LETTERS TO THE EDITOR

Scope
Heart welcomes letters commenting on papers published in the journal in the previous six months. Topics not related to papers published earlier in the journal may be introduced as a letter: letters reporting original data may be sent for peer review.

Presentation
Letters should be:

– not more than 600 words and six references in length
– typed in double spacing (fax copies and paper copy only)
– signed by all authors

They may contain short tables or a small figure. Please send a copy of your letter on disk. Full instructions to authors appear in the July 1999 issue of Heart (page 116).

Management of scorpion sting

EDITOR—We read with great interest the haemodynamic pattern in patients with scorpion envenomation.1 We have studied this acute time sensitive medical emergency since 1976 and have tried various regimens including antiscorpion venom.2 Since the advent of prazosin (1983–84)—an α adrenergic blocker which acts as an antagonist to venoms—the mortality of scorpion sting victims is less than 1%.3

In the pre-prazosin era (1961–83) a fatality rate of 25–30% was reported from western India,4,5 acute pulmonary oedema causing death. We were therefore surprised by the 25% mortality reported by Karnad,6 that two victims died on the third day of hospitalisation; we have similar findings in 1978–82—that is, before prazosin treatment.6

We have reported that the severity of scorpion sting depends on the victim's age, the season, and the time between sting and administration of prazosin. The symptoms following the sting are hypertension, tachycardia, pulmonary oedema, and shock (autoimmune storm).7 We believe that the transport of Karnad's patients to the nearest hospital and referred to their destinations of seven to eight acute pulmonary oedema owing to a delay in reaching a tertiary care hospital.8 Scorpion venom inhibits angiotensin converting enzyme (ACE), resulting in accumulation of bradykinin, which is implicated in the development of pulmonary oedema and acute reversible pancreatitis.9 Captopril (an ACE inhibitor) has a similar action resulting in hypotension resistant to dopamine agonists.10 Bradykinin further enhances noradrenaline (norepinephrine) release by a presynaptic mechanism.11

Alpha receptor stimulation plays a major role in the pathogenesis of pulmonary oedema.12 It causes hyperkalaemia and hyperglycaemia (inhibition of insulin secretions). Angiotensin II stimulates α adrenergic receptors in the myocardium and hypoxia results from coronary spasm as well as accumulation of free radicals and free radicals injurious to myocardium leading to cardiac arrhythmias and sudden death.13

At a general hospital at Mahad we successfully treated 658 cases of severe scorpion sting with oral rehydration, oral prazosin, and oxygen and mannitol-phyleline: 362 (55%) had hypertension, 178 (27%) had pulmonary oedema, 118 (18%) had tachycardia; no patient had lethal arrhythmias. Seventeen patients who died on the way to Mahad had been referred 24 hours after being stung while 13 cases admitted with multigorgan failure and were moribund and comatose; they died 30–60 minutes after admission despite treatment with dopamine, nitroprusside, oxygen, and calcium chloride. The remaining 56 cases with massive pulmonary oedema recovered after treatment with intravenous sodium nitroprusside.

We travelled throughout western Maharashtra where Mesobuthus tamulus scorpions flourish, and taught all peripheral doctors how to treat scorpion sting victims. There has not been any deaths over the past two years due to scorpion sting reported from this region. Moreover, only two patients had massive pulmonary oedema, which was treated with intravenous sodium nitroprusside. Captopril failed to correct haemodynamic abnormalities in two cases who had cardiac arrhythmias. We believe that this delay would have been life saving in the two patients treated with captopril who died in Karnad's report.7 As a potent inhibitor of phosphodiesterase, prazosin causes accumulation of cGMP, a second messenger of nitric oxide, in vascular endothelium and myocardium, inhibits the formation of inositol triphosphate, and activates venom inhibited calcium dependent potassium channel.14

Thus prazosin reverses both inotropic (hypertension), and hypokinetic (pulmonary oedema, hypotension, tachycardia) phases evoked by scorpion envenoming.15

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7 Imami M, Faraji AJY, Debies TT. Experimental treatment protocols for scorpion envenomation review of common therapies and an effect on kaliuretic-kain inhibitors. Toxicon 1992;30:1257–70.

