StarluxTM (Palomar, Burlington,MA)is not only a model of IPL system, but also a multi functional skin rejuvenation system. This system acts as a multifunctional device for treating vascular and pigmented lesions(LuxG, LuxY), inflammatory acne(LuxV), hair removal(LuxRs), photofacial/photorejuvenation(LuxG, LuxY, Lux1540 Fractional), leg vein treatment(LuxG, Lux1064:Nd YAG), and as a noninvasive facial lifting(LuxIR Fractional). Due to the strong cooling effect the pain is very much decreased, and the panel control system is designed user-friendly. The skin is cooled throughout treatment, permitting the operator to deliver high-energy pulses while providing maximum comfort and safety to the patient. The flashed light passes absorption and dichromatic filtration in its system, which eventually provides more protection to the skin. The StarLux™ delivers pulsed light in one smooth pulse, rather than the train of multiple power spikes. Its smooth pulse technology prevents a rapid rise in skin temperature for far more comfortable treatments. StarLux™ is able to deliver high energy to the target pigment and oxyhemoglobin due to its active contact cooling feature, which chills the handpiece's sapphire tip to as low as 4°C. A variety of handpieces in Starlux™ system tailored for specific indications makes treatment easy. Actually, we need pay attention more to the evolution of IPL, because of the progress of IPL is quite remarkable,

THE Q-SWITCHED LASERS

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The Q-switched lasers including the Q-switched ruby (694nm), Q-switched Alexandrite (755nm), Q-switched Nd:YAG (1064/532nm) are effective in removing pigmented lesions, by selectively targeting melanosomes. Regardless of what system is used, pigment laser treatment should be initiated at the threshold fluence, which causes an immediate tissue-whitening effect that signals appropriate energy deposition in the melanosome. For darker skin tones, like in the Asian population, the Q-switched Nd:YAG has the lowest incidence of side effects (e.g. hypopigmentation) since its wavelength is more weakly absorbed by melanin than the other laser systems.

The following conditions can be treated with the Q-switched lasers: lentigines, nevus of Hori, labial melanosis, tattoos and certain birthmarks e.g. café-au-lait macules, nevus of Ota and nevus of Ito. There is conflicting evidence on the use of Q-switched lasers for melasma.

In Asian patients with dermal melasma and where associated Hori nevus is present, the Q-switched Nd: YAG laser may be useful. The use of the Q-switched Nd: YAG laser for non-ablative skin resurfacing will be briefly discussed.

In conclusion, the Q-switched lasers have become a common tool in the treatment of a wide variety of benign pigmented lesions and we look forward to even more powerful and effective systems that will lead to improved clinical outcomes.

FRACTIONATED LASERS

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For the purpose of skin rejuvenation or acne scar, laser resurfacing has been regarded one of the best method. Due to ablative resurfacing lasers like pulsed carbon dioxide and erbium YAG lasers, more precise skin surface remodeling could be achieved. Because they have been provided the predictable results, they played a key role for laser resurfacing until the beginning of this century. But, when we think about the drawbacks like prolonged recovery time, considerable social downtime, or significant side effects, such as postinflammatory hyper or hypopigmentations, ablative resurfacing lasers is not always preferred by patients and doctors. Cooling system installed nonablative lasers can transfer thermal damage only to the targeting areas like upper dermis or the appendegeal organs in upper dermis. The epidermal protection and downtimeless procedure were possible by these lasers, but efficacy is less and unpredictable compared with ablative lasers. And, the treatment depth does not reach deep inside to dermis without downtime.

To get over the drawbacks of both ablative and non-ablative devices, the new concept of fractional photothermolysis was developed for skin remodeling in 2004. Actually fractional photothermolysis is based on the concept of creating focal or partial thermal damages. It is designed to create microscopic thermal wounds to achieve skin rejuvenation without significant side effects. The Fraxel(tm) SR750 laser(Reliant Technologies, Palo Alto, CA), which employs 1550 nm, is the first true fractional laser. It has been cleared FDA approval for the treatment of pigmented lesions, periorbital rhytides, skin resurfacing, soft tissue coagulation, and recently for acne and surgical scars. The effect of the Fraxel(tm) SR750 laser demonstrated by a great number of peer group review. The next generation the Fraxel(tm) SR1500 laser was released on the market in 2006 and the new version can deliver higher fluences, wider microthermal zones, and save treatment time. The Fraxel(tm) SR1500 laser has an optical spot size that is adjusted at each pulse energy level for optimizing depth of thermal damage.

