LETTERS

High rate of immediate systemic hypersensitivity reactions to tiger snake antivenom

Geoffrey K Isbister, Alan S Tankel, Julian White, Mark Little, Simon G A Brown, David J Spain, Chris F Gavaghan and Bart J Currie

To the Editor: During a national multicentre study of snake bites — the Australian Snakebite Project (ASP), involving over 40 hospitals — we have recently noted a high rate of early allergic reactions following the administration of tiger snake antivenom in Australia. People with suspected or definite snake envenoming are recruited to ASP, and laboratory and clinical data and serial blood samples are collected to measure venom and antivenom concentrations.

From 1 November 2005 to 31 January 2006, 14 patients who had been given tiger snake antivenom (CSL Limited, Parkville, VIC) were recruited. These patients are briefly described in the Box, and include bites from several different groups of snakes. Of the 14 patients, 11 exhibited immediate systemic hypersensitivity reactions to antivenom infusion. Reactions were mild in five patients, moderate in three, and severe in three, according to the grading system by Brown.[1] The six patients in the moderate and severe groups fulfilled the criteria for anaphylaxis according to a recent consensus definition.[2] All patients required specific treatment in addition to ceasing antivenom therapy, and nine were treated with adrenalin. Antivenom was recommenced in all patients at a slower rate, although an adrenalin infusion was required in four of these and repeat doses of intramuscular or subcutaneous adrenalin in another four while the antivenom infusion continued.

Over the same period, there were seven administrations of brown snake antivenom (over 30 vials of antivenom) reported to ASP without any hypersensitivity reactions.

There has been a previous report of allergic reactions to tiger snake antivenom in a single hospital,[3] and we are concerned that there may be a particular problem with tiger snake antivenom. The reaction rate in this series is similar to reported rates in parts of the world where high reaction rates have been attributed to relatively impure antivenom preparations.[4,5] The reactions here were traced to at least four different batches of tiger snake antivenom.

Fourteen patients administered tiger snake antivenom for snake envenoming

Age/sex	Previous antivenom	Snake	Clinical features	Grading	Treatment of reaction
47 M	No; SH	BHS	No reaction	Nil	Nil
13 M	No	TSG	No reaction	Nil	Nil
17 M	No	TSG	Nil	Nil	Nil
20 M	No	TSG	Generalised erythema, urticaria, tachycardia	Mild	IM adrenalin (0.5 mg), then IV adrenalin infusion
12 M	No	RBBS	Generalised erythema	Mild	IM adrenalin (0.2 mg × 3)
12 M	No	RBBS	Generalised erythema, urticaria	Mild	IM adrenalin (0.25 mg × 2)
28 F	No	TSG	Pruritus, erythema and moist cough (no wheeze)	Mild	Promethazine (10 mg)
53 M	No	TSG	Generalised pruritus	Mild	Promethazine (25 mg)
32 M	No	TSG	Dizziness, chest tightness, tachycardia, vomiting	Mod.	SC adrenalin (0.3 mg)
21 M	Yes; SH	SBS	Generalised rash and pruritus, vomiting	Mod.	IV adrenalin infusion for 1 hour
9 M	No	SBS	Urticarial rash, chest tightness	Mod.	IV adrenalin infusion
55 M	No; SH	PHS	Generalised pruritus, diaphoresis, confusion, hypotension	Severe	SC adrenalin (0.5 + 0.5 + 1 mg), IV fluid, IV hydrocortisone (100 mg)
M	No	RBBS	Rash, wheeze and hypotension	Severe	Adrenalin, IV fluid, antihistamines, steroids
45 F	No	TSG	Hypotension, sweaty and unwell appearance	Severe	IV adrenalin infusion

BHS = Broad-headed snake (*Hoplocephalus bungaroides*); IM = intramuscular; IV = intravenous; Mod. = moderate; PHS = Pale-headed snake (*H. bitorquatus*); RBBS = Red-bellied black snake (*Pseudechis porphyriacus*); SBS = Stephens' banded snake (*H. stephensii*); SC = subcutaneous; SH = snake handler; TSG = Tiger snake group (any snake from the *Notechis*, *Hoplocephalus*, *Tropidechis*, and *Austrelaps* genera). ◆

We have informed CSL of this high rate of reactions and the antivenom batch numbers, and we have encouraged the treating doctors to make formal reports of each adverse reaction to CSL and the Adverse Drug Reactions Advisory Committee.

