Cord blood collection

Should cord blood be collected for the future benefit of the child? The current debate about stem cell research has focused attention on cord blood, and commercial firms are cashing in by offering to collect and store cord blood for future purposes.

Companies are advertising collection as a biological insurance whereby the blood is kept for possible transfusion if the child develops leukaemia or some metabolic disease. Claims, which are currently speculative, suggest that future medical advances will enable the blood to be used to cure diseases such as diabetes, breast cancer, ovarian and testicular cancer, melanoma and rheumatoid arthritis or for the regeneration of damaged heart valves. More accurate predictions would be that better treatments for childhood leukaemias will be found that do not require autologous cells. In any event, donor cord blood can be used.

The scientific arguments are in fact pseudoscience in that they talk about future 'yet to be discovered' developments. Maybe there will be inventions that will need the patient's own cord blood, but research will be extremely difficult as trials testing 'own versus other' blood will be a recruiting nightmare. At present, the likelihood of stored blood being used is very low – quoted at between 1 in 1 400 and 1 in 20 000 (Edozien, *BMJ* 2006; 333: 801-804).

The Royal College of Obstetricians and Gynaecologists says storage cannot be recommended because of insufficient scientific evidence and logistic problems. The American and Canadian Colleges are also critical of the process, as are midwifery, paediatric and ethical bodies. There are also medico-legal issues, like whose responsibility is it to take the blood, ensure it is free of contamination, obtain consent to its collection, and correctly label it, store it, and test it for viral and other dangers? To whom does the blood belong – mother or child? Does the collection process take priority over other labour ward procedures?

It is clear that it cannot be a routine practice, but should those with sufficient resources be advised to pay for it? Parents-to-be want the best for their unborn child and can be considered vulnerable to promotion of this 'just in case' philosophy. Yes, personal cord blood may be useful in future situations, but at present it is more likely that other measures will overtake autologous transfusions. Medical science says 'no' right now, but there are other sciences and other beliefs, so it is up to individuals to decide whether recommending cord collection is medical paternalism or the way of the future.

It sounds more like a get-rich venture for the companies selling the idea than sound advice.

When to clamp the cord

It appears that the practice of early cord clamping is about to change. Traditionally, midwives and doctors clamp the cord immediately after delivery and pass the baby off as soon as possible, but there is little evidence that this unnatural practice has any benefits to the baby. All studies from developing countries show that at 6 months of age infants who had delayed cord clamping had better haematological parameters than those who had early cord clamping (van Rheenan and Brabin, *BMJ* 2006; 333: 954-958). Superior iron stores from the placental blood reaching the neonate lead to less anaemia and improved childhood survival in resource-poor settings.

The authors recommended 3 minutes' delay from delivery to clamping with the infant at the same level as the mother (± 10 cm). Lowering the baby speeds blood crossing from the placenta.

There are various theoretical objections to delayed cord clamping, but these are dealt with as follows:

- Preterm infants may be polycythaemic and could be at risk from hyperbilirubinaemia if extra blood crosses to the neonate. There is no evidence from trials to support this possibility, and no infants required phototherapy in the studies published.
- Growth-restricted fetuses can be polycythaemic from chronic hypoxia, but again the trials of delayed clamping show no adverse effects. In developing countries such babies have low ferritin levels, strengthening the case for delayed clamping.
- The active management of the third stage of labour could be compromised by delayed clamping. The use of oxytocics to reduce blood loss is not affected by delayed clamping and the combination is beneficial to mother and baby.
- When neonatal resuscitation is needed, delayed clamping is also acceptable. When assisted ventilation is required, this decision is usually taken at 60 seconds, during which time the infant should be placed between the mother's legs and oxygen given.

A strong case for delayed clamping at 3 minutes can be made for all deliveries in developing countries. The marginal benefits in wealthier nations may mean resistance to changing entrenched labour ward habits, despite the fact that early clamping is an artificial intervention. It will be interesting to watch institutional responses to this new information.

Acute uterine bleeding

There is surprisingly little written about the management of acute uterine bleeding. Excessive bleeding that is unrelated to pregnancy is a fairly common occurrence in premenopausal women and can occur as part of an irregular cycle or unexpectedly in a woman with an otherwise normal menstrual pattern. The definition of excessive bleeding is not volume dictated, but rather sufficient loss to require urgent or emergency management.

The correct approach after excluding gestationally related problems is to question the patient about drugs and bleeding dysfunction, exclusion of a local cause and basic haematological tests. Following a normal gynaecological examination, endometrial sampling and/or ultrasound investigation may or may not be deemed appropriate. If the patient is haemodynamically stable with a haemoglobin concentration greater than 8 g/dl, both surgical and medical options are available. Because of anxiety or lack of confidence in medical therapy, women are frequently admitted to hospital and subjected to surgical interventions or transfusion, or both, with dilatation and curettage, endometrial ablation, uterine artery embolisation or hysterectomy considered.

