August 2009 pp379–84). We would like to add that xanthomatoses, especially xanthelasmas, are also an important marker for diabetes, propensity to coronary artery disease (CAD)[1] and gout[2] apart from cholestasis and hyperlipidemia as mentioned. Besides xanthaelasma and xanthoma, presence of arcus juvenilis in young people (age ⩽40 years) may also be considered as a clinical sign for premature CAD.[3] Premature graying and/or balding in chronic smokers has also been shown to be associated with premature CAD.[4] Other cutaneous signs like ear lobe crease, ear canal hair, and nicotine staining should be considered as valuable clinical markers of CAD for the benefit of the readers.[1] Recently, hyperpigmented palm and digits of hand associated with central obesity in betel quid sellers has been shown to predispose to early CAD.[5] There may be a clinical scenario where one sibling in the family has xanthoma, other has xanthelasma or arcus juvenilis and some suffering from CAD. The clinical implication of such a finding is that one must actively look for such signs in all the family members for early identification of persons predisposed to premature CAD.

AMITESH AGGARWAL
Lecturer
Department of Medicine/Preventive Cardiology
University College of Medical Sciences
University of Delhi, India

References

1 Chan HL. Cutaneous manifestations of cardiac diseases. *Singapore Med J* 1990;31:480–5.
2 Storey GO. Xanthomatosis, hyperlipoproteinaemia (type II, Fredrickson), gout, cardiac infarction. *Proc R Soc Med* 1971;64:59–60.
3 Chambless LE, Fuchs FD, Linn S *et al.* The association of corneal arcus with coronary heart disease and cardiovascular disease mortality in the Lipid Research Clinics Mortality Follow-up Study. *Am J Public Health* 1990;80:1200–4.
4 Dwivedi S, Aggarwal A. Risk factors and cutaneous markers of coronary artery disease in young in north Indian population. *Atherosclerosis Supplement* 2009;10:e1406.
5 Dwivedi S, Dwivedi G. Betel quid seller syndrome. *Occup Environ J* 2009;forthcoming.

Using umbilical cord blood stem cells for myocardial infarction and stroke is ethically challenging

Editor – It is disingenuous for stem cell researchers such as Copeland *et al* (*Clin Med* August 2009 pp 342–5) to claim that 'hUCB (human umbilical cord blood) is readily available, and presents little ethical challenges'. They must be aware that until the feto-placental circulation is interrupted by human professional intervention, that blood has a life-sustaining function. Without cord clamping, placental transfusion occurs and most of the blood then resides in the neonate. Pressure to separate mother and baby has created an apparent 'waste product' that may be valuable to researchers (and vested commercial interests). The earlier the cord is clamped, the more hUCB is 'readily available' for collection and the less is available for the neonate. Growing awareness of the impact of this irreversible intervention during the transitional circulation has led professionals responsible for the health and wellbeing of the new mother and baby to take a more cautious view.[1] In view of findings of long-term developmental problems in children apparently successfully resuscitated after birth, we hypothesised that early clamping may lead both to neonatal depression and inadequate cerebral oxygenation.[2,3] Physicians caring for adults and concerned about the alleviation of damage to adult vital organs must be aware of the ethical concerns about the use of vital material taken at birth.

SUSAN BEWLEY
Consultant obstetrician/maternal-fetal medicine
Guy's & St Thomas' NHS Foundation Trust, London

JUDITH MERCER
Clinical professor, University of Rhode Island, College of Nursing;
Adjunct professor, Department of Pediatrics, Brown University;
Research scientist, Women and Infants Hospital Rhode Island, USA

Conflict of interest: SB was a member of the Royal College of Obstetricians and Gynaecologists working party on umbilical cord stem cell collection. JM is PI of a research study into the protective effects of delayed cord clamping in very low birth weight infants.

References

1 Scientific Advisory Committee. *Opinion paper 2. Umbilical cord blood banking.* London: Royal College of Obstetricians and Gynaecologists, 2006.
2 Odd DE, Lewis G, Whitelaw A, Gunnell D. Resuscitation at birth and cognition at 8 years of age: a cohort study. *Lancet* 2009;373:1615–22.
3 Mercer J, Bewley S. Could early cord clamping harm neonatal stabilisation? *Lancet* 2009;374:377–8.

In response

Our comments were meant to indicate that cord blood stem cells, as compared to embryonic stem cells, present 'little ethical challenge' (particularly in the USA). Cord blood is readily available with more than four million births per year in the USA; many more than there are monies available for collection in both public and private banks. Therefore, in the USA it is common practice to not alter in any fashion the standard birthing procedures for the collector. If for some reason, inadequate volumes are collected the samples may be discarded. We firmly agree that the health and well being of the infant and mother are always of primary importance. Further, as was noted in our article, cord blood stem cell therapies have shown promise for treatment of adult as well as neonate disease such as cerebral palsy.[1]

Having said that many professionals argue that early clamping (within the first 30 seconds of birth) allows for more immediate care of the newborn and mother while others argue that late clamping (after two minutes or more) may allow for increased transfer of blood from the placenta to the newborn. There is evidence to support both sides of this argument, derived from studies conducted in North America, England, Australia and South America, including increased deleterious haemoglobin content, increased incidence of jaundice and polycythemia in infants delivered using late clamping.[2–5] However, early clamping has been thought to possibly deprive the newborn of potentially needed red cells and iron.[2–5]

Regardless, in the USA it has been common practice for more than 50 years to deliver infants utilising what would be

© Royal College of Physicians, 2010. All rights reserved.

termed early clamping. Anecdotally, there has been no evidence of significant harm to these infants. Scientifically, the changes that have been noted are of arguable long-term medical consequence. If it were clearly detrimental to the health of the child to perform clamping in one fashion or another, surely legislation would have been instituted by now. Therefore, we leave the decision of when to clamp and collect the cord blood up to the preferences of the mother and her physician or midwife. In our experience, we have not found that the difference in time involved makes for a significant difference in collection.

