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 paper by the Indian group on the management of scorpion sting.1 We were therefore surprised by the 25% mortality reported by Karnad,2 which we were unable to confirm in the present series. We have analysed the last 1000 cases of scorpion sting at our centre, from January 1988 to June 1999. There were 54 deaths (5.4%). The scorpions in question were taken for analysis in 658 cases of severe scorpion sting. We believe that the transport of the scorpion venom is done after being stung. We have reported that the severity of scorpion sting depends on the victim's age, the season, and the time between sting and admission of the patient.3 The symptoms following the sting are hypotension, tachycardia, pulmonary oedema, and shock (autoimmune storm).4 We believe that the transport of Karnad's patients to the nearest hospital may have contributed to their death. Seven of eight had acute pulmonary oedema owing to a delay in reaching a tertiary care hospital.

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.5 Captopril (an ACE inhibitor) has a similar action resulting in hypotension resistant to dopamine agonists. Bradykinin further enhances noradrenaline (norepinephrine) release by a presynaptic mechanism.6 Alpha receptor stimulation plays a major role in the pathogenesis of pulmonary oedema.7 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.8

At a general hospital at Madh we successfully treated 658 cases of severe scorpion sting with oral rehydration, oral prazosin, and oxygen and mannitol: 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 Madh had been referred 24 hours after being stung while 13 cases were admitted with multigorgan failure and were moribund and comatose; they died 30–60 minutes after admission despite treatment with dopamine, nitroprussiade, oxygen and hydralazine-drip. The remaining 56 cases with invasive 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. Further investigations would have been life saving in the two patients treated with captopril who died in Karnad's report.9 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 trisphosphate, and activates venom inhibited calcium dependent potassium channels. Thus prazosin reverses both inotropic (hyperpension), and hypokinetic (pulmonary oedema, hypotension, tachycardia) phases evoked by scorpion envenoming.

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2 Bawaskar HS, Bawaskar PH. Envenoming by scorpion venom: their pathophysiological manifestations and therapeutic approach. Trop Doct. [In press.]
3 Bawaskar HS, Bawaskar PH. Prazosin in the management of scorpion envenoming: a review of common therapies and their neurotoxins and therapeutics. Trop Doct. [In press.]

EDITOR,—The study by Karnad1 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 artery 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 1980,2 and confirmed by numerous series in human subjects.3 All of these series performed a haemodynamic study and concluded that they were 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 envenomed patients and the treatment strategy he suggests. A haemodynamic, echocardiographic, and angiosciographic studies have shown that severe scorpion envenomation impairs left and right ventricles to the same extent.4 Echocardiographic studies showed that LV systolic function might be deeply depressed with a mean LV fractional shortening as low as 12%.5 Regarding the right ventricle, in eight patients we recorded a mean RV ejection fraction of 24%.6 In fact, severe scorpion envenomation evokes acute heart failure which tends to recover in a few days. The heart failure might be concealed in some patients by the simultaneous hypovolaemia that occurs in envenomed patients as a consequence of vomiting and sweating. Hence, the patterns II, III, and IV described by Karnad should not be regarded differently from the multiple facets of the same and only haemodynamic feature that is the profile of acute heart failure (patterns II and IV) that might be mitigated by simultaneous hypovolaemia (pattern III). Moreover, the three reported patients who had simultaneous hypovolaemia exhibited a worsening in their pulmonary oedema with fluid infusion, suggesting an exaggerated increase in PAWP resulting from altered LV function.

Although attractive from a pathophysiological standpoint, Karnad challenges the usefulness of inotropic drugs and claims that they improve only transiently the circulatory failure observed in scorpion envenomation with no effect on mortality. We are unaware of any study specifically addressing this issue. Nevertheless, owing to the clearly established haemodynamic pattern of severe scorpion envenomation and on the basis of a pathophysiological approach, we have therefore treated envenomated patients exhibiting pulmonary oedema and/or peripheral circulatory failure with dobutamine. The physiological effects were as expected, those usually observed in the treatment of heart failure: an increase in cardiac output as a consequence of an increase in stroke volume with enhanced LV performance, a substantial decrease in PAWP, and an increase of arterial pressure.

Finally, Karnad suggests that RV failure occurs late in the terminal phase of scorpion envenomation and combines with pre-existing LV failure to produce severe cardiogenic shock. This speculation is not supported by Nouria et al who used a modified Swan–Ganz catheter equipped with a fast response thermostance.7 This study showed that scorpion envenomation evokes simultaneous impairment of the LV as well as the RV, the latter being depressed to the same extent as the former. Infusion of dobutamine enhances RV as well as LV performance.

In conclusion, scorpion envenomation kills thousands of patients in developing coun-
tries. First line clinicians need comprehensive and meaningful insights regarding the pathophysiology and valuable treatments of this dreaded accident. The clearer and simpler the message on this issue the better the effect in daily clinical practice.

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These letters were shown to the author, who replies 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 is impressive. They cite their personal experience with 388 patients treated with prazosin, of whom only 30 (4.5%) died. They had previously reported 526 patients treated with prazosin up to 1992; in this series 28 patients died.1 They are surprised that two of the eight patients reported in my paper died. However, it must be understood that as the objective of my paper was to describe haemodynamic patterns, only eight patients in whom detailed serial haemodynamic data were available were reported; these cases are not the entire experience of our unit with captopril in scorpion envenomation.