It is difficult to be called true fractional resurfacing laser without some essential factors, those are microscopic thermal wounding, mid infrared wavelength for optimal water absorption, and sufficient capacity of power to reach up to 1000 _m. Since 2006, some devices employed fractional concept. But, without histologic studies that support the clinical result, we may classify them in another group, "quasi" nonablative fractional resurfacing. To be called true fractional laser, sufficient epidermal and dermal changes should be revealed clinically and histologically.

THERMAGE CRF - APPLICATIONS FOR NON-INVASIVE ABDOMINAL TISSUE TIGHTENING

Nantapat Supapannachart
Thailand

The Thermage capacitive radio frequency (CRF) device, widely acknowledged to be the gold standard in tissue tightening technology, has greatly extended its range of applications to treat loose and sagging skin and renew facial and body contours. New treatment tips and improved generator technology make treatments faster and more versatile. Thermage is fully FDA cleared and clinically proven to deliver superior results in skin tightening and contouring on all areas of the body.

Thermage has recently introduced new treatment tips specifically designed for the treatment of larger body areas, such as abdomen, thighs and legs. The latest Thermage applications and treatment outcomes are being discussed.

VAGINAL REJUVENATION - HYPE OR HEAL?

Lee Keen Whye
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Vaginal rejuvenation is a surgical art to enhance the vagina functionally and aesthetically. Rejuvenation is a catchy term in anti-aging and aesthetic medicine. It embodies reconstruction, giving the organ a fresh breath and a lease of new life. Hence, in vaginal reconstruction surgery, there is a functional aspect and an aesthetic aspect to be attained. In gynaecology, the focus is on operating on diseased organs and correcting anatomical defects e.g. vulva cancer and uterovagina prolapse. In vaginal rejuvenation, an added focus is on the patient's expectations. This is the essence of aesthetic gynaecology.

It has been said that the most powerful sex organ is the brain. But, this power is not harnessed by mere thinking or dreaming. It requires an interaction of all our senses, sight, touch, sound and so on. I will showcase my personal selection of cases in vaginal rejuvenation like hymen repair, labiaplasty and vaginoplasty. At the same time debunk the hypocritical statement of "size does not matter."

Vaginal rejuvenation empowers women with a new lifestyle option. The answer of whether it is hype or heal is a personal order.

FACTORS ASSOCIATED WITH BREASTFEEDING PRACTICES & DURATION: A PROSPECTIVE COHORT STUDY

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Background
The initiation rate of breastfeeding conducted in 2001 in Singapore (Foo et al, 2005) was high at 94.5%, but the duration of exclusive breastfeeding was extremely low (7% at 4 months and almost zero at 6 months). Other local studies were conducted more than 5 years ago and studies from other countries on factors influencing breastfeeding practices may differ with our local situation.

Methods
Participants from a large maternity hospital were interviewed prior to discharge from the hospital and subsequently follow-up interviews were conducted at six weeks, four months and six months postnatal using questionnaire with a mixture of closed and open-ended questions.

Results
The exclusive breastfeeding at six weeks was 22.6%, and the rate fell to 17.3% at four months and 3.1% at six months, At six weeks postpartum, the most common maternal and infant related reason for cessation of breastfeeding was 'not enough milk' (49.8%) and 'baby unable to latch' (21%). Malay mothers compared with Chinese mothers (OR=0.61, 95% CI=0.41-0.89) were significantly less likely to cease breastfeeding at six weeks postpartum. Mothers with no intention to exclusively breastfeed were found to be 6 times more likely to cease breastfeeding compared with exclusive breastfeeding at six weeks postpartum. Mothers who did not initiate breastfeeding within 1 hour of birth were more likely to cease breastfeeding at six weeks postpartum.

Conclusion
Modifiable factors such as early initiation within one hour after birth and intention to breastfeed exclusively were found to be significantly associated with continuation of breastfeeding and exclusive breastfeeding at six weeks postpartum.

CLOSER TO BREASTMILK: THE "IDEAL" MILK FORMULA?

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Research into the functional constituents of breastmilk has led to a number of recent additives to infant formulas which include nucleotides, prebiotics, probiotics, long chain polyunsaturated fatty acids (LCPUFA) and sialic acid.

