Letters to the Editor

Hyponatraemic rhabdomyolysis in Addison's disease

Sir,

The protean manifestations of rhabdomyolysis include, not only the biochemical derangements listed in the case report by Egan *et al.*¹ but also a spectrum of haematological manifestations, ranging from disseminated intravascular coagulation² to non-specific pancytopenia,³ which can obscure recognition of this syndrome, with consequent diagnostic delay. This was exemplified by an 81-year-old woman admitted to this hospital in February 1993 with a recent fall preceded by generalised aches and pains of a few days' duration. She had clinical stigmata of congestive cardiac failure and a temperature of 38°C. She was taking bumetanide 10 mg, enalapril 5 mg, isosorbide mononitrate 60 mg, and a variable dose of cocodamol daily. Her haemoglobin (Hb) was 9.3 g/dl, mean corpuscular volume = 86.7 fl, mean corpuscular haemoglobin = 27.4 pg, white blood count (WBC) = 1600/mm³, with 84% neutrophils and 4% metamyelocytes. Platelet count = 97000/mm³. The blood film showed a moderate degree of anisocytosis, and many non-segmented neutrophils. Although the electrocardiogram only showed non-specific ischaemia, the total creatine phosphokinase (CPK) level was 3338 with absence of the MB isoenzyme. Other biochemical investigations are shown in the table. Blood and urine cultures were sterile, and the urinary dipstick test showed no abnormality. On admission, and on follow up, significant hepatotoxicity was ruled out by the fact that serum bilirubin and γ -glutamyl transferase levels were normal. In view of pancytopenia, she was also investigated for vitamin B₁₂ and folate deficiency (see table). Her subsequent biochemical tests showed transient hypocalcaemia, and her WBC and platelet counts eventually reverted to the normal range (table). Her management included cessation of enalapril, due to renal dysfunction, and the use of sustained-release morphine for relief of disabling muscle pains. Sixteen days later, she was afebrile, pain free, and independently mobile.

Comment

The association of disabling muscle pains, marked elevation of non-cardiac creatine phosphokinase, transient hypocalcaemia, and reversible renal failure formed the basis for the diagnosis of rhabdomyolysis,⁴ notwith-

standing the normal urinary dipstick tests,⁵ although confirmation by serum myoglobin assay had not been sought because the index of diagnostic suspicion was low, due to the fact that the clinical picture was dominated by the haematological derangements. The latter were initially perceived to be the result of septicemia, or deficiency of vitamin B₁₂ and/or folate. In the event, as in the case reported by Feldman,² pancytopenia appeared to be entirely consistent with rhabdomyolysis *per se*, the haematological profile possibly being a component of multiple organ dysfunction.⁶ The spurious elevation of serum vitamin B₁₂ might have been the result of the fact that this vitamin, which is stored not only in the liver but also in skeletal muscle,⁷ had been released into the blood stream as a result of rhabdomyolysis.

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- Egan JJ, Davies AJ, Jones MC. Hyponatraemic rhabdomyolysis in Addison's disease. *Postgrad Med J* 1994; 70: 830-2.
- Prendergast D, George CF. Drug-induced rhabdomyolysis: mechanisms and management. *Postgrad Med J* 1993; 69: 333-6.
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- Marcus EL, Rudensky B, Sonnenblick M. Occult elevation of CK as a manifestation of rhabdomyolysis in the elderly. *J Am Geriatrics Soc* 1992; 40: 454-6.
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- Chanarin I. Vitamin B₁₂ - nutritional aspects. In: *The megaloblastic anaemias*. Oxford, Edinburgh: Blackwell Scientific Publications, 1969; p 48.

This letter was shown to the authors, who responded as follows:

Sir,

Drs Jolobe and Sen emphasise the importance of recognising occult rhabdomyolysis in clinically complex patients. In a similar fashion to our report, their case demonstrates that unless there is a high index of suspicion, particularly in elderly patients with multi-organ dysfunction, rhabdomyolysis may go unrecognised and contribute to renal impairment in the absence of urinary myoglobinuria.

In our publication we have suggested a causal relationship between severe Addi-

sonian hyponatraemia and the subsequent onset of rhabdomyolysis. In contrast their case appears to describe an association, not a causal relationship, between pancytopenia and rhabdomyolysis in an elderly patient with multiorgan dysfunction.

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Clinical guidelines

Sir,

The recent discussion of clinical guidelines¹ is most welcome. As guidelines are developed and introduced with increasing frequency it is important that clinicians become familiar with the issues surrounding them. I would like to make some additional points.

