#### News & Views

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#### 1. Carbetocin at caesarean section

Carbetocin is a synthetic analogue of oxytocin with a longer biological half life. As such it may have advantages over the standard 5 IU intravenous dose of oxytocin given at caesarean section once the baby is delivered. The routine 5 IU of oxytocin is frequently augmented by a further infusion of the drug prophylactically against post-partum haemorrhage in patients the surgeon considers to be at high-risk.

A report by Attilakos et al (BJOG 2010; 117:929-36) showed that 100 mg of carbetocin was more effective than an ampoule of 5 IU oxytocin in reducing the need for additional oxytocin infusions. There were no differences in the incidence of haemorrhage or blood transfusion requirements. Despite its higher cost carbetocin may find a place in the armamentarium of uterotonic agents used in first world obstetrics but continuous oxytocin infusion and rectal mesoprostol will delay its entry to our country.

## 2. Genetic susceptibility to breast cancer

It is seductive to believe that genetic testing could hold the key to breast cancer risk prediction. There are ten environmental factors that influence risk: age at menarche, parity, age at first birth, breastfeeding, menopausal status, age at menopause, use of hormone replacement, body mass index, height and alcohol consumption.

There are also a dozen single nucleotide polymorphisms (SNPs) that are known to be associated with breast cancer risk so it might be possible to marry the environmental factors with the SNPs to come up with a gene-environment rubric that would really identify those at risk. To test this hypothesis Travis et al (Lancet 2010;375:2143-51) used the data from the UK Million Women Study to investigate over 7000 women who developed breast cancer and see if combining environmental plus SNP information lead to a definable interaction that would be a useful predictor of risk.

Unfortunately it did not reveal any significant combinations of the possible 120 interactions despite formidable statistical pyrotechnics so genome-wide association studies are unlikely to yield progress (Narod Lancet 2010;375:2123-4). It is exactly a decade since the human genome was mapped and although a scientific success in decoding our 3 billion base pairs, the clinical benefits remain scarce. Maybe the next 10 years will be more fruitful.

## 3. Surgery for stress urinary incontinence

As women age their chances of urinary incontinence increase until about one in three will have her lifestyle affected. The social cost can be expressed by patients saying "Incontinence doesn't kill you, but it takes your life away". An article in JAMA (Goode et al 2010; 303: 2172-81) and a commentary by Wagner and Subak (2184-5) give data about the magnitude of the problem and the options available that may be helpful to those trying to address their difficulties with their doctor's help.

The number of operations for stress urinary incontinence has increased markedly over the last few years. Not only are women living longer and anticipating a higher quality of life but the procedures available offer more choice, are simpler and are less likely to cause complications.

The changes came 15 years ago when the synthetic midurethral sling was introduced using tension-free vaginal tape (TVT). Unlike the Burch urethropexy or the suburethral fascial sling the new operation was less invasive, did not require a traditional abdominal incision and could be performed as an out-patient procedure. This retropubic TVT proved immensely popular because of its simplicity and excellent results but randomised trials of its efficacy were slow in following. Its "obvious" advantages remained unchallenged until, 5 years later a different type of midurethral sling appeared that was not placed in the retropubic space but through the obturator foramen. It was suggested that it had advantages over the TVT in that it had fewer complications and bladder perforation was less common.

There is a clinical impression that the two procedures are roughly equivalent in efficacy in terms of their outcomes and complication rates (Rogers NEJM 2010;362; 2184-5). Clinical equivalence is a challenge to prove but Richter et al (NEJM 2010; 362: 2066-76) did carry out such a trial comparing midurethral retropubic and transobturator slings. They

recorded objective and subjective measurements of cure rates after one year as well as the complication rates and the need for additional treatment. The research showed remarkably similar findings for the 300 women in each group giving objective positive results around 80% at 12 months follow-up. The subjective results were around 60% with the retropubic sling being slightly more satisfactory than the transobturator sling.