EDITOR—The study by Karnad on the haemodynamic patterns encountered in scorpion envenomation raises important concerns. Karnad claims that the mechanism of pulmonary oedema observed in scorpion envenomation had not previously been established as pulmonary arterial wedge pressure (PAWP) had not been measured. However, the haemodynamic mechanism of pulmonary oedema in scorpion envenomation was suggested in animal studies as early as 19801 and confirmed by numerous series in human subjects. All of these series performed a haemodynamic study and PAWP.2–4 We are therefore not surprised with Karnad's findings and observe that they are consistent with our previous reports suggesting similar effects of the Indian red scorpion Mesobuthus tamulus and the yellow scorpion of North Africa (Androctonus australis).

We are particularly concerned by Karnad's interpretation of the haemodynamic records in the envenomated patients and the treatment strategy he suggests. The haemodynamic, echocardio-graphic, and angiointer-
tries. First line clinicians need comprehensive and meaningful insights regarding the pathophysicsology and valuable treatments of this dreaded accident. The clearer and simpler the message on this issue the better the effects in daily clinical practice.

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**These letters were shown to the author, who echoes as follows:**

The efforts of Bawaskar and Bawaskar in popularising prazosin treatment in western India are truly commendable, and the effect on mortality following scorpion envenomation: combined haemodynamic and echocardiographic study. *Intensive Care Med* 1995;21:629–35. In this series 28 patients treated with prazosin, of whom only 30 (4.5%) died. They cite their personal experience with captopril. In India, scorpion envenomation occurs almost exclusively in rural areas, and is particularly common in the coastal regions of western India where Dr Bawaskar's hospital is located. Patients stung by scorpions are likely to consult local doctors first, especially if envenomation is mild, explaining why 18% of patients had tachycardia alone and 55% had hypertension. Pulmonary oedema, resulting from more severe envenomation, was seen in 27% of patients. In contrast, our experience is from a tertiary referral centre in Bombay. Most patients treated in our unit were referred from rural areas 80 to 150 km away, 6–36 hours after the sting. Moreover, the pattern of disease had not improved despite receiving treatment at primary care centres. Consequent to this referral pattern, a greater proportion of our patients had severe envenomation and presented late—18 of 31 patients treated in our unit with captopril in the past 10 years had pulmonary oedema with hypotension. Four patients (all had severe pulmonary oedema with hypotension) died. In Dr Bawaskar's series, 178 patients with pulmonary oedema were treated with prazosin and 30 (17%) died. This is not significantly different from the 22% mortality in our experience with captopril.

I agree with Abroug and colleagues that patterns II, III, and IV described in my paper are facets of the same underlying abnormality. For this reason, they were all grouped under the category of predominant myocardial effects. Haemodynamic abnormalities in patterns II and III differ only in terms of the patients' fluid balance, but the clinical features of the two patterns are so different as to need separate discussion. Pattern II is characterised by severe pulmonary oedema and mild or no hypotension. Pattern III is seen in dehydrated patients and manifests as severe hypotension, with little or no pulmonary edema following scorpion envenomation. *Chess* 1991;100:109–7.

**Abroug et al have, in a previous study, shown that left ventricular ejection fraction measured by echocardiography was severely depressed (26%) following scorpion envenomation. They showed a threefold improvement to 75% during recovery.** In another study, they assessed right ventricular function using a pulmonary artery catheter; right ventricular ejection fraction was 24% following envenomation and improved to 39% during recovery. Unfortunately simultaneous right and left ventricular functions have not been studied.

Our patients with pattern II showed severely raised PAWP and subnormal left ventricular stroke work index, while right ventricular stroke work index and right atrial pressures were normal, suggesting that the left ventricle was more severely aected than the right. In pattern IV, however, as well as right ventricular stroke work indices were severely depressed and both PAWP and right atrial pressures were grossly raised suggesting that at this stage right ventricular function was also severely deranged.

Abroug et al mention that they have been using dobutamine in scorpion envenomation with good results. Their patients also received antivenom, which is not available in India. It may be possible that antivenom favourably alters the response to inotropic catecholamines. The experience of Bawaskar and Bawaskar suggests that inotropic treatment given to patients who have not received antivenom does not decrease mortality. Although no controlled studies exist, studies using historical controls treated conventionally, including intravenous drugs, have shown that vasodilators like prazosin, calcium channel blockers, ACE inhibitors, and sodium nitroprusside have been used. However, whether any one of them is superior has not been studied. Currently available evidence indicates that these are equally effective and the suggestion that prazosin may have been effective in patients who did not improve with captopril as suggested by Bawaskar can only be considered speculative.