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 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, their pattern did not improve and we did not receive 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 hypertension. Four patients (all had severe pulmonary oedema with hypertension) 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 were 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 oedema.

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.1 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.2 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 affected 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 inotropic drugs, have shown that vasodilator therapy improved the treatment of cardiovascular manifestations of scorpion envenomation.3 4 Vasodilators like prazosin, calcium channel blockers, ACE inhibitors, etc, have been used.3 4 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.

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 predictor of mortality.1 They measured BNP in 25% of patients surviving AMI who did not improve with captopril.2 The objective of my paper was to describe haemodynamic patterns, only eight patients being studied.3

Using a pulmonary artery catheter, right ventricular stroke work index, while right ventricular ejection fraction was 24% following envenomation and improved to 39% during recovery.2 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 affected 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 inotropic drugs, have shown that vasodilator therapy improved the treatment of cardiovascular manifestations of scorpion envenomation.4 5 Vasodilators like prazosin, calcium channel blockers, ACE inhibitors, etc, have been used.4 5 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.


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

Dr Khan’s letter raises a number of interesting points. First, when the site of myocardial infarction (anterior or inferior) is included in multivariate analysis of data reported in our recent paper, plasma BNP remains an independent prognostic indicator for both death and development of heart failure. This is not surprising as division of patients according to inferior or anterior site of infarction creates crude categories, which both include a broad spectrum of injury from mild to very severe. In contrast, plasma BNP is a continuous variable and is related to the severity of myocardial injury across the entire group. This finding is also predictable in view of the fact that already published reports have indicated BNP has prognostic power independent of left ventricular ejection fraction (LVEF). Moreover, our report also makes it very clear that the possible upper limit for BNP above this level is very wide (that is, BNP above the normal range within the early postinfarction period is a weak predictor of reduced LVEF), and we do not recommend the routine use of plasma BNP as a substitute for measurement of left ventricular ejection fraction.

The most important and insightful part of Dr Khan’s letter is that he stresses the possible potential for BNPs together with ejection fraction to identify high risk populations in whom some sort of intervention is feasible before development of “clinical end points”. He states correctly that at present there is no evidence to suggest that treating a high plasma BNP in the presence of a normal ejection fraction improves outcome. In a manuscript now in preparation, the Christchurch Group is able to report follow up data on over 500 MI patients with a mean follow up period of approximately two years. This group has been divided according to both plasma BNP and radionuclide LVEF. Notably, over 20% of the group have an early postinfarct LVEF in excess of 40% but a concomitantly high BNP of over 25 pmol/l. (2.5 times the upper limit of normal). This subgroup has a significantly greater risk of mortality and of developing heart failure than the group with LVEF above 40% and plasma BNP < 25 pmol/l. Furthermore, in patients who have ejection fractions below the 40% threshold but BNP < 25 pmol/l, there is a very high increase in risk of either death or heart failure over two years compared with that group with low BNP concentrations and high ejection fraction. In other words, reduction in ejection fraction only predicts a higher level of mortality or mortality in the presence of neurohormonal activation as indicated by raised plasma BNP. Our findings concur with data from colleagues in Sweden and Norway (T Omland, C Hall, personal communication), and it is becoming clear that a randomised controlled trial of treatment in asymptomatic patients with LVEF > 40% but clear neurohumoral activation should be done.

Transfusion associated graft versus host disease

Editor,—Ahye et al reported a case of transfusion associated graft versus host disease (TA-GVHD) in a non-immunocompromised patient resulting from blood transfusion for coronary artery bypass grafting (CABG). 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 common conditions such as sepsis and malignancy. Moreover, histological diagnosis needs specialist expertise in tissue typing.

We report another patient with TA-GVHD acquired following elective four-vessel CABG and periperooperative 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 sputum. He had an extensive erythrodemic maculopapular 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 maximal support he died within seven days of readmission.

Although TA-GVHD does occur in immunocompetent individuals who had blood transfusion following other 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 unlikely to be multifactorial. Preoperative surgery, use of fresh blood with more frequent following cardiopulmonary bypass surgery, use of fresh blood with lymphocytes, immunosuppressive effect of multiple transfusions, and transient reduction in interleukin 2 production may all have roles in the pathogenesis of this disease. TA-GVHD should be considered in patients who develop unexplained multiorgan failure following major surgery, and a high index of suspicion is required. We agree with the authors that the published literature is conflicting and we reiterate the need for further research into the prevention of this distressing complication.


cardiopulmonary bypass may all cause a degree of immune dysfunction. If the donor's blood happens to be homoygous 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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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 establishing catheter facilities on this site and the link with 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 septic defects (both atrial and ventricular). As uncomplicated, 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 had various other conditions from complex congenital heart disease including tricuspid atresia with Fontan op-eration (1.3%), single ventricle with total cavopulmonary connection (TCPC) (1%), complex pulmonary atresia with right ventricular outflow tract reconstruction (2.6%), septated double outlet ventricles (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 dilation of aortopulmonary collaterals, 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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