The retropubic sling had more complications, often related to mesh exposures or bladder perforations whereas the transobturator sling gave rise to more neurological side effects such as numbness and weakness. Given that up to one third of women having a procedure for incontinence require another manoeuvre at some time in their lives, there is no guarantee that the long term outcomes will be equivalent. It seems both operations are comparable in efficacy and complication rates after one year so other considerations can be taken into account for individual cases.

In Egypt and other countries with limited resources, cheaper tapes cut from surgical mesh are used frequently with no reported complications. Transobturator tapes do provide very good results and are most often successful when there has been no previous incontinence surgery and where the woman did not suffer from prior urge incontinence

#### 4. Neonatal care

Perinatal mortality rates have improved with more advanced neonatal care and neonatal intensive care units (NICU) in our country — in Cairo and other cities - are accepting earlier and earlier gestationally aged infants for treatment. In sophisticated NICUs there is about a 75% survival rate of babies born between 24 and 27 weeks and 6 days gestation but there is a high prevalence of neurodevelopmental problems in survivors — approximately 50%. Naturally all statistics improve as the neonate's age approaches 28 weeks

Neonatologists are constantly reviewing their strategies, especially those of pulmonary function support. Two articles by the SUPPORT Group (NEJM 2010;362:1959-69 & 1970-9) address the issues of intubation plus surfactant and the percentage oxygen saturations that are best for these tiny infants. It seems that nasal continuous positive airway pressure (CPAP) is a viable alternative to immediate intubation plus surfactant administration so it is worth considering even if later intubation does become necessary.

Answering the second question – that of target oxygen saturations – has proved problematic. Keeping levels between 85 & 90% resulted in fewer cases of severe retinopathy of prematurity but more babies died compared with the group whose oxygen saturations were kept between 90 & 95%. It is also essential to provide long-term follow up on neurodevelopmental outcomes as many subtle characteristics only become apparent in later years.

There is clear evidence that resuscitation of 22 -23 weekers is very rarely successful and should only be undertaken after counselling which must consider that non-survivors will have to endure long periods of intensive care and this is part of a "hidden morbidity" especially in our private practice and that survivors will, more likely than not, suffer permanent cerebral damage (Swamy et al Arch Dis Child 2010;95:F293-4).

# 5. Maternal vitamin A

Adequate maternal levels of vitamin A are essential in early pregnancy for normal lung development in the fetus. Vitamin A regulates growth through cell proliferation and differentiation and children born to mothers in areas of deficiency may suffer from suboptimal alveolar development.

In the 1990s mothers in Nepal were given vitamin A, beta-carotene or placebo as part of a trial on the effects of supplementation on pregnancy outcomes and then 10 years later their children had their pulmonary function studied (Checkley et al NEJM 2010;362:1784-94). There were improved lung function results in those whose mothers (and as newborns) had received vitamin A compared with those given beta-carotene or placebo as measured by their forced expiratory volume. Populations experiencing chronic vitamin A deprivation should be provided with supplementation antenatally as well as subsequently through the child's school years for optimal lung development.

On the other side of the coin, vitamin A supplementation has been shown not to reduce maternal mortality in Ghana (Kirkwood et al Lancet 2010;375:640-9). Although it has one of the highest maternal mortality rates in the world, the people of Ghana seldom suffer from night blindness which is a manifestation of vitamin A deficiency so it may be that supplementation did not benefit the women in a clinically discernable manner.

Supplementation is not going to be the magic bullet which will allow deprived nations to achieve their Millennium Development Goat of a 75% reduction in maternal mortality ratios by 2015. Progress toward the goals is reported by Hogan et al (Lancet 2010;375:1609-23) and deserves to be read by all those concerned about women's health globally

### 6. OCs & mortality

One of the longest running surveys is the UK General Practitioners' study of the effects of oral contraceptives (OCs). Forty years ago GPs started tracking the health of OC users and a control group of non-users to see of OCs were linked to increased or decreased mortality rates (Hannaford et al BMJ 2010;340:c927). Initial reports suggested an increased risk of cardiovascular problems in older women and smokers but the latest data show users to be at a lowered risk compared with never-users. There were fewer in deaths from cancer and circulatory disease leading to an overall reduction in all-cause mortality of 52 per 100 000 woman years.

