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ORAL MISOPROSTOL FOR LABOUR INDUCTION

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Oral misoprostol as an induction agent is effective at achieving vaginal delivery, and may have benefits over both vaginal and intra-cervical dinoprostone. Although oral misoprostol does not achieve vaginal delivery as quickly as vaginal misoprostol, the rates of hyperstimulation are lower when using comparable doses. Given that the primary consideration should be safety of induction rather than speed, the oral regimens (using a maximum of 50 mcg) are recommended as the optimal route of administration. This is especially important in situations where the risk of ascending uterine infection is high and staffing levels often result in less than optimal monitoring of induced labour (i.e. not having one-to-one care and/or electronic fetal monitoring).

The relatively high rate of uterine hyperstimulation that is seen even with relatively low doses remains a worry. Although the trials so far (which include over 8 500 women) have not shown any increase in adverse fetal outcomes, much more data are needed before we can be confident that there are really no adverse fetal effects. This is true for all prostaglandin induction agents including currently licensed products.

CERVICAL CERCLAGE

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Several observational studies in the last 50 years have claimed high rates of successful pregnancy outcome in women who had a poor obstetric history attributed to cervical incompetence in whom cerclage was used. Our recent Cochrane review of randomised trials analysing outcomes including miscarriage, perinatal loss, maternal infection, minor maternal morbidity, major maternal morbidity, antepartum haemorrhage, and preterm delivery found no conclusive evidence of benefit. Significant statistical heterogeneity was present for some of the important clinical outcomes including preterm delivery and maternal infection. Possible explanations for this heterogeneity are the inconsistency in the clinical definitions employed in the trials, including the cut-off for gestational age defining preterm delivery, and the different patient populations studied.

To address some of these concerns we have analysed more than 2 000 individual patient data obtained from the principal investigators of 9 randomised trials included in the original Cochrane review.

We confirmed that cervical cerclage tended to reduce neonatal mortality although the effect was not statistically significant. Importantly, there was no difference in the likelihood of a baby being healthy at discharge from hospital. The intervention appears to reduce the risk of preterm delivery to the same extent at all gestations but is also associated with an increased risk of maternal pyrexia.

Despite additional analyses, uncertainty regarding the true effectiveness of elective cervical cerclage persists.

RECOMBINANT FACTOR VII AND MAJOR POSTPARTUM HAEMORRHAGE

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Major haemorrhage during pregnancy and after delivery is the commonest cause of maternal morbidity and mortality worldwide. The World Health Organisation estimated that 585 000 maternal deaths occur annually, of which around 25% are due to severe bleeding. In addition, an annual total of 20 million significant maternal morbidities result from haemorrhage. Even in the developed world, major postpartum haemorrhage (usually defined as > 1 000 ml) occurs in 1 - 6% of deliveries.

If established medical therapy and conservative surgical measures fail, the usual last resort is hysterectomy, which is itself associated with significant medical and psychological morbidity. Alternative approaches are constantly being sought, and recombinant activated factor VII (rFVIIa), a potent haemostatic agent used to control bleeding in haemophilic patients, is one of them. Recently its use has been extended to control life-threatening bleeding in surgery, trauma and postpartum haemorrhage.

These is a growing number of reports in the literature that rFVIIa – often in a single dose – can produce dramatic reductions or cessations of bleeding under these circumstances, so it is hardly surprising that clinicians are increasingly acting upon the advice of a recent editorial in the *Journal of the American College of Obstetricians and Gynecologists* that 'desperate hemorrhagic circumstances should prompt us to think of rFVIIa'.

We will present the difficulties in setting up controlled clinical trials of factor VII for major postpartum haemorrhage and efforts to gather data from isolated cases in a systematic manner to inform clinical practice.

DOES ANEUPLOIDY SCREENING IMPROVE OUTCOME OF ASSISTED REPRODUCTION TECHNOLOGY?

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Preimplantation genetic diagnosis (PGD) is an early alternative to prenatal diagnosis (PND) and is suitable for a small group of patients who are at substantial risk of conceiving a pregnancy affected by a known genetic disorder. To label PGD the pursuit of 'designer babies' is to misunderstand its methodology, and the serious and often lethal genetic diseases that can be prevented by its use. This technique may be helpful for those patients who are childless as a result of recurrent miscarriage caused by an inherited rearrangement of their chromosomes, such as reciprocal or Robertsonian translocation, especially where the translocation has caused severe reduction in sperm quality.

Whereas PGD tests for a known genetic abnormality with a high transmission rate, usually in fertile couples, the techniques of embryo biopsy and chromosome testing have been extended in order to try to improve likelihood of successful pregnancy

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in infertile couples. For those already being treated by IVF or ICSI, PGS (preimplantation genetic screening or aneuploidy screening), is employed in an effort to detect and thus not to replace embryos carrying some of the common sporadic or age-related chromosome abnormalities that may prevent implantation, promote miscarriage, or result in liveborn but disabled offspring. Despite the high expectations of this technique, improvement in outcome for the older patient, or those with implantation failure, largely has not been realised when subjected to rigorous scrutiny.