Health care professionals treating patients with tiger snake antivenom need to be aware of the possible higher risk of anaphylaxis with tiger snake antivenom and be prepared to treat with adrenalin. Recommendations for the diagnosis and treatment of anaphylaxis have recently been reviewed.[6] However, this current problem with CSL tiger snake antivenom should not cause health professionals to reduce or cease its use. In all patients described here, control of the adverse reaction and continuation of antivenom was possible. The rapid identification of this problem over a short period was only possible because of our large multicentre collaborative study, and supports such studies for recognising uncommon envenoming syndromes.

Competing interests

Julian White is employed by the Women's and Children's Hospital, Adelaide, which is paid by CSL Ltd to provide a clinical toxinology service for users of CSL antivenom and venom detection products.

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Jane Leong

Comment: Thank you for the opportunity to comment on the letter by Isbister et al regarding hypersensitivity reactions to tiger snake antivenom.

CSL has been notified about the cases of hypersensitivity reactions to tiger snake antivenom in general, but has only received two individual case reports. We have been in contact with the study investigators and have requested more detailed information on the other patients so that we can further our investigations.

A thorough check of product manufacturing records revealed no deviations from approved specifications for tiger snake antivenom.

It is important to note Isbister et al have advised health professionals not to reduce or cease the use of tiger snake antivenom. We would like to draw physicians' attention to the approved Product Information before use of the product. The tiger snake (and other antivenom) Product Information lists the possibility of both anaphylactic and anaphylactoid reactions. Hypersensitivity and skin reactions (including urticaria, rash, hypotension, bronchospasm, anaphylaxis and delayed serum sickness) are listed as common, and are more likely to occur in people who have had previous exposure to equine-based products.

In addition, the Product Information describes an anaphylactoid reaction which can occur because the antivenom has the ability to bind complement. The risk of this reaction can be minimised by adequate dilution of the antivenom (1 : 10 for adults and 1 : 5 in small children) before infusion. Further, the Product Information states that a syringe already loaded with 1 : 1000 adrenalin must be available during antivenom therapy.

CSL is continuing to monitor this situation closely and is awaiting further details on the patients from the reporting physicians. In the meantime, we encourage users of all antivenom products to report any untoward reaction to CSL so that these can be fully evaluated.

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An African strain of community methicillin-resistant *Staphylococcus aureus* in a Burundi refugee

Annabelle Donaldson and Iain B Gosbell

To the Editor: Community strains of methicillin-resistant *Staphylococcus aureus* (MRSA) are increasingly seen in Australia, particularly in certain population subgroups, such as Pacific Islander[1] and Aboriginal[2] people. We report the case of an African with community MRSA to highlight its existence in yet another subgroup. Given the increase in people arriving in Australia from Africa under the Humanitarian Program (with around 8500 arrivals from Africa in 2004–2005)[3] and their wide dispersal around the country, it is possible that African community MRSA will be seen increasingly in Australia.

A 53-year-old Burundi refugee presented with an infected wound overlying the left lateral malleolus after laceration 6 weeks previously in a Tanzanian refugee camp. An unknown antibiotic was given for 2 weeks before travel to Australia. On the patient's arrival in this country, the wound appeared purulent, erythrocyte sedimentation rate was 82 mm/h (reference range [RR] < 10 mm/h), and C-reactive protein level was 9 IU/L (RR < 5 IU/L). Plain x-rays and bone scans suggested osteomyelitis.