**Letters**

Is BNP ready for use in clinical practice?

**Editor,—Richards et al suggest that brain natriuretic peptide (BNP) measured 24–96 hours after acute myocardial infarction (AMI) is a powerful independent indicator for subsequent development of left ventricular failure and death.**

In their multivariate analysis the site (anterior v inferior) and type (Q wave v non-Q wave) of infarction do not appear to have been included. The important prognostic value of these indicators has been established. One might expect the anterior infarcts (39% of their study population) to demonstrate greater left ventricular dysfunction, higher BNP concentrations, and a poorer prognosis than the inferior infarcts (31%). A similar relation may exist between type of infarct and outcome, although figures for each type are not given. It would be interesting to see whether BNP is still a powerful prognostic variable if site and type of AMI were included in their analysis.

Two further confounding variables that may have weakened the association between BNP and outcome are the timings of the radionuclide ventriculography and blood sampling (1–4 days after AMI). Assessment of ventricular function in the first 24–48 hours after AMI can lead to an overestimation of damage due to the phenomenon of myocardial stunning. The time course of BNP shows a peak at 16 hours followed by a significant decline in the next 48–72 hours. A narrower and standardised time frame for ventriculography and venesection may have improved the correlations.

It would have been useful to know the area under their receiver operating characteristic (ROC) curve for BNP, which is highly relevant in assessing the true value of a test. They demonstrated a negative predictive value of 100% for BNP at a threshold of 20 pmol/l, but they used different thresholds for looking at the sensitivity and specificity and predictive power for left ventricular ejection fraction and left ventricular failure (25 and 33 pmol/l, respectively). Although these values were derived from their ROC analyses, it is difficult to envisage how a BNP result should identify a high risk population in whom some sort of intervention is feasible before development of “clinical end points”. However, at present, there is no evidence to suggest that treating a high plasma BNP in the presence of a normal ejection fraction improves outcome. Clearly this should be an area for further investigation.

BNP and its prohormone derivative (N-terminal proBNP) offer exciting prospects for non-invasive assessment of myocardial function and outcome following infarction. Richards et al have clearly demonstrated the prognostic superiority of BNP over other neurohumoral markers thus supporting their initial hypothesis. Their concluding statement, however, suggests that plasma BNP “could reasonably be included in the routine clinical workup of a patient following myocardial infarction” seems premature.
Transfusion associated graft versus host disease

EDITOR,—Ahya et al reported a case of transfusion associated graft versus host disease (TA-GVHD) in a non-immunosuppressed patient resulting from blood transfusion during coronary artery bypass grafting (CABG).1 They concluded that this devastating complication of transfusion is probably underreported. There is no doubt that diagnosing this condition needs a high index of suspicion because its manifestations can be seen in other more common conditions such as sepsis, immunosuppression, and is likely to be multifactorial. Stress of surgery. This type of major surgery appears to induce a transient immunodeficiency state, which is poorly understood.

We report another patient with TA-GVHD acquired following elective four-veeular CABG and perioperative transfusion of a total of six units of blood. A 68 year old man was admitted three weeks after surgery with a seven day history of skin rash, breathlessness, cough, and expectoration of brown sputum. He had an extensive erythromedic mucopurulent eruption, oral thrush, tachycardia, hypotension, general chest crepitations, and mild hepatomegaly. His condition worsened progressively with development of profound pancytopenia, disseminated intravascular coagulation, metabolic acidosis, hepatitis, and acute renal failure. His bone marrow was aplastic and skin biopsy showed mononuclear infiltration with cellular apoptosis supporting the clinical diagnosis of TA-GVHD. Treatment with high dose steroids, ciclosporin, and OKT3 was initiated, but despite maximum support he died within seven days of readmission.

Although TA-GVHD does occur in immunocompetent individuals who had blood transfusion for other conditions, it is more frequent following cardiopulmonary bypass surgery. This type of major surgery appears to induce a transient immunodeficiency state, the mechanism of which is poorly understood and likely to be multifactorial. The use of fresh blood with more lymphocytes, immunosuppressive effect of multiple transfusions, and transient reduction of Interleukin 2 but not Interleukin 3 may contribute to the development of this condition. The role of transfusion is controversial but may enhance the risk of TA-GVHD.


cardiopulmonary bypass may all cause a degree of immune dysfunction. If the donor’s blood happens to be homozygous for one of the recipient’s major HLA types, this transient immune dysfunction may facilitate donor’s lymphocyte engraftment and development of TA-GVHD.