Additional reading

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THE PROMISES AND PITFALLS OF HUMAN STEM CELL THERAPY

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The use of human embryonic stem cells is being hailed as the next major step in the battle against serious degenerative disorders like diabetes, heart disease and some neurological diseases. Reading promotional material on websites and news reports conveys the impression that this therapy is now available or imminently so.

Derivation of human embryonic stem cell lines has increased dramatically in the past two years, despite either total bans in some countries, or partial bans on use of embryos in others. Fortunately some other countries have been foresighted enough to see the potential in these therapies, and allowed regulated embryo research.

There are however still major hurdles to be overcome that will require substantial investment and research. The growth of stem cells under pharmaceutical GMP conditions is yet to be achieved. Surprisingly, even the embryos from which they would be derived are still cultured in the presence of human or animal products. The premature use of cell therapy could put many patients at risk of major viral or prion illness unless appropriate tests and quality systems are put in place. The lessons of the premature application gene therapy, and the huge disaster of HIV in the haemophiliac population, should not be forgotten. Animal experiments need be conducted to further understand destination, integration and risks of neoplasia, but the transfer of human stem cells into animal hosts has also caused substantial ethical disquiet.

A logical progressive approach to the development of lines and their rational therapeutic use is required for this promising therapy to be realised. The danger is that the drive to be first could see it spiral into the realms of quackery and fraud, as demonstrated by the recent scientific fraud in Korea in this area.

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PREIMPLANTATION GENETIC DIAGNOSIS AS AN ALTERNATIVE TO PRENATAL DIAGNOSIS

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Preimplantation genetic diagnosis (PGD), the removal of a single cell for genetic testing during preimplantation development *in vitro*, has become an established alternative to prenatal diagnosis (PND) for couples carrying **recurrent genetic conditions** that may affect their offspring. The advantage of PGD over PND is that it allows diagnosis prior to implantation, thus avoiding the initiation of an affected pregnancy and the couple being faced with the difficult decision about terminating a wanted pregnancy. PGD is relatively expensive, is technically demanding and is time-consuming. It is therefore a procedure offered only in a few specialised centres worldwide. To be successful, it requires close collaboration between clinicians and scientists specialising in assisted reproduction technology (ART), clinical geneticists, molecular and cytogeneticists, and clinicians from other specialities. Clinicians need to be aware of what can and cannot be delivered by the technology, and especially to appreciate the real success in terms of live birth rate per cycle started, a denominator not often given in results tables. Generally, these couples are fertile and are not in need of assisted conception technology other than for the PGD. Thus the decision that must sometimes be faced is whether to embark on the easier route to conception, but with the risk of termination thereafter, or to accept a reduced chance of pregnancy because of the need for ART, but if successful, the likelihood of unaffected offspring.

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MODERN MANAGEMENT OF THE AZOOSPERMIC MALE

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Azoospermia (absence of sperm from the semen) can be caused by hypothalamic-pituitary failure, testicular failure, or testicular obstruction. Testicular size and concentration of follicle-stimulating hormone determine the clinical diagnosis. Although azoospermia is uncommon, 75% of men with the condition now have the opportunity of biological fatherhood through assisted conception techniques.

Since pregnancy can be achieved with very few sperm using ICSI, it now behoves both gynaecologists and urologists to be aware of the appropriate means for diagnosing aetiology, and the methods for retrieving and preserving even small numbers

of mature sperm. They should also be aware of the genetic conditions that may cause azoospermia, such as cystic fibrosis, Kleinfelter syndrome and certain Robertsonian translocations, and that PGD can be used to prevent transmission of these to resulting offspring.

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IMPROVED FETAL GROWTH – THE ROAD TOWARDS MACROSOMIA

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While macrosomia may suggest excellent fetal growth, a pregnancy with a big baby is not good news. Complications include cephalopelvic disproportion requiring caesarean section, uterine rupture, shoulder dystocia, infant brachial plexus injury and increased neonatal mortality. Macrosomia is most frequently defined as a birth weight of 4 000 g or more. The frequency of such births varies from 3% in sub-Saharan Africa, to 10% in the United Kingdom, and 20% in Denmark. Other associations with macrosomia include prolonged pregnancy, increased maternal weight and pregnancy weight gain, increased parity, maternal diabetes mellitus and glucose intolerance, and a male fetus.

Primary prevention of macrosomia could be achieved by promoting exercise and judicious eating in women. Treatment of gestational diabetes is effective in reducing the rate of macrosomia. Induction of labour to prevent birth of a large baby may prevent macrosomia but is of no clinical value.

If macrosomia can be detected before the onset of labour, or even during labour, complications can theoretically be anticipated and averted. Prediction of macrosomia is inaccurate, however, with no advantage with ultrasound as opposed to a clinical estimate. No useful symphysis-fundal height cut-off has been described as a simple clinical screen. Elective caesarean section for women with suspected macrosomia, to prevent shoulder dystocia and brachial plexus injury, is frequently performed but may do more harm than good. The threshold for elective caesarean section can however be lowered in women with diabetes mellitus and in those with a previous history of shoulder dystocia.