The article did not define guidelines. The definition of 'practice guidelines' proposed by the Institute of Medicine² may reduce anxieties about them: 'systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances (my italics)'. This definition emphasises the positive role guidelines may play when appropriately developed and implemented. Thus defined they are not the coercive managerial instruments some clinicians fear.

The second point concerns guideline development. Systematic reviews should be pivotal in guideline development. Guidelines based on other types of review or on consensus are prone to bias and may reflect this bias rather than the 'best' evidence. Everyone involved in guideline development or use should ensure that guidelines are not having a detrimental effect on patients, a potential danger of inappropriately developed guidelines. Guidelines based on consensus may have a further drawback. In order to reach agreement the wording of such guidelines may be so vague as to render the guideline useless: 'Consensus means that lots of people say collectively what nobody believes individually.' (Abba Eban)

My final point concerns the effectiveness of practice guidelines. Ideally the impact of a new guideline on patient outcome should be prospectively evaluated. If adverse events are infrequent, and if there is very strong evidence to support a guideline's recommendations, the process of care (the level of

Table Serial biochemical and haematological tests

Date	Sodium (mmol/l)	Potassium (mmol/l)	Urea (mmol/l)	Creatinine (μ mol/l)	Calcium (mmol/l)	Albumin (g/l)	CPK (IU/l)	Hb (g/l)	WBC (mm^{-3})	Platelets (mm^{-3})	Vitamin B ₁₂ (ng/l)
20/2/93	138	4.7	26.0	225			3338	9.3	1600	97 000	
22/2/93	127	4.2	36.1	308	1.94	34.5	2888				2255
2/3/93	133	5.0	34.5	320	2.21	37.9	129	10.1	11 400	417 000	
28/4/93	140	4.4	11.6	161				10.3	5700	285 000	
16/11/94	144	4.7	9.6	116							
23/11/94								11.6	9000	240 000	392
Reference range	135-146	3.5-4.8	2.5-6.5	40-110	2.12-2.63	37-50	38-148				170-900

adherence to the guideline) may be a reasonable, albeit surrogate, end point. The recent article did not distinguish between process and outcome. In the review by Grimshaw and Russell³ the *process* of care was improved in all but four of the 59 studies (in an updated review⁴ improvements were found in 81 of 89 studies). Nine of the 11 studies evaluating effects on the *outcome* of care found a significant improvement (12 of 17 studies in the updated review found an improvement). All 14 studies carried out in the UK noted significant improvements in compliance with guidelines.

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- 1 Onion CWR, Walley T. Clinical guidelines: development, implementation, and effectiveness. *Postgrad Med J* 1994; 71: 3–9.
- 2 Institute of Medicine. *Clinical practice guidelines: directions for a new program*. Field MJ, Lohr KN, eds. Washington, DC: National Academy Press, 1990.
- 3 Grimshaw JM, Russell IT. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet* 1993; 342: 1317–22.
- 4 Effective health care. *Implementing clinical practice guidelines*. Bulletin No 8. Leeds: University of Leeds, 1994.

This letter was shown to the authors, who reply as follows:

Sir,
The approach proposed to guideline development by the correspondent requires scientific rigour, but is idealistic. A problem arises concerning the many areas of medicine where such clear scientific evidence does not exist.¹ Are such areas not proper subjects for guidelines? It is in precisely these areas that guidelines may be most valuable, when evidence is uncertain or conflicting, as a means of ensuring consistent and acceptable practice. Most guidelines will involve elements of firm evidence and of opinion, and should make clear which is which. Users of guidelines must recognise that, as new evidence arises, the parts based on opinion should change. For instance, in drawing up guidelines on indications for endoscopy, a working party used a mixture of literature review and consensus opinion.² The well known British Thoracic Society guidelines on asthma are quite clear on the lack of firm evidence that increased use of inhaled steroids would decrease mortality in asthma.³ But both groups appropriately drew up guidelines on what they consider best medical practice despite this lack of hard evidence. Clinicians and purchasers of health care need guidelines of this kind, based on evidence where available but if not available, on what might be considered acceptable practice, to face everyday clinical problems with a little less uncertainty.

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- 1 Naylor CD. Grey zones of clinical practice: some limits to evidence based medicine. *Lancet* 1995; 345: 840–2.
- 2 Axon A, Bell G, Jones R, Quine M, McCloy RF. Guidelines on appropriate indications for upper gastrointestinal endoscopy. *BMJ* 1995; 310: 853–6.
- 3 British Thoracic Society and others. Guidelines for the management of asthma. *Thorax* 1993; 48 (suppl): S1–24.