Impact of additives on immune responses
There is increasing evidence that LCPUFAs influence the inflammatory immune response. In a recent study, docosahexaenoic acid (DHA) supplementation was associated with a significant reduction in the incidence of bronchitis in the first year of life. Nucleotide-supplemented formulas have been associated with fewer and shorter episodes of diarrhoea, and in one landmark trial, infant formula fortified with nucleotides enhanced Haemophilus influenzae type b and Diphtheria humoral antibody responses in immunized infants. Supplementation of infant formulas with Fructo-oligosaccharides (FOS) has also been associated with decreased severity of diarrhoeal illness and constipation, and reduced symptoms of irritable bowel syndrome. Probiotic Supplementation with probiotics (cultures of bacteria beneficial to a healthy gut microflora) not only results in intestinal immunostimulation, and decreased gastrointestinal infections but also reduces by 50% the incidence of eczema at 2 years.

Neurodevelopment
Supplementation with LCPUFAs increases the early rate of visual maturation in preterm infants, and also confers a beneficial effect on information processing. Several variables can influence the impact of LCPUFA intake, including the quantitiy and the source of DHA and arachidonic acid (ARA) in formulas. There is emerging evidence of the long-term effects of LCPUFA supplementation on not just preterm but also full-term infants.

Long-term impact of infant formula supplements
Infant formulas should also protect from long-term complications such as osteoporosis, obesity and hypertension. Breastfed infants generally have a lower fat mass than formula-fed infants even at 1 year of life, and further follow-up is needed to assess if this difference is sustained and also as to whether there is any impact on maturity-onset chronic diseases.

Breastfeeding and dietary supplementation with LCPUFAs during infancy has been associated with lower blood pressure in later childhood. In a follow-up study of children at age 6 years, those fed LCPUFA supplemented formula in infancy had significantly lower blood pressure than control subjects. The diastolic pressure of breastfed children was significantly lower than that of the non-supplemented formula group, but did not differ from the LCPUFA formula group. Dietary modification ie early exposure to LCPUFAs may thus reduce cardiovascular risk in adulthood.

IMPACT OF INFANT NUTRITION ON OBESITY

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We compared growth, skin-fold measurements and fat mass in breast-fed (BF, n=21) versus formula-fed (FF, n=14) full-term infants from birth until 12 months of age. The BF group was exclusively breastfed up to 2 months of age, while the FF group was predominantly or exclusively formula-fed. Anthropometry, skin-fold measurements at 4 different sites and percentage fat mass as determined by the Deuterium Oxide dilution technique for measuring total body water were performed at 3, 6 and 12 months of age. All 35 babies were full-term at birth ((BF) 39.3±1.2 weeks vs (FF) 39.0±0.8 weeks). Weight, length, head circumference and mid-arm circumference at birth were similar. There were no significant differences between the 2 groups with regards to anthropometry, mid-arm circumference (MAC), skin-fold measurements or percentage fat mass (% Fat) (mean±SD, $p>0.05$):

Age (mth)	Diet	MAC (cm)	Triceps (mm)	Biceps (mm)	Subscapular (mm)	Suprailiac (mm)	% Fat
3	BF	14.5±0.8	8.3±1.8	6.8 ±1.4	8.1±1.4	7.7±1.7	25.3±5.8
	FF	14.3±0.7	7.9±1.1	7.3±1.3	8.3±1.6	7.9±1.6	25.5±6.2
6	BF	15.2±1.4	8.3±1.9	5.7±1.1	7.4±1.5	5.9±1.0	24.0±8.9
	FF	15.5±0.7	8.0±0.8	6.0±1.5	7.5±1.2	7.1±0.9	24.9±8.6
12	BF	16.0±1.0	9.0±3.4	5.6±0.8	9.4±1.9	7.0±2.7	19.8±1.9
	FF	15.5±0.9	7.7±2.5	4.3±0.9	7.5±1.7	6.1±2.5	20.2±1.7

Conclusion: There was a trend towards breastfed infants being leaner when compared to formula fed infants. Early nutrition may have an effect on infant adiposity later on in life.

FREE PAPERS

DEVELOPMENT OF NON-INVASIVE PRENATAL EXCLUSION OF ALPHA THALASSAEMIA USING FETAL DNA FROM MATERNAL PLASMA

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Objective

Couples with the α-thalassaemia double gene deletions(αα/—SEA, αα/—FIL and αα/—THAI) are at-risk of carrying fetuses with the fatal HbBart\'s hydrops fetalis. We aim to exclude HbBartís hydrops non-invasively using cell-free fetal DNA from the maternal plasma and prevent miscarriages of at-risk mothers with unaffected fetuses from unnecessary invasive procedures.