Most research on the prediction and management of suspected macrosomia has been done in the USA. In view of the high frequency of pelvic contraction in sub-Saharan Africa, local recommendations will have to be made based on local research and experience.

MANAGEMENT OF ACUTE HYPERTENSION IN PREGNANCY

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Presentation of a pregnant woman with a blood pressure ≥ 160/110 mmHg is an obstetric emergency. Severe hypertension associated with pre-eclampsia or eclampsia is associated with stroke, pulmonary oedema, acute renal failure, HELLP syndrome, abruptio placentae and fetal anoxia. Treatment with antihypertensives may reduce the risk of stroke.

Women with severe hypertension should be transferred immediately to hospitals that have appropriate facilities. Administration of magnesium sulphate for transfer to hospital is probably sufficient, as additional antihypertensives may be unsafe given in an uncontrolled environment.

Acute hypertensive crises in pregnancy must be treated in a properly equipped high-care area. There should be a complete clinical assessment, with testing for platelet count, renal function and liver enzymes, and fetal assessment while starting specific management. Magnesium sulphate is indicated for patients who have proteinuria or other evidence of pre-eclampsia. Antihypertensive drugs are used as emergency agents if the BP exceeds 160/110 mmHg. Intravenous hydrallazine is not easily obtained in South Africa and many institutions have had to revise their protocols. Oral nifedipine and intravenous labetalol seem to be the most suitable agents. Diazoxide and sodium nitroprusside are not advised. Nicardipine is an intravenous calcium channel blocker that has potential for the future. While a fluid bolus to precede drug therapy is advised, plasma volume expansion is not. Close monitoring of blood pressure response is mandatory, as excessive blood pressure reduction may result in fetal distress or maternal cerebral hypoperfusion.

Following initial control of the blood pressure, attention must be given to timing and mode of delivery, and maintenance antihypertensive therapy.

SEVERELY ILL OBSTETRIC PATIENTS: HOW FAR SHOULD WE GO?

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Despite advanced medical technology and better understanding of diseases, critical illness in pregnancy still poses a challenge. While some patients may have pre-existing disease, others develop conditions unique to pregnancy that can progress to such severity that the patient's life is threatened. It is estimated that 1 to 9/1 000 pregnancies may be complicated by acute and potentially fatal disorders directly related to physiological processes unique to pregnancy. HIV, on the other hand, complicates the situation further.

When confronted with such a situation, taking into account our ethical duty of caring, how does one draw boundaries in providing care for these severely ill patients? Often resources are a limiting factor and patients have to compete for the available resources – are there guidelines to help one handle such a situation? Should we advocate obstetric ICUs to maximise care for this unique group of patients?

A detailed look at these challenges will be the focus of discussion.

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SCREENING FOR OVARIAN CANCER

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In spite of an overall incidence of only about 1 - 4%, ovarian cancer remains a major reason for morbidity and death due to gynaecological cancer. The disease carries a poor prognosis, especially in the late stages at which the diagnosis is usually made.

The diagnosis of ovarian cancer, and specifically the radiological diagnosis of peritoneal involvement, remains very inaccurate even when this situation is suspected and when new and sophisticated radiological techniques are used. Biochemical tumour markers are very useful in the management of ovarian cancer. Ca-125 is now invaluable in the follow-up of epithelial ovarian cancer and is also used increasingly as a screening test. The test is more accurate after the reproductive years, used in conjunction with radiology. In the reproductive years differentiating benign and functional ovarian changes from early epithelial cancer is still notoriously difficult.

Considering the low incidence of the disease and difficulties with diagnostic modalities, screening for ovarian cancer in the general population and in low-risk population subgroups is generally unsuccessful. However, screening is indicated in high-risk subgroups and has been reported successful in terms of downstaging and some resultant improved survival.

Identifying high-risk groups and individuals who would potentially have a reasonable cost-benefit ratio can be difficult and is currently based mainly on the family history. It is expected that traditional family history criteria will identify at most 10% of ovarian cancer cases. If screening is expected to have an effect on the incidence or survival of ovarian cancer, it must therefore also be aimed at the medium-risk group. The very high morbidity and mortality rate of the disease may warrant such a screening programme, expected to have a very low yield.

Combining biochemical and radiological testing is currently recommended to have a reasonable sensitivity and specificity. Transvaginal ultrasound in combination with Ca-125 is used with intervals between 6 and 12 months, and often the two tests are alternated. Techniques using ovarian morphology, morphology indices, Doppler flow studies, ovarian volume measurements and three-dimensional ultrasound are all acceptable methods with comparable results. Other radiological tests have not been proven to have similar accuracy and are certainly not superior. Ca-125 measurements using both trend and an absolute value above 34 are done regularly and always following an abnormal ultrasound. More sophisticated diagnosis of sonographic anomalies and repeat ultrasound can often prevent unneccessary surgical exploration.

Defining the various risk categories and specific management guidelines for these groups will be discussed. The role of oophorectomy and the management of younger high-risk patients will also be further explored.