MOHAMED GABALLA
Director, Cardiology Research
Sun Health Research Institute
Phoenix, AZ, USA

DAVID T HARRIS
Professor of immunobiology
Director, Stem Cell Bank
The University of Arizona
Tucson, AZ, USA

NATHAN COPELAND
Medical student, MD-Candidate Class of 2012
The University of Arizona
Tucson, AZ, USA

References

1 Meier C, Middelanis J, Wasielewski B *et al.* Spastic paresis after perinatal brain damage in rats is reduced by human cord blood mononuclear cells. *Pediatr Res* 2006;59:244–9.
2 Ceriani Cernadas JM, Carroli G, Pellegrini L *et al.* The effect of timing of cord clamping on neonatal venous hematocrit values and clinical outcome at term: a randomized, controlled trial. *Pediatrics* 2006;117:e779–86.
3 Hutton EK, Hassan ES. Late vs early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. *JAMA* 2007;297:1241–52.
4 McDonald SJ, Middleton P. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Cochrane Database Sys Rev* 2008;(2):CD004074.
5 Neilson, JP. Cochrane update: effect of timing of umbilical cord clamping at birth of term infants on mother and baby outcomes. *Obstet Gynecol* 2008;112:177–8.

Discrepancies between histology and serology for the diagnosis of coeliac disease (1)

Editor – Sweis and colleagues showed discrepancies between histology and serology in the diagnosis of coeliac disease (CD) (*Clin Med* August 2009 pp 346–8), and suggest we reduce our reliance on serology testing in diagnosing and excluding CD. However, we feel there are major reasons to reconsider this.

The numbers reported here must be interpreted carefully: 10 out of 26 CD patients who received serologic testing were seronegative. This 38.5% occurrence of seronegative CD is misleading. In the spirit of Bayes theorem, the more common the condition we are testing, the greater the percentage of false negative results.[1] In this case, all 26 patients were selected due to the diagnosis of CD, meaning the prevalence in this group was already 100%. Therefore, this group is bound to have a high number of false negative tests. The authors correctly state that a small number of cases of CD will be missed by relying on serology alone, but the true prevalence is unknown, and this number is likely to be much lower than 38.5%.

In addition, the predictive value of using an ELISA-based method to detect tissue transglutaminase autoantibody (tTG) remains open to discussion. There are currently numerous tTG assays available, all with varying performances. The International tTG Workshop for CD performed head-to-head comparisons of various commercial and laboratory-based tTG assays. For this workshop, assays reported sensitivities ranging from 82% to 93%, underscoring the marked variability in assay performance.[2] Given these findings, the lack of positive serology in a proportion of their biopsy-proven coeliacs could be assay dependent.

Finally, even though intestinal biopsy is the gold standard method to diagnose CD, it is not without its short comings. The sensitivity of histology is largely dependent on the site and number of biopsy samples taken.[3,4] Negative histology often excludes a diagnosis of CD. However, a proportion of these patients have CD-like gastrointestinal symptoms, which might be attributed to the subtle changes seen in microscopic enteritis that could go undetected.[5]

In all, we agree that it is important not to rely on serology alone for the diagnosis of CD, but to allow serology to increase or decrease your estimation of risk of disease. However, considering the lifelong implications of a diagnosis of CD, one should still maintain a degree of suspicion and also take great care in interpreting villous atrophy in the absence of autoantibodies in any patient.

DEVASENAN DEVENDRA
Consultant physician and honorary senior lecturer
NHS Brent, Central Middlesex Hospital
and Imperial College, London

CHUKWUMA UDUKU
Research assistant and 6th year medical student
Department of Investigative Sciences
Imperial College, London

EDWIN LIU
Associate professor, pediatrics
Section of Gastroenterology,
Hepatology and Nutrition
The Children's Hospital,
University of Colorado at Denver

YANNOULLA WILSON
Laboratory manager, Autoimmune Serology
Northwest London Hospitals NHS Trust

References

1 Shapiro D. The interpretation of diagnostic tests. *Stat Methods Med Res* 1999; 8(2):113–34.
2 Li M, Yu L, Tiberti C *et al.* A report on the International Transglutaminase Autoantibody Workshop for Celiac Disease. *Am J Gastroenterol* 2009;104:154–63.
3 Bonamico M, Mariani P, Thanasi E *et al.* Patchy villous atrophy of the duodenum in childhood celiac disease. *J Pediatr Gastroenterol Nutr* 2004;38:204–7.
4 Pais W, Duerken D, Pettigrew N *et al.* How many duodenal biopsy specimens are required to make a diagnosis of celiac disease? *Gastrointest Endosc* 2008;67:1082–7.
5 Rostami K, Villanacci V. Microscopic enteritis: novel prospect in coeliac disease clinical and immuno-histogenesis. Evolution in diagnostic and treatment strategies. *Dig Liver Dis* 2009;41:245–52.

Discrepancies between histology and serology for the diagnosis of coeliac disease (2)

Editor – Discrepancies between histology and serology for the diagnosis of coeliac disease (CD) (*Clin Med* August 2009 pp 346–8)

© Royal College of Physicians, 2010. All rights reserved.