Are blood tests of value in the primary assessment and resuscitation of patients in the A&E Department?

Sir,
The guidelines issued to senior house officers by consultant staff in the A&E Department of Southampton General Hospital following the clinical audit of the value of blood tests in the assessment of their patients may not be widely applicable.¹ The audit assumption that patients are immediately admitted from A&E Departments following an initial diagnosis may not be valid elsewhere. The guidelines appear overly restrictive.

The practice in this hospital differs in many ways. When a raised amylase is found in a patient with abdominal pain, the serum alanine aminotransferase and alkaline phosphatase is provided to A&E as an indicator of the likelihood of the presence of bile duct stones.² An admission serum calcium is also useful as a factor in the prediction of the severity of disease.³

Cardiac enzymes were also reported to be of no benefit to patients in A&E. It is surprising that there were no occasions where Coronary Care beds were full or whether the patient's history or electrocardiogram (ECG) was equivocal. Cardiac enzymes can aid in the selection of patients for intensive care and for thrombolytic therapy but the sensitivity and specificity of cardiac enzymes in the diagnosis of myocardial infarction in relation to the duration of chest pain must be considered.⁴ A speedy laboratory turnaround time for cardiac enzymes is important and the interval in this department is 20 to 35 min.

Alcohol may be a significant contributory factor in trauma, poisonings and coma and should be listed in the clinical guidelines. Cost switching between units within hospitals should not be allowed to interfere with patient investigations.

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- 1 Pennycook A. Are blood tests of value in the primary assessment and resuscitation of patients in the A&E department? *Postgrad Med J* 1995; 71: 81–5.
- 2 Steinberg WM. Acute pancreatitis – never leave a stone unturned. *N Engl J Med* 1992; 326: 635–7.
- 3 Moosa AR. Diagnostic tests and procedures in acute pancreatitis. *N Engl J Med* 1984; 311: 639–43.
- 4 Collinson PO, Young LJ, Foo AY, Rosalki SB. Early diagnosis of acute myocardial infarction. *Ann Clin Biochem* 1994; 31: 301–2.

This letter was shown to the author who replied as follows:

Sir,
Dr Tormey suggests the guidelines that were issued to the senior house officers might not be widely applicable.¹ Clearly local circumstance and practice must be taken into account when such guidelines are introduced and moreover agreement reached between directorates. However, it is best clinical practice after assessment and resuscitation to admit patients promptly from the A&E department.

This has been reinforced in the new national patients' charter,² which specifies a maximum trolley waiting time. Delaying admission for inappropriate blood tests that do not actually influence clinical management cannot be justified. Cost savings on unhelpful investigations made in one directorate can be spent elsewhere within a Trust.

The majority of amylase tests undertaken in an A&E Department are negative. While a serum alanine aminotransferase, alkaline phosphatase and calcium are of use in a patient with pancreatitis, these tests are more appropriate to the in-patient environment and do not belong in A&E guidelines.

I would disagree with regard to the value of cardiac enzymes in the A&E Department. The diagnosis of acute myocardial infarction is made from the patient's history and especially the ECG which forms the basis for the thrombolytic regimes currently used. Cardiac enzymes, eg, creatinine kinase do not rise for 8–10 hours after coronary occlusion. In terms of myocardial salvage the maximum benefit from thrombolysis is gained in the first six hours. Enzymatic diagnosis of myocardial infarction is therefore essentially retrospective.^{3,4} If the initial ECG is normal or equivocal then the patient requires a repeat ECG every 15 minutes to exclude infarct. When the coronary care unit or other inpatient area is full, prompt thrombolysis in the A&E Department is mandatory.

Finally, alcohol measurement is rarely of use in an A&E Department as it must never be presumed to be the sole cause of a patient's depressed conscious level. What is required is the effective support of the patients' vital functions and the exclusion of serious head injury and other causes of coma.

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- 1 Pennycook A. Are blood tests of value in the primary assessment and resuscitation of patients in the A&E department? *Postgrad Med J* 1995; 71: 81–5.
- 2 *The National Patients' Charter for the NHS*. London: HMSO; 1995.
- 3 *Advanced cardiac life support – the practical approach*. Advanced Life Support Group. Chapman and Hall, 1993; p19.
- 4 *Advanced life support manual*. 2nd edn. Resuscitation Council UK. Burr Associates 1994; p3.