PREVENTING COMPLAINTS

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There is no easy or apparent solution for the medicolegal problems that pose a big threat to the discipline of Obstetrics and Gynaecology. There are, however, things that the practitioner can do to decrease risk for complaints or lawsuits.

In this presentation the complaints process with the HPCSA will be outlined as well as new steps put in place by the HPCSA to speedily deal with such matters.

Steps to be taken by the individual practitioner will be discussed. This will include the guidelines for ethical practice, notekeeping, communication skills, billing techniques and dealing with complications.

DATG AND SCREENING FOR BREAST CANCER

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As breast cancer has now become the most common cancer of women in South Africa, the absence of a screening programme has come under the spotlight more than previously. The inability of self-examination to increase the rate of diagnosis of breast cancer as shown in randomised controlled trials adds to this problem. In many developed countries there are guidelines on breast cancer screening utilising mammography and ultrasound to be used in certain age brackets. This is done with full understanding of the limitations of mammography: not useful in young women, difficult in women with dense breast tissue, and a fail-to-detect rate of up to 20%. Where high technology is readily available even MR screening is under consideration to improve on this situation. All this comes into perspective when mammography (potentially to be abandoned in some countries as a screening method) has not even been used in South Africa as a national screening tool.

DATG (dynamic angiothermography) is a relatively new screening tool for the detection of breast cancer and even *in situ* carcinoma. A film-coated plate is used to visualise the arteries of the breast by pressing the plate onto the breast. Abnormal vascular patterns appear (as part of angioneogenesis) where *in situ* and invasive cancers grow in the breast. The technique has been used for some years in Italy, where thousands of women have been screened this way. Currently this is the subject of comparative studies in South Africa, Brazil, France and New Zealand. In Pretoria a SA Menopause Society-supported study on peri- and postmenopausal women is in progress as well as a study on high-risk women with BRCA abnormalities or a family or own history of breast cancer where DATG is compared with mammography. The technique as well as the available data will be presented.

DATG is a simple technique with almost no patient discomfort, and it has a very high detection rate with high specificity. Pending confirmatory results from the international and local studies, this technique may prove very valuable for breast cancer screening.

HOW SHOULD WE SCREEN FOR GESTATIONAL DIABETES?

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Should we screen for gestational diabetes? This question has recently been answered with the study published by Crowther et al. In a randomised controlled trial they randomised women with gestational diabetes to treatment or no treatment. Their conclusion was that treatment of gestational diabetes reduced serious perinatal morbidity and may also improve women's health-related quality of life.[1]

This leads to a new problem, namely what is the best way to screen for gestational diabetes? There are different screening methods and cut-off values, all supported by leading expert panels and organisations. The oral glucose tolerance test (OGTT) is regarded by many as the gold standard diagnostic test. In a study published by Agarwal *et al.* they used the

75 g OGTT and applied the diagnostic criteria of six well-accepted expert panels to diagnose gestational diabetes. They concluded that these guidelines showed major discrepancies in the ability to diagnose women with gestational diabetes.[2] Some authors felt there should be different cut-off values for different ethnic groups. Their study used a 100 g OGTT and showed that African Americans had the highest positive predictive value and whites the lowest positive predictive value throughout the range.[3] A new diagnostic tool for gestational diabetes might be the measurement of insulin in early pregnancy while doing a 75 g OGTT in women who had one or more risk factors for gestational diabetes. An increased fasting insulin value above 30 mU/l and an increased 2-hour value above 70 mU/l indicted an increased risk of developing gestational diabetes, even with a normal OGTT at less than 16 weeks.[4] Agarwal and co-workers evaluated an alternative cost-effective and patient-friendly test. They concluded that an abbreviated 100 g OGTT doing a fasting plasma glucose > 5.3 mmol/l and 2-hourly > 8.6 mmol/l had a sensitivity of 98.5% and a specificity of 84.7%. For a fasting plasma glucose > 5.6 mmol/l and 2-hourly > 8.6 mmol/l, sensitivity was 92.5% and specificity 89.3 %.[5]

All this studies illustrate the problem the practising obstetrician faces. Although it is necessary to make the diagnosis of gestational diabetes, there is currently no clear gold standard that is practical for use in practice. Until a test has been proven with large trials the obstetrician should decide on a screening test knowing the sensitivity, specificity and predictive values of the test. Another issue is whether wide-based screening or risk-based screening should be followed. The answer to this depends on the available resources. The risk-based screening is possibly more appropriate for the public health sector. The future lies in identifying a good screening test and not debating whether we should be screening.

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CAESAREAN SECTION 2006

A P Macdonald

Caesarean section (CS) rates have been have been escalating rapidly over the past 10 years, causing concern to obstetric governance and those responsible for funding. These changes have occurred without improvement in maternal and perinatal mortality or morbidity rates and have therefore been difficult to justify obstetrically.

The reasons for the rising CS rate (patient request, breech presentation, twin pregnancy, delivery after caesarean section, convenience and defensive obstetrics) will be discussed.

The evidence relative to the safety and short- and long-term complications of vaginal and CS delivery will be summarised. While there are differences, these are rare occurrences that will not dictate that one delivery method is safer. One of the difficulties is that information is available for single aspects but it is impossible to obtain an overview that proves comprehensively that vaginal birth or CS is superior.