We emphasise the relation of this highly dangerous condition with cardiopulmonary bypass surgery. One can only speculate as to the nature of this association.

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First the transfused units may contain an insufficient number of immunocompetent lymphocytes; second, some recipients may be able to destroy the donor lymphocytes on the basis of subtype differences in the class I or other minor histocompatibility antigens between the donor and recipient. Finally, it is possible, and quite likely, that some cases have remained unrecognised and unreported. We hope that our publication in Heart of two cases of TA-GVHD after cardiac surgery will heighten awareness of this complication of transfusion, and result in full investigation and reporting of all suspected cases to SHOT (serious hazards of transfusion). It is necessary to establish the true incidence of TA-GVHD in cardiac surgery so that cost-benefit analysis and informed review of guidelines for the irradiation of cellular blood products for this indication can be completed.


Outpatient clinics for adults with congenital heart disease

EDITOR,—We agree with the views expressed by Gatzoulis et al concerning the need for dedicated clinics for adults with congenital heart disease.1 We started such a clinic in 1993. Initially this was once a month, becoming semimonthly in 1995 and weekly in 1999. The clinic is in a district general hospital serving a population of 650 000, and the initial numbers may have been present because of the early work of Bill Oliver in Great Ormond Street visiting cardiologists. One of us also runs a paediatric clinic and the other has experience in adult congenital heart disease.

Forty three per cent of our 260 patients are male, and 25% of the patients have septal defects (both atrial and ventricular). As there are complicated cases, closed defects are not followed up all these patients have additional lesions or residual sequelae of the original repair.

12% have had a tetralogy of Fallot repaired
11.5% have bicuspid aortic valves
8.7% have had a coarctation repaired
11% have cyanotic heart disease (5% with the Eisenmenger complex)
5% have left ventricular outflow tract abnormalities
5% have transposition of the great arteries—all of whom have had the Mustard repair
12.1% of patients have Marfan’s syndrome (although patients with Marfan’s are also seen in general clinics).

The remaining 9.9% have various conditions from complex congenital heart disease including tricuspid atresia with Fontan operation (1.3%), single ventricle with total cavopulmonary connection (TCPC) (1%), complex pulmonary atresia with right ventricular outflow tract reconstruction (2.6%), separted double outlet ventriciles (2.6%) to abnormal AV valves (mitral clefts and Ebstein’s anomaly) (2.1%), corrected transposition, pulmonary valve and pulmonary branch stenoses.

33.6% have had no previous interventions
58.5% have had a single surgical repair of which 10.9% have had one or more reoperations
7.9% have had palliative procedures only.

There have been a few patients with complex cyanotic heart disease who we have referred for their first operative intervention in their 20s, including TCPC in a patient with single ventricle, and right ventricular outflow tract reconstruction in a patient with complex pulmonary atresia.

2.1% have had catheter interventions such as dilatation of aortopulmonary collars, coil obliteration of residual shunts, etc 2.1% have had pacemaker implantations.

One patient has already been transplanted (atrial septal defect and restrictive cardiomyopathy), three are waiting (two heart–lung and one heart transplant), and one died on the waiting list.

We use transoesophageal echocardiography and magnetic resonance imaging in selected patients in addition to the more routine use of echocardiography, ECGs, Holter monitoring, and exercise testing. Very complicated cases are usually sent to a tertiary centre for catheterisation, with whom we have a close liaison; indeed in some cases the patient care is shared and discussion of difficult problems in other cases is helpful. The patients do seem to value a dedicated clinic in their local hospital, particularly when given the time to discuss contraception, employment, insurance, housing, inheritance, and pregnancy.

New patients transferred from the paediatric service are also introduced to the GUCH (grown up congenital heart) association, which has newsletters, helplines, and area meetings. We try to maintain an emergency slot for patients if they become worried about symptoms. “At risk” pregnancies are also supervised within the clinic, with close liaison with obstetricians and anaesthetists. Fetal echocardiography is performed at 20 weeks. We would concur with Gatzoulis et al that structured transitional requirements for these patients must be introduced so that they are not lost to follow up when the leave the paediatric service and, as we hope we have shown, a dedicated clinic within a region does fulfil a need, a point purchasers may care to note.

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