The hormonal options are oestrogens alone, progesterone alone, or combinations and, since there are no published trials, a group from California chose to compare two regimens of progesterone only, or progesterone plus oestrogen in the form of a standard preparation oral contraceptive (Munro *et al., Obstet Gynecol* 2006; 108: 924-929). The regimens were: 20 mg medroxyprogesterone acetate (MPA) 3 times a day for 7 days followed by 20 mg daily for 3 weeks or an OC containing 35 mg ethinyl oestradiol plus 1 mg norethidrone 3 times a day for 7 days followed by 1 OC daily for 3 weeks.

It was a small trial, but both treatments proved effective in that none of the 40 women required surgical intervention and the mean time to cessation of acute bleeding was 3 days with low drop-out rates for both regimens.

The women were mostly in their 40s and tended to be overweight or obese, so the underlying mechanisms were presumably anovulatory cycles. Those taking the progesterone-only tablets experienced some bloating, while those taking the OCs had more nausea and vomiting, especially in the start-up week.

Tranexamic acid was not evaluated, nor were intravenous hormones. It was a pragmatic trial that now allows some science to back up 'distilled experience' in the medical management of acute uterine bleeding.

Misoprostol for PPH prevention

There is genuine debate concerning the use of oral misoprostol for the prevention of postpartum haemorrhage (PPH) in resource-poor settings. The gold standard of injectable oxytocin requires sterile needles and syringes, which are not readily available in the situations where most morbidity from PPH occurs.

The purists say 'Why should the poor expect lower standards since trials have shown oxytocin to be superior to misoprostol and it does not have fever or shivering as a side-effect?' The pragmatists say 'Do what's do-able', or, as Chong and Su quote, 'The side-effects may be unpleasant but so is bleeding to death when you've just had a baby' (*Lancet* 2006; 368: 1216-1217).

So the arguments have gone, with Cochrane siding with the oxytocin group because of lack of evidence of misoprostol's efficacy when tested against a placebo. Now Derman *et al.* have published such a trial run by midwives in rural India (pp. 1248-1253) which shows a lower mean blood loss plus lower rates of PPH and severe PPH. The 600 mg of oral misoprostol reduced acute bleeding by 50% and acute severe bleeding by 80% compared with placebo. The authors accept that oxytocin is superior in hospital settings but argue for misoprostol for home deliveries by local attendants where something is better than nothing, and lives can be saved. Let us hope this science from the countryside echoes right to the top of the ivory towers.

Plan B

Plan B is the delightful name given to the American emergency contraceptive package containing two 0.75 mg tablets of levonorgestrel. It has a colourful history, being championed and distributed by the Women's Capital Corp in Washington DC who want to make wider options available to women to prevent the 3 million unintended pregnancies that occur in their country each year. More than 40% of these end in elective abortions (Gilliam, *Obstet Gynecol* 2006; 108: 1060-1061).

One would have thought that any means to reduce unwanted pregnancies would have been welcome, but for religious reasons US thinking about sex does not work in straight lines. The Bush administration promotes abstinence rather than contraception, opposes abortion at every level, and propounds moral responsibility based on dogma not education.

If you ever wondered about President Bush's derisory attitude towards women, then read the editorial in the *New York Times* of 24 November. It is called 'Family Planning Farce' and will either make you laugh or cry, and is summarised as follows.

This beloved champion of world human liberty has just appointed Dr Keroack as the head of family planning of the Department of Health and Human Services, whose office finances birth control, pregnancy testing and screening programmes for over 5 million of the poorest in the US. The only problem is that Dr Keroack is associated with a group vehemently opposed to birth control.

Among Keroack's associations have been the directorship of 'Women's Concern', which tries to dissuade women from having an abortion because it steeply increases the risk of breast cancer (*sic*). They also say contraception is demeaning and degrading to women, with adverse effects on health. He is now trying to distance himself from these statements, but when speaking at abstinence conferences he propounds his theory that sex with multiple partners alters brain chemistry, making it harder for women to form bonding relationships.

It seems the Bush administration is unchastened by its political defeats in recent months and is pressing gaily on with its repressive policies against its own women.