Various interventions have been suggested to attempt to bring the rate down to internationally accepted norms without success. It is possible that medical insurances will attempt to curb the rising rate by not paying for CS done for non-obstetric indications (as is the case with cosmetic surgery), and this will be implemented by profiling practices using the Robson classification for CS. This possible intervention will be discussed.

It is unlikely that the CS rate will come down, and current trends will become accepted practice.

MANAGING THE PREGNANT WOMAN WITH HIV/AIDS

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HIV infection is one of the most commonly encountered conditions in pregnancy in South Africa. HIV-infected women must be assessed and treated appropriately for their own infection, and to reduce the risk of mother-to-child transmission of HIV (MTCT).

Women who require ongoing highly active antiretroviral therapy (HAART) for their own health should receive this during pregnancy, which will also be very effective in preventing transmission. Where resources allow, combination HAART can also be used for preventing MTCT in those women who do not yet need to receive ongoing treatment. Concerns remain about the choice of regimen and potential side-effects of HAART regimens.

Significant reductions in the rates of transmission of HIV from mother to child have been achieved with increasing complexity of antiretroviral regimens in pregnancy in developed countries. With the use of HAART through pregnancy, and avoidance of breastfeeding, transmission rates have dropped to below 2%.Where such treatment is feasible, the almost complete eradication of perinatal HIV infection is possible in identified HIV-positive pregnant women, and the current challenge is to ensure early access to HIV testing and care for HIV-infected pregnant women, who are often marginalised and in vulnerable circumstances. Routine HIV testing ('opt-out') testing in pregnancy has been promoted as a way to achieve this.

Despite these advances, mother-to-child transmission of HIV (MTCT) is responsible for 1 800 new infections in children daily across the world. Where HAART is not possible, a dual combination regimen of antepartum zidovudine with single-dose nevirapine to mother and baby can reduce transmission to below 5%. In many places the only available option is single-dose nevirapine to mother and baby, which is effective in halving transmission risk, although the effectiveness in practice will be influenced by continued infection through breastfeeding and by programme factors such as uptake of HIV testing. Exposure to nevirapine for MTCT prevention can select for resistant virus in the majority of women. While the long-term implications of this are not completely clear, this selection can be reduced by the addition of short courses of postpartum zidovudine and lamivudine.

THROMBOPHILIAS AND FETAL LOSS

Claire McLintock

An estimated 15% of confirmed pregnancies end in miscarriage, but recurrent fetal loss, i.e. loss of > 3 pregnancies, affects only 1 - 2% of couples. After excluding genetic, anatomical, endocrine, infective and immune mechanisms, in 75% of couples the aetiology of recurrent miscarriage is unknown. The placenta in some, but not all, pregnancies complicated by fetal loss shows evidence of thrombosis and infarction. However, placental thrombosis is unlikely to explain all cases of fetal loss, especially early loss as the maternal spiral arteries are blocked by cells of placental origin, trophoblasts, until 10 - 12 weeks' gestation. However, while thrombotic mechanisms

may not explain all cases of placental insufficiency leading to fetal loss, procoagulant mediators such as thrombin may affect placental development by augmenting the inflammatory response. Recent studies using animal models also suggest that protein C plays a key role in early placental development.

Thrombophilia describes an increased tendency to form clots and in about 50% of individuals who experience venous thrombosis we can demonstrate a procoagulant laboratory marker, such as factor V Leiden, the prothrombin gene mutation. These markers can be either inherited or acquired. Given the evidence for thrombosis complicating cases of fetal loss, there have been a multitude of studies examining the association between fetal loss and laboratory markers of thrombophilia. Systematic review of these studies suggests that women who have experienced fetal loss, especially late loss or stillbirth are more likely to have a laboratory marker of thrombophilia than women who have uncomplicated pregnancies (Table I).

The inclination to translate Odds Ratio into Relative Risk – viz. a woman with late fetal loss is 2.7 times more likely to have factor V Leiden, ergo all women with FVL are 2.7 times more likely to have a late fetal loss – as well as being statistically inaccurate, is not confirmed in prospective studies of general obstetric populations.

There is an increasing tendency to test all women with fetal loss for laboratory markers of thrombophilia, without good evidence that the presence of a thrombophilia marker increases a woman's risk of recurrent loss. Similarly, assumptions are being made that a woman who has experienced fetal loss and has a thrombophilia marker requires different treatment to a woman with the same obstetric history but no thrombophilia marker. Studies of women who have experienced fetal loss and have positive antiphospholipid antibodies have shown no improvement in pregnancy outcome with low-dose aspirin alone, but randomised clinical trials have demonstrated benefit with the addition of heparin. To date there are no data from randomised clinical trials that show benefit in women

Table I. Systematic review of prevalence of laboratory markers of thrombophilia in women with fetal loss compared with women with uncomplicated pregnancy (not all studies allowed sub-categorisation to examine gestation fetal loss occurred)

