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

- 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.
- 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.<sup>3,4</sup> 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.<sup>5</sup>

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

- 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)