# 7. Cardiovascular disease prevention

As women age their cardiovascular disease risk becomes more similar to that of men. Indicators of risk such as dyslipidaemia or elevated C-Reactive protein levels have been successfully used in men as triggers for the initiation of preventative medication—like statins. Evidence that primary prevention in women is now starting to appear (Mora et al Circulation 2010; 121: 1069-77) and rosuvastatin looks a promising agent.

In the JUPITER trial nearly 7 000 women over the age of 60 with hematological risk factors were allocated to rosuvastatin or placebo. The statin did significantly reduce coronary events in women in much the same ration as it did for men – results which are supported by meta-analyses of primary prevention statin trials. It seems that sex differences for CVD do become less far apart with age and medical interventions have a similar protective effect.

Hysterectomy and urinary symptoms

The effects of hysterectomy on urinary tract symptoms are difficult to evaluate. After recovering from the operation women generally feel better and report an improved quality of life but long-term follow up has suggested a predisposition to urinary symptoms. Whether this increased incidence of symptoms is due to natural aging processes or the operation is a matter of debate.

A study from Finland adds some clarity (Heliovaara-Peippo et al BJOG 2010;117:602-9). The researchers randomised women with a mean age of 43 years to either hysterectomy or the lev-

onorgestrel releasing intrauterine system (LN-IUS) for the management of the menorrhagia. Diligent follow-up over the next decade of their lives allowed deductions to be made as to the effect of hysterectomy on urinary tract symptoms. Detailed questionnaires were filled in at baseline, 6 and 12 months, 5 years and 10 years with over 90% of participants completing the programme.

They found that those allocated to hysterectomy had more urinary tract infections and used more medication for urinary incontinence than those treated with LN-IUS. The sensation of incomplete bladder emptying was also more common in the surgically treated women allowing the trial to conclude that a hysterectomy increases the risks of women experiencing incomplete emptying, lower urinary tract infections and stress incontinence.

### 8. Post-operative DVT

Men and women are at increased risk of venous thromboembolism postoperatively. This is well known and preventative measures should be used in all women undergoing major gynaecological surgery. Evidence is accumulating that the risk lasts longer than two weeks after surgery – and may extend to day-care surgery.

Sweetland et al (BMJ 2009;339:b4583) report on data derived from the UK Million Women Study and show that the risk of venous thromboembolism (VTE) reaches its peak 3 weeks after surgery and remains elevated for 12 weeks.

A middle-aged woman having an operation is 70 times more likely to be admitted to hospital with a VTE than someone not operated on. This is in the first 6 weeks after inpatient surgery and the risk is still present for another 6 weeks thereafter. These facts are "a wake-up call to all surgeons" say Cohen (BMJ 2009;339:b4477) because most prophylaxis is confined to hospital stays or the week thereafter, missing the most at risk period. Even the latest figures are probably an under-estimate as most VTEs are undiagnosed, untreated and managed outside of hospitals.

The UK National Institute for Health and Clinical Excellence (NICE) has published recommendations for all patients in hospital and estimate only half of those who should received prophylaxis actually get it. The summary by Hill et al (BMJ 2010;340:C95) enumerates the following risk factors: cancer patients, age over 60 years, admission to critical care, dehydration, thrombophilia, obesity, common comorbid medical conditions such as heart disease, metabolic, endocrine or respiratory pathology, infections or inflammatory diseases, a personal or close family history of VTE, hormone use or smoking.

Preventative strategies include practical measures of mobility and hydration, mechanical devices to aid circulation plus drugs like low molecular weight heparin (or unfractionated heparin). These drugs should be continued till "the patient is no longer at increased risk of VTE". Given the most recent data this is clearly longer than has previously been thought. It is essential that the active discharge management should be given to every woman leaving hospital after surgery.