Thrombophilia	Complication	Studies (N)	Cases (N)	Controls (N)	OR (95% CI)
APCR	Fetal loss (all gestations)	14	2 439	1686	3.3 (2.5 - 4.3)
	Early fetal loss	4	1 066	409	1.7 (1.1 - 2.7)
	Late fetal loss	7	594	961	3.3 (2.3 - 4.8)
	Stillbirth	3	262	522	3.2 (1.7 - 6.2)
FVL	Fetal loss (all gestations)	44	4 722	1 296	2.6 (2.2 - 3.0)
	Early fetal loss	13	1 812	1 296	1.7 (1.3 - 2.3)
	Late fetal loss	19	1 054	2 363	2.7 (2.0 - 3.6)
	Stillbirth	13	640	1 646	2.7 (1.9 - 3.9)
Hyperhomocysteinaemia	Fetal loss (all gestations)	3	198	178	3.9 (1.8 - 8.2)
	Early fetal loss	1	59	70	4.2 (1.3 - 3.9)
	Late fetal loss	1	18	44	1.0 (0.2 - 5.6)
	Stillbirth	1	18	44	1.0 (0.2 - 5.6)
5,10-MTHFR	Fetal loss (all gestations)	26	2 119	3 166	1.3 (1.1 - 1.6)
	Early fetal loss	6	438	467	1.2 (0.8 - 1.9)
	Late fetal loss	11	603	1 437	1.4 (1.1 - 1.9)
	Stillbirth	10	571	1 315	1.4 (1.1 - 1.9)
PT20210	Fetal loss (all gestations)	32	2 665	4 034	2.0 (1.5 - 2.5)
	Early fetal loss	9	808	981	2.2 (1.3 - 3.6)
	Late fetal loss	15	765	2 018	2.3 (1.5 - 3.5)
	Stillbirth	13	642	1 788	2.2 (1.4 - 3.2)
AT deficiency	Fetal loss (all gestations)	11	1 284	1 389	1.4 (0.5 - 3.5)
	Early fetal loss	0	0	0	Not estimable
	Late fetal loss	6	414	773	1.6 (0.2 - 0.3)
	Stillbirth	5	374	693	1.6 (0.2 - 0.3)
Protein C deficiency	Fetal loss (all gestations)	10	1 266	1 345	2.5 (0.8 - 8.0)
	Early fetal loss	0	0	0	Not estimable
	Late fetal loss	5	396	729	2.2 (0.4 - 2.1)
	Stillbirth	4	362	649	2.2 (0.4 - 2.1)
Protein S deficiency	Fetal loss (all gestations)	11	1 274	1 308	3.1 (1.8 - 5.2)
	Early fetal loss	0	0	0	Not estimable
	Late fetal loss	6	414	773	3.7 (1.7 - 6.9)
	Stillbirth	5	380	693	3.4 (1.6 - 7.1)

Early loss: 1st trimester loss; Late loss: 2nd or 3rd trimester loss; Stillbirth: > 20 - 24 weeks (definitions vary among studies).

Claire McLintock – unpublished data.

with fetal loss without antiphospholipid antibodies, but the SPIN study, being run in centres in the UK and Auckland, aims to compare the effect of intensive surveillance with or without low-dose aspirin and enoxaparin, 40 mg in women who have had two or more previous pregnancy losses prior to 24 weeks.

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MODERN SLING TECHNIQUES FOR TREATMENT OF URINARY STRESS INCONTINENCE

A Smith

Sling techniques for surgical treatment of stress incontinence have been described for over a century. The literature indicates that slings are effective, but often techniques described involved complex, extensive surgery that in some reports carried a higher risk of postoperative voiding dysfunction than other procedures. The introduction of the tension-free vaginal tape (TVT), based on a new theory of the mechanism of stress incontinence, has radically changed the surgery of stress incontinence, although the technique is in reality simply an evolution of previous techniques. The evidence to support this change in surgical practice will be discussed. The introduction of numerous 'me-too' slings will be discussed. The introduction of trans-obturator slings has produced a further change in practice. The evidence to support this change will be critically reviewed.

MANAGEMENT OF UTERO-VAGINAL PROLAPSE

A Smith

Prolapse and its management was first described in Egyptian writings 4 000 years ago. Surgical treatment has only been described during the last 150 years. This lecture will describe the evolution of conservative and surgical treatment of prolapse and illustrate how this influences present-day approaches. A third of pelvic floor reconstructive procedures fail to produce long-lasting anatomical cure, and more recent studies evaluating functional outcome and quality of life issues have provided further insight into the limitations of surgical treatment. Reasons for the failure of surgery will be discussed. Clarification of the definition of prolapse using structured examination techniques (Pelvic Organ Prolapse Quantification Questionnaire, POPQ) and improvement of the understanding of the aetiology of prolapse should enable treatment to be modified. The relationship between pelvic floor anatomy and lower urinary, gastro-intestinal tract and sexual function is still poorly understood. The lecture will discuss why and how our management needs to be refined to improve functional outcome from our treatment.

