Howard recounts many surgical dilemmas and difficulties, not least the inability to always remove musket balls weighing up to 5 lbs. Although amputations were restricted in civilian life, they were soon found to provide better results than attempts at conservative treatment and actually reduced suppuration, blood loss and surgical shock. Shattered bones and extensive soft tissue damage to muscles, arteries and nerves were the main indications. Larrey led the way in surgical techniques, and advocated early, rather than delayed, high amputations where possible: 'However cruel an operation may be, it is an act of humanity in the hands of a surgeon'. He was opposed to closure of the skin flap and attempts to secure healing by first intention – as practised by British surgeons. Chest, abdominal and head wounds were common and each presented its own problems to Larrey and his team, who were extraordinarily courageous and inventive in their techniques, but also judicious in selecting conservative methods when surgery proved too risky.

But surgical wounds were not the only problems confronting Napoleon's doctors. On the eve of the Revolution the overall life expectancy was 28 years, with those surviving childhood living to 44 years. Soldiers and civilians were at risk of tuberculosis, typhus, malaria, smallpox as well as malnutrition. Syphilis, gonorrhoea, dysentery, bubonic plague, and other infectious fevers all took their toll. Only antiphlogistic remedies, purging and bloodletting were in use.

The final chapter is a revealing account of daily life 'on the road with Napoleon,' providing us with the sort of details which enable us to visualise and understand the terrible existence of his soldiers and doctors. Martin Howard's scholarly book is eminently readable: a worthy successor to his *Wellington's doctors.*[1]

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Reference

1 Howard M. *Wellington's doctors: the British Army medical services in the Napoleonic Wars.* Stroud: Tempus Publishing Ltd, 2001.

letters
TO THE EDITOR

Please submit letters for the Editor's consideration within three weeks of receipt of the Journal. Letters should ideally be limited to 350 words, and sent by e-mail to: Clinicalmedicine@rcplondon.ac.uk

Monitoring of cardiotoxicity during immunotherapy with Herceptin using simultaneous continuous wave Doppler depending on N-terminal pro-brain natriuretic peptide

We read with great interest the current work of Routledge and coworkers regarding the cardiotoxicity monitoring during immunotherapy with trastuzumab (Herceptin) among patients with metastatic breast cancer (*Clin Med* September/October 2006 pp 478–81). Cardiotoxicity after trastuzumab therapy was first monitored during a phase III clinical trial[1] with cardiac dysfunction evident in 4%, with 0.9% deaths attributed to cardiac dysfunction. The combination with anthracycline plus cyclophosphamide to trastuzumab increased the occurence of cardiac dysfunction to 27%.[2,3]

Current detection and management of trastuzumab-related cardiotoxicity is based on physical examination, electrocardiography and repetitive echocardiography on a six-week basis by a cardiologist.[3] Echocardiographic examination is without doubt of utmost importance to monitor and identify patients with cardiac failure. However, it is usually performed before or hours and days later following the trastuzumab infusion based on a single ejection fraction.

We therefore hypothesised that using an instantaneous real-time continuous wave (CW) Doppler ultrasound device (USCOM, Sydney) with quantitative determination of cardiac output as well as the afterload as systemic vascular resistance in combination with n-terminal pro-brain natriuretic peptide (NT-pro BNP)[4] might identify patients at risk of a possible cardiotoxic event. Forty-eight women with metastatic breast cancer were allocated to a trastuzumab (Herceptin) antibody therapy concerning their HER2-positive staining. Depending on the NT-pro BNP levels <125 pg/ml, which is the normal range of the Roche Diagnostics NT-pro BNP test (group A, n=34, 51±10.5 years) versus NT-pro BNP 125 pg/ml or more (group B, n=14, 63±7.5 years).

Systemic vascular resistance prior to the trastuzumab infusion in normal level NT-pro BNP was significantly increased with 1919±620 dyne/sec × cm^{-5} with even higher values in the high-level NT-pro BNP group (2680±774 dyne/sec × cm^{-5}). During the infusion of trastuzumab (at 30 min after start of the infusion) systemic vascular resistance was decreased to 1758±461 dyne/sec × cm^{-5} and 2350±889 dyne/sec × cm^{-5}, respectively (p=0.061). Ten minutes after the end of the trastuzumab infusion the systemic vascular resistance declined further. The higher systemic vascular resistance in the high-level NT-pro BNP group B indicates the higher sympathetic activity in patients at higher risk for cardiac failure.

Using the CW-Doppler USCOM a different haemodynamic response to trastuzumab is evident depending on the level of NT-pro BNP. The high-level NT-pro BNP group had a significantly higher stroke volume and cardiac output immediately after the end of trastuzumab-infusion indicating a stronger haemodynamic response after the possible cardiodepressant drug. During trastuzumab therapy no immediate changes of NT-pro BNP were noted following trastuzumab infusion.

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References

1 Hudis C, Seidman A, Paton V *et al.* Characterization of cardiac dysfunction observed in the Herceptin (trastuzumab) clinical trials. *Breast Cancer Res Treat* 1998;50:232.
2 Slamon DJ, Leyland-Jones B, Shak S *et al.* Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer overexpresses HER2. *N Engl J Med* 2001;344:783–92.