Material and Method

Detection limit of quantitative fluorescence(QF)-PCR of polymorphic microsatellite markers within the breakpoints of the α-thalassaemia deletions was optimised using spiked(1:50) DNA samples consisting of αα/αα, αα/—SEA, —SEA/—SEA, αα/—FIL and αα/—THAI genotypes. The optimised protocol was performed on 28 families each consisting of maternal plasma, parental(paternal/maternal) and fetal DNA. Presence of fetal paternally-inherited microsatellite markers in maternal plasma DNA would exclude HbBartís hydrops fetalis.

Result

Fetal paternally-inherited microsatellite markers were detected in 10 maternal plasma later confirmed unaffected by HbBartís hydrops. Absence of fetal markers in the remaining 18 samples required further analysis with pure fetal DNA. Of these, 1 fetal sample was confirmed HbBartís hydrops(—SEA/—SEA). Paternally-inherited fetal alleles were detected in 10 of 26 maternal plasma unaffected by HbBartís hydrops.

Conclusion

HbBartís hydrops was excluded non-invasively with 100% accuracy using fetal DNA from maternal plasma. Thirty-eight percent(10/26) of the screened population would have avoided unnecessary invasive prenatal testing. The ability to differentiate between maternally- and paternally-inherited microsatellite markers is useful for the identification of fetal alleles amongst the overriding maternal DNA in the maternal plasma. In conclusion, fetal DNA in maternal plasma can be used to exclude HbBartís hydrops fetalis noninvasively.

QUANTITATIVE FLUORESCENCE-POLYMERASE CHAIN REACTION (QF-PCR) OF UNCULTURED AMNIOCYTES: INCREASED STRINGENCY IN THE PRENATAL DIAGNOSTIC CRITERIA OF CHROMOSOMAL ANEUPLOIDIES

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Objective
Diagnostic results of chromosomal aneuploidies using QF-PCR are considered valid with the presence of two or more informative microsatellite markers per chromosome. Our aim is to evaluate and improve this current diagnostic criterion for increased accuracy of molecular genetics diagnosis.

Material and Method
QF-PCR of 19 microsatellite markers on chromosomes 13 (n=5), 18 (n=5), 21 (n=6), X and Y (n=3) were performed on 812 amniotic fluid samples. Samples with two or less informative microsatellite markers per chromosome were repeated.

Result
The number of informative markers per chromosome increased to 3 in all trisomic samples (n=38) in the repeated run, resulting in distinct biallelic (1:2 or 2:1) or triallelic (1:1:1) ratios which were otherwise, not observed during the first run for 3 samples. Eight out of 25 normal samples with previously uninformative microsatellite markers (<2) showed a distinct biallelic (1:1) ratio with ≥2 markers in the repeated run. Eleven out of 87 samples with two informative markers per chromosome during the first run showed an increase to 3 informative markers in the repeated run.

Conclusion
We have shown that the minimum number of informative markers per chromosome for valid QF-PCR results can be increased from the current 2 to 3. This increase in stringency of diagnostic criterion will increase the confidence of reporting accurate QF-PCR diagnostic results.

RAPID AND COST EFFECTIVE MODEL FOR PRENATAL DIAGNOSIS

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Objectives To propose a cost-effective model, which could merge rapid molecular tests (fast Fish) with Karyotyping for prenatal diagnosis.. We aim to test the hypothesis that if we test for trisomy 21 routinely, but for trisomy 13 and 18 only if the ultrasound abnormalities were present, we would rapidly detect more than 90% of these fetal aneuplodies using fast FISH with considerable cost saving.

Methods Modeling study based upon 211 cases of trisomy 13, 18, 21 diagnosed between January 1992 to October 2004 was performed. Presence or absence of structural abnormalities were analyzed. Fast FISH protocol was tested through optimisation of hybridisation time and temperature.

Results 80.3% of trisomy 18 (n=53) and 90% of trisomy 13 (n=18) fetuses had ultrasound abnormalities. However, 42.4% of trisomy 21 fetuses (n=53) had no detectable ultrasound abnormalities. Testing for chromosomes 21, X and Y routinely but for chromosomes 18 and 13 only in the presence of ultrasound abnormalities allow 93% of these aneuploidies to be identified rapidly ($z=3.2$; $p=0.001$). Through optimisation of the hybridisation time and temperature, our modified FISH protocol allows FISH results to be obtained within 2 hours.

Conclusion Fast FISH allows results to be available within two hours. Routine rapid molecular testing for trisomy 21, but targeted testing for trisomy 13 and 18 based upon ultrasound abnormality, allows rapid detection of more than 90% of significant fetal aneuploidies. This novel approach of fast FISH and targeted testing lead to faster speed and lower cost in prenatal diagnosis.