NEW DEVELOPMENTS IN THE SURGICAL MANAGEMENT OF VAGINAL PROLAPSE

A Smith

Anatomical failure following surgical treatment is reported in a third of cases, and this may represent an underestimate of reality. The reasons for failure are probably multiple, but weakness of the supporting tissues used in reconstructive surgery is relevant in a substantial proportion of cases. Reconstructive surgery has for many years employed tissue implants from other parts of the body, cadavers and other animals to improve the quality of the repair. In recent years synthetic meshes have been used more frequently and mesh development has resulted in changes to materials aiming to produce a repair more suited to the vagina. More extensive mesh repairs have now been introduced that may radically change our approach to pelvic reconstructive surgery. Such a change needs careful evaluation, and the risks of widespread adoption before robust clinical studies have been performed will be discussed.

CHALLENGES FACING SURGICAL INNOVATION

A Smith

This lecture will describe the life and work of J Marion Sims, one of the father figures of gynaecological surgery. Sims's pioneering work in surgery has been both lauded and more recently criticised on account of some of the ethical issues viewed rather differently today. The lessons from the life and work of Sims will be analysed in the context of modern practice, in particular the introduction of new surgical techniques and devices. Regulation of the pharmaceutical industry and the medical device industry will be compared. How clinical governance is managed, and how regulation, public scrutiny and attitudes towards the medical profession are changing, will be discussed.

THE MODERN GYNAECOLOGICAL CONSULTATION

L Snyman

Many women present to gynaecologists in private practice on a regular basis for a so-called routine gynaecological examination. It is not known what proportion of patients go for routine gynaecological check-ups in South Africa, but it does form a significant proportion of the non-obstetric duties performed by gynaecologists in private practice. There are numerous reasons motivating patients to undergo routine gynaecological examinations. Whatever the reasons might be, it is a golden opportunity for the identification of health risks and early intervention that can make huge differences to women's health, especially after the menopause.

What exactly are the boundaries of a routine gynaecological examination? The impact that can be made on women's health in a holistic approach towards this type of routine examination is far reaching compared with an approach defined by boundaries defined by the female genital tract.

Gynaecologists are in the fortunate position of regularly seeing healthy patients who prefer to have routine examinations. It is our responsibility to holistically assess these patients in an effort to identify all their health-related problems and risks. The routine gynaecological examination in this day and age should not be restricted to the boundaries as defined by

the female genital tract, but it should only be defined by the patient's health needs.

THE ROLE OF SPECIAL INVESTIGATIONS IN UROGYNAECOLOGY

P Swart

The diagnosis of POP is based on the clinical examination and the use of the POP Quantification system (POPQ). Additional imaging methods are of limited value. Ultrasound is useful for identifying the anatomy of the bladder neck and anterior or posterior vaginal wall prolapse, but the technique is limited to use in patients with genital prolapse beyond the hymeneal ring . Magnetic resonance imaging is an excellent radiological tool for the assessment of prolapse. On an everyday basis, however, no advantage has been found over a careful history and physical examination. Its use is mainly experimental or in complex prolapse cases.

Women with severe POP may also have stress urinary incontinence. Whether this needs to be investigated with urodynamic evaluation is controversial; it is probably unnecessary. It is crucial to understand though that if the diagnosis is uncertain, when you are going to perform repeat surgery and if the patient leaks at very low pressures urodynamic evaluation is mandatory for a number of reasons. When anti-incontinence surgery is to be performed in the absence of hypermobility it would also be wise to use urodynamics to try to diagnose intrinsic sphincter deficiency.

PROPHYLAXIS IN THE PATIENT UNDERGOING GYNAECOLOGICAL SURGERY

Piet Wessels

We need to briefly answer four questions regarding this issue:

A. Why do we need to give prophylaxis? Are there specific issues different in gynaecological patients?

B. Which prophylactic measures are appropriate?

C. When should we start prophylaxis?

D. How long should prophylaxis be continued?

A. Why do we need to give prophylaxis?

Risk factors to consider in patients undergoing surgical procedures[1]

- *Stasis:* Increased age, previous thrombosis, surgery, pregnancy, puerperium, immobility, paresis, trauma (major or lower extremity), acute medical illness, heart or respiratory failure.
- *Endothelial damage:* Increased age, previous thrombosis, oobesity, smoking, varicose veins, previous VTE, central venous catheterisation.
- *Hypercoagulability:* Inherited or acquired thrombophilia, pregnancy and the postpartum period, antiphospholipid syndrome, underlying malignancies, cancer therapy (hormonal, chemotherapy, or radiotherapy), oestrogen-containing oral contraception or hormone replacement therapy, inflammatory bowel disease, nephrotic syndrome, myeloproliferative disorders, paroxysmal nocturnal haemoglobinuria.

Are there specific issues different in gynaecological patients?