3 Keefe DL. Trastuzumab-associated cardiotoxicity. *Cancer* 2002;95:1592–600.
4 Maisel AS, Krishnaswamy P, Nowak RM *et al.* Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 2002;347:161–7.

In response

Change in left ventricular ejection fraction (LVEF) as a method for detecting cardiotoxicity, whether by echocardiography, cardiovascular MR, or equilibrium-gated radionuclide ventriculography, is a blunt instrument. LVEF is not a direct measurement of myocardial contractility and physiological compensatory changes may mask significant early cardiac damage. Variability in measurement does not only occur as a result of methodology but also due to changes in loading conditions. Nevertheless, such testing has been of fundamental importance in many landmark studies because the individual variation and interpretative artefacts are largely equalised when large populations are studied. The technique becomes more problematic when attempting to guide individual therapy, particularly when testing is performed every three months and detection of cardio toxicity becomes to some extent 'retrospective'.[1]

Brain natriuretic peptide (BNP) and N-terminal pro-brain natriuretic peptide (NT-pro BNP) have an extensive evidence base in the diagnosis of heart failure[2] and for the assessment of prognosis.[3] Elevations in both biomarkers have been shown in stable coronary artery disease, unstable coronary syndromes and in valvular heart disease.[4] One potential use is therefore in the screening of patients prior to initiation of cardiotoxic chemotherapy to exclude those with pre-existing disease. A second option with greater potential is hinted at in the letter from Knobloch *et al* – that of using such a biomarker during chemotherapy infusion to provide immediate feedback regarding risk of subsequent dysfunction. As yet, however, there are limited data available that focus on the therapeutic implications derived from BNP and NT-pro BNP assessment. It is known that levels increase with age and this may confound study of trastuzumab toxicity, which is also age-dependent. Levels can also be altered by a number of other factors, including renal dysfunction.[5] There are studies of BNP and NT-pro BNP currently underway for screening and risk assessment in patients with malignant disease being treated with cardiotoxic chemotherapeutic agents. The major difficulty will be the identification of a 'cut-off' for abnormality, since there is no age-adjusted normal range, although serial comparisons may partially overcome this.

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References

1 National Institute for Health and Clinical Excellence. *Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer.* London: NICE, 2006. www.nice.org.uk/TA107.
2 de Lemos JA, McGuire DK, Drazner MH. B-type natriuretic peptide in cardiovascular disease. *Lancet* 2003;362:316–22.
3 Anand IS, Fisher LD, Chiang YT *et al.* Changes in brain natriuretic peptide and norepinephrine over time and mortality and morbidity in the Valsartan Heart Failure Trial (Val-HeFT). *Circulation* 2003;107:1278–83.
4 Weber M, Hamm C. Role of B-type natriuretic peptide (BNP) and NT-proBNP in clinical routine. *Heart* 2006;92:843–9.
5 Redfield MM, Rodeheffer RJ, Jacobsen SJ. Plasma brain natriuretic peptide concentration: impact of age and gender. *J Am Coll Cardiol* 2002;40:976–82.

A pain tool for people with communication difficulties is no closer

Jackson *et al* have produced a novel variation of a pain scale (*Clin Med* November/December 2006 pp 580–85). Sadly their hope that this scale might be applied to people with communication impairments is based on a misunderstanding of the issues involved.

With regard to patients unable to qualitatively describe the cause of their distress, there is increasing evidence that pain tools will respond as much to non-pain distress as to pain.[1,2,3] Jackson and colleagues acknowledge this, but fail to ask a vital question: is there any evidence that pain produces any specific signs and behaviours?[4] To date, no such evidence has been found,[3,5] suggesting that pain assessment is not a feasible goal in a person with a severe communication impairment. This lack of evidence sits uncomfortably with the multitude of pain tools that have been developed for people with cognitive or communication impairments. Very few of these tools have been validated,[3] however, while those that claim to have been validated have failed to address two key issues. Firstly, a 'pain' tool will be correct on many occasions, not because it is measuring pain but because pain is so common. Secondly, pain tools will pick up causes of distress other than pain.[3] If an analgesic is given for non-pain distress then any sedation will settle the distress, giving the false impression that pain has been relieved. There are two consequences of using a pain tool in these patients. Non-pain distress will be misinterpreted as pain resulting in inappropriate analgesic use; and non-pain causes of distress will be missed and remain untreated. No one would agree to the suggestion that a distressed patient with severe communication impairment should be given morphine, and yet administering a pain tool could have the same effect.

Jackson *et al*'s tool could be a useful communication aid in patients with mild to moderate communication impairments who are able to explain the cause of their distress. For patients who lack this communicative or cognitive ability, however, it will be necessary to work through a process of documenting the signs and behaviours of their distress,[3] and then placing the distress in context, identifying a pattern and trying interventions for the likeliest causes.[5] Such a process is beneficial for patients and is empowering for staff.[5]

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References

1 Herr KA, Mobily PR, Kohout FJ, Wagenaar D. Evaluation of the Faces Pain Scale for use with the elderly. *Clin J Pain* 1998;14:29–38.
2 McGrath PA, Seifert CE, Speechley KN, Booth JC. A new analogue scale for assessing children's pain: an initia; validation study. *Pain* 1996;64:435–43.
3 Herr K, Bjoro K, Decker S. Tools for