But back to the saga of Plan B, which began when the FDA was asked to approve its over-the-counter sale status. Since its effectiveness to prevent pregnancy decreases linearly over time, clearly the sooner it is obtainable the better. By 72 hours most of its activity has disappeared, so quicker access is crucial. The FDA's own committee recommended over-the-counter availability, but their advice was unexpectedly turned down – on the spurious grounds that it had not been proven safe for teenagers. What followed was pure American politics, with indignant resignations, obfuscatory requisitions for unnecessary data, refusals by pharmacists to provide Plan B even on prescription, plus political posturing by Hilary Clinton, who refused to accept the new FDA's new commissioner until Plan B was approved – and its eventual acquiescence 3 years later.

The probable explanation for this unseemly bickering is the underlying misconception that Plan B prevents implantation and is therefore an abortifacient rather than a contraceptive – a sort of 'do-it-yourself' abortion pill. It is not. It does not work by post-fertilisation action – if it did, it would be just as effective 72 hours post-coitally as immediately. There is neither histological nor biochemical evidence of endometrial hostility after taking Plan B in the second half of the cycle. Davidoff and Trussell (*JAMA* 2006; 296: 1775-1778) state that Plan B's ability to interfere with implantation is speculative and that there is adequate scientific evidence that it does not cause abortions, a point supported by the fact that progesterone is given to prevent early miscarriage.

It is highly unlikely that Plan B affects tubal function, as ectopic rates for its users are slightly lower than national averages.

It is likely that it works by one of the following mechanisms:

- Interference with sperm activity. Progesterone alkalinises uterine cavity fluid, which immobilises sperm 5 hours after ingestion. This will not have an effect on the first wave of sperm migration, but will on later waves of capacitated sperm which begin 10 hours after intercourse and continue for several days.
- It produces thickening of the cervical mucus after 9 hours.
- If taken just before anticipated ovulation it interferes with the LH surge, inhibiting ovum maturation and release.

Amniocentesis and pregnancy loss

The standard risk quoted for pregnancy loss after a mid-trimester amniocentesis is 1 in 200. This figure is largely historical, and the First and Second Trimester Evaluation of Risk for Aneuploidy trial (FASTER) now allows revision of the statistics (Eddleman *et al., Obstet Gynecol* 2006; 108: 1067-1072).

The FASTER Consortium in the US looked at 35 000 pregnancies between 10 and 14 weeks' gestation who were being followed for Down syndrome evaluation. A control group of 32 000 did not have an amniocentesis, and they had a miscarriage rate of 0.94% before 24 weeks' gestation. The group of 3 000 that did have a genetic amniocentesis had a miscarriage rate of 1%, making a difference of 0.06%, which translates into a risk of 1 in 1 600. The trial was conducted in 15 clinical centres throughout the US, without prescribed needle size, and the procedure was carried out by clinicians with varied experience. It thus reflects current rather than research circumstances, which improves the generalisability of the results for quoting in routine practice.

A sensible approach to Down screening is described by Rozenberg *et al.* (*AJOG* 2006; 195: 1379-1387), who surveyed an unselected French population of 15 000 women. They performed routine maternal serum marker tests in the first trimester and reacted to positive values. At the 20-week ultrasound scan, structural features were sought that are associated with Down syndrome, thus providing a follow-up safety net while checking the fetus for non-chromosomal abnormalities. Detection and screen-positive rates were 90% and 4% respectively using this method, which seems highly acceptable.

These summaries were extracted from **Journal Article Summary Service (JASS)**, which can be accessed at **www.jassonline.com**

Athol Kent
Editor

Improving women's health in Africa

A new charity is being created in the UK called TASK Women's Health (Towards African Solutions through Knowledge in Women's Health).

The aim of the charity is to facilitate the development of affordable and sustainable interventions in Women's Health, to improve Women's Health across the African Continent.

The Trustees of the charity are Mr John Osborne (Chairman), MB BS, FRCOG, of University College, London, Prof. John Guillebaud, MA, FRCS Ed, FRCOG, Hon FFFP, Hon FCOG (SA), Emeritus Professor, UCL, Prof. Eric Jauniaux, MD, PhD, UCL, Miss Sohier ElNeil, BSc Hon, MB ChB, DFFP, MRCOG, PhD (Cantab), Consultant Gynaecologist, UCLH, and Miss Adeola Olaitan, MD, FRCOG, Consultant Gynaecological Oncologist, UCLH.

A meeting is planned for early October 2007 to bring together interested professionals from across Africa to discuss the most significant problems affecting Women's Health and to develop strategies and pilot projects for which the charity can raise funds.

Further information about the meeting may be obtained from our website on www.TASKforwomen.org or email addresses info@TASKforwomen.org and osbornes.chiswick@virgin.net Please contact John Osborne at the email address above if you have ideas that need sponsoring to be put into practice, or just if you are interested.