- Rates of DVT, PE, and fatal PE comparable to those seen after general surgical procedures.[2]
- Specific factors appear to increase the risk of VTE following gynaecological surgery:
  - previous VTE,
  - older age
  - malignancy
  - prior pelvic radiation therapy
  - an abdominal surgical approach.[3]
  - Hormonal therapy plays an important additional role

B. Which prophylactic measures are appropriate?

1. *Aspirin:* Grade 1a recommendation: We recommend *against* the use of aspirin alone as prophylaxis against VTE for any patient group.[1]
2. *Warfarin:* Practical issues regarding individual response, drug interactions, side-effects.
3. *Mechanical prophylaxis.* We recommend that mechanical methods be used primarily in patients who are at high risk of bleeding (**grade 1C+**) or as an adjunct to anticoagulant-based prophylaxis (**grade 2A**), and also that careful attention be directed toward ensuring the proper use of, and optimal compliance with, the mechanical device (**grade 1C+**).[1]
4. *LMWH and unfractionated heparin:* drugs of choice. Anti-FX activity levels to monitor (pregnancy, children, renal failure and obese).

C. When do we need to start prophylaxis?[4]

- Pre-operative initiation is not required for good efficacy. If < 2 h: increases major bleeding.
- Initiation > 6 h postoperatively effective, not associated with increased major bleeding.
- Initiation < 6 h postoperatively increases major bleeding, without improved efficacy.
- Initiation 12 - 24 h postoperatively may be less effective than at 6 h.

Most work has been done in orthopaedic surgery.

For major orthopaedic surgical procedures, we recommend that a decision about the timing of the initiation of pharmacological prophylaxis be based on the efficacy-to-bleeding tradeoffs for that particular agent (**grade 1A**). For LMWH, there are only small differences between starting preoperatively or postoperatively, and both options are acceptable (**grade 1A**).[1]

D. How long should prophylaxis be continued?

For major gynaecological procedures, we suggest that prophylaxis continue until discharge from the hospital (**grade 1C**). For patients who are at particularly high risk, including those who have undergone cancer surgery and are > 60 years of age or have previously experienced VTE, we suggest continuing prophylaxis for 2 to 4 weeks after hospital discharge (**grade 2C**).[1]

Prolonged secondary prophylaxis in a subset of patients:[5]

- male gender
- increasing patient age
- and increasing body mass index
- neurological disease with extremity paresis, and
- active malignancy
  - Inherited thrombophilia (PS, PC, AT)
  - antiphospholipid syndrome as well as possibly
  - persistent residual deep-vein thrombosis.

Table. Group-specific prophylaxis summary for the surgical patient[1]

Level of risk	DVT, % calf	DVT, % proximal	PE, % clinical	PE, % fatal	Successful prevention strategies
Low risk					
Minor surgery in patients < 40 yrs with no additional risk factors	2	0.4	0.2	< 0.01	No specific prophylaxis; early and 'aggressive' mobilisation
Moderate risk					
Minor surgery in patients with additional risk factors Surgery in patients aged 40 - 60 yrs with no additional risk factors	10 - 20	2 - 4	1 - 2	0.1 - 0.4	LDUH (q12h), LMWH (≤ 3 400 U daily), GCS, or IPC
High risk					
Surgery in patients > 60 yrs, or age 40 - 60 with additional risk factors (prior VTE, cancer, molecular hyper-coagulability)	20 - 40	4 - 8	3 - 4	0.4 - 1.0	LDUH (q8h), LMWH (> 3 400 U daily), or IPC
Highest risk					
Surgery in patients with multiple risk factors (age > 40 yrs, cancer, prior VTE) Hip or knee arthroplasty, HFS Major trauma; SCI	40 -80	10 - 20	4 - 10	0.2 - 5	LMWH (> 3 400 U daily), fondaparinux, oral VKAs (INR, 2 - 3), or IPC/GCS + LDUH/ LMWH

Summary on recommendations for gynaecological patients undergoing surgery:

- Brief procedures of ≤ 30 minutes for benign disease: we recommend against the use of specific prophylaxis other than early and persistent mobilisation (**grade 1C**).
- Laparoscopic gynaecological procedures, in which additional VTE risk factors are present: we recommend the use of thromboprophylaxis with one or more of the following: LDUH, LMWH, IPC, or GCS (**all grade 1C**).
- Thromboprophylaxis be used in all major gynaecological surgery patients (**grade 1A**).
- Major gynaecological surgery for benign disease, without additional risk factors: we recommend LDUH, 5 000 U bid (**grade 1A**). Alternatives include once-daily prophylaxis with LMWH, 3 400 U/d (grade 1C), or IPC started just before surgery and used continuously while the patient is not ambulating (**grade 1B**).
- Extensive surgery for malignancy, and for patients with additional VTE risk factors: we recommend routine prophylaxis with LDUH, 5 000 U tid (**grade 1A**), or higher doses of LMWH (i.e. 3 400 U/d) (**grade 1A**). Alternative considerations include IPC alone continued until hospital discharge (**grade 1A**), or a combination of LDUH or LMWH plus mechanical prophylaxis with GCS or IPC (**all grade 1C**).
- Major gynaecological procedures: we suggest that prophylaxis continue until discharge from the hospital (**grade 1C**). For patients who are at particularly high risk, including those who have undergone cancer surgery and are > 60 years of age or have previously experienced VTE, we suggest continuing prophylaxis for 2 to 4 weeks after hospital discharge (**grade 2C**).[1]

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