

## Commentary: Liver function tests: defining what's normal

Paul Roderick

Chronic liver disease and hepatocellular carcinoma are major worldwide public health problems in countries with endemically high levels of viral hepatitis (B and C).<sup>1</sup> However, even in western countries chronic liver disease is an emerging problem, due not only to viral hepatitis but also to the effects of lifestyle factors such as heavy alcohol consumption and obesity.<sup>2-3</sup>

Liver function tests are widely performed blood tests used in patients with suspected liver disease or unexplained illness and in some specific situations such as screening of blood donors. The most widely used tests are those used to detect the aminotransferases—alanine and aspartate—which are associated with hepatocellular injury. Raised concentrations may indicate serious underlying chronic liver disease, recognition of which is important for guiding interventions to modify lifestyle and use of specific therapies such as interferon for hepatitis C to prevent the risk of progression to cirrhosis.

The sensitivity, specificity, and predictive values are important in assessing the clinical utility of such tests. Normal ranges have been based on distributions from healthy volunteers with two SD above the mean (that is, top 2.5% cut-off) being considered the upper normal range. Aminotransferase concentrations maybe within the normal range in people with chronic liver disease.<sup>4-5</sup> There is ongoing debate about whether to lower the normal range to take account of changing lifestyle factors that influence aminotransferase concentrations, particularly obesity, which in Western countries would increase the detection of hepatitis C and alcoholic and non-alcoholic fatty liver disease (NAFLD).<sup>6-7</sup>

Kim and colleagues have analysed the association between aminotransferase concentrations and mortality from liver disease in a large prospective cohort in Korea.<sup>1</sup> They found that there was a graded increase in risk of mortality from liver disease even within the normal range (20–40 IU/l) compared with the lowest concentrations (<20 IU/l) for both sexes. The performance of the test in identifying future risk of mortality from liver disease was maximised by lowering the threshold to about 30 IU/l. They propose identifying a borderline level of aminotransferase of 30–39 IU/l, suggesting that patients in this category should be

further investigated with more specific diagnostic tests for chronic liver disease.

What are the implications for countries with lower levels of chronic liver disease than Korea? Test utility is affected by disease prevalence. In countries with lower prevalence the negative predictive value (that is, the ability of a negative test to exclude disease) will be higher and the positive predictive value (that is, the ability of a positive test to predict disease) will be lower. Lowering the upper normal range for aminotransferase or including borderline cases will increase sensitivity at the expense of specificity, so detecting more cases of chronic liver disease but with a lower positive predictive value. These effects would be less marked in those with suspected liver disease compared with the population as whole. The cost effectiveness of further investigation of borderline cases is not known but requires evaluation. A crucial diagnostic issue is how to identify severe chronic liver disease (indicated by inflammation and fibrosis), which is associated with high risk of progressing to cirrhosis. Definitive evaluation currently relies on liver biopsy. Research is needed to evaluate combinations of non-invasive measures to predict severe liver disease; this could include patients with borderline concentrations of aminotransferase.

Competing interests: Research collaboration with Bayer Health-Care.

- 1 Kim HC, Nam CM, Jee SH, Han KH, Oh DY, Suh I. Normal serum aminotransferase concentration and risk of mortality from liver disease: prospective cohort study. *BMJ* 2004 doi/10.1136/bmj.38050.593634.63
- 2 Clark JM, Brancati FL, Diehl AM. The prevalence and etiology of elevated aminotransferase levels in the United States. *Am J Gastroenterol* 2003;98:960-7.
- 3 Department of Health. *On the state of the public health. The annual report of the chief medical officer*. London: Department of Health: 2002.
- 4 Kyrlagkitis I, Portmann B, Smith H, O'Grady J, Cramp ME. Liver histology and progression of fibrosis in individuals with chronic hepatitis C and normal elevated ALT. *Am J Gastroenterol* 2003;98:1588-93.
- 5 Pratt DS, Kaplan MM. Evaluation of abnormal liver-enzyme results in asymptomatic patients. *N Engl J Med* 2000;342:1266-71.
- 6 Prati D, Taioli E, Zanella A, Della Torre E, Butelli S, del Vecchio E, et al. Updated definitions of healthy ranges for serum alanine aminotransferase levels. *Ann Intern Med* 2002;137:1-9.
- 7 Kaplan MM. Alanine transferase levels: what's normal. *Ann Intern Med* 2002;137:49-50.

Community Clinical Sciences Research Division, University of Southampton, B Floor, South Academic Block, Southampton General Hospital, Southampton SO16 6YD

Paul Roderick  
senior lecturer in public health

Correspondence to:  
P Roderick  
pjr@soton.ac.uk

### NHS change management (or how many people it take to change a light bulb)

When a fluorescent tube in our office began to flicker irritatingly I was intrigued at how complex the process of change became. In other words, I wanted to find out exactly how many people it takes to change a light bulb in a large inner city teaching hospital. My research led me as follows.

I reported the fault to my personal assistant (two people). She telephoned the estates department helpdesk (three people). The helpdesk passed on the information to the maintenance supervisor (four), who allocated the job to an electrical assistant (five). The electrical assistant approached the general stores clerk

(six), who selected the required item from the store stocked by the general stores manager (seven). The fault was then rectified.

Apparently, the process is more complex for non-standard light bulbs, and I have not yet performed an economic analysis on the number of financial staff required to process the purchasing costs.

My conclusion from this brief research is that change within an organisation like the NHS is complex.

Verbal consent only was obtained from participants.

Graham Ellis *clinical research fellow, Glasgow Royal Infirmary*