A wound swab grew *S. aureus*, *Streptococcus pyogenes* and *Pseudomonas* species. The patient was initially given intravenous cefazolin, and then definitive therapy (for MRSA and *S. pyogenes*, ignoring the colonising pseudomonad) with oral clindamycin (450 mg three times daily). Clinical resolution was complete, and levels of acute-phase reactants returned to normal.

The antibiotic sensitivity pattern of the *S. aureus* isolate raised suspicion that it might be an unusual strain: it was resistant to methicillin, tetracycline and trimethoprim–sulfamethoxazole, but sensitive to erythromycin, clindamycin, ciprofloxacin, gentamicin, vancomycin, linezolid, mupirocin, rifampicin, fusidic acid and chloramphenicol.

The *mecA* gene was detected by polymerase chain reaction testing, confirming methicillin resistance. The organism possessed staphylococcal cassette chromosome *mec* (SCC*mec*) element type IV. The Panton–Valentine leukocidin gene, staphylococcal enterotoxins A to E and toxic shock syndrome toxin-1 were not detected. As DNA fingerprinting with standard pulsed-field gel electrophoresis showed a novel banding pattern, the "gold standard" of multilocus sequence typing was used for identification. This confirmed an ST140 allelic profile, which has not been seen previously in Australia.[4] On the balance of probabilities, the isolate represents an African community MRSA strain, not previously detected in Australia.

Non-multiresistant community MRSA is not widely recognised in African countries. Hospital MRSA rates vary widely in Africa (eg, between 21% and 30% of all *S. aureus* isolates in Nigeria, Kenya and Cameroon, and fewer than 10% in Tunisia and Algeria[5]), but most are multiresistant.

Medical practitioners in Australia who treat African refugees need to be aware that pyogenic soft tissue infections could be caused by community MRSA, and these MRSA strains may have a different antibiotic sensitivity profile to Australian community MRSA strains. It is essential to take appropriate specimens for microbiological analysis (wound swabs and possibly blood cultures and/or tissue samples), as antibiotic susceptibility profiles are increasingly unpredictable.

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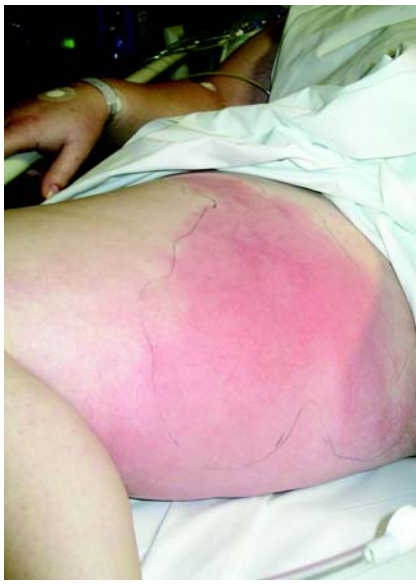
Invasive meningococcal disease presenting with cellulitis

Karina J Kennedy, Jhumur Roy and Paul Lamberth

To the Editor: We recently treated two patients with invasive meningococcal disease presenting with cellulitis. This presentation contributed to a delay in diagnosis and appropriate antibiotic treatment.

Cellulitis in Patient 1



Cellulitic area on the right thigh of a 33-year-old woman with Neisseria meningitidis *meningitis.* ◆

The first patient was a 33-year-old woman, recently diagnosed with nephrotic syndrome, who had been unwell for a week with mild upper respiratory tract symptoms. During this time, her nephrologist began treating her with prednisolone (15 mg daily). The day before presentation, she developed abdominal pain, vomiting, chills, myalgia and headache. A rash developed on the day she presented to hospital. The temperature was 39.2°C, heart rate 148 beats per min, and blood pressure 146/57 mmHg. She had an area, measuring 20 cm × 20 cm, of tender cellulitic rash on the right thigh (Box) and mild neck stiffness.

The diagnosis was initially unclear, leading to a delay of several hours before ceftriaxone was administered, and a lumbar puncture performed. Cerebrospinal fluid (CSF) examination revealed a leukocyte count of 4500×10^6/L (98% polymorphs) (reference range [RR], $< 5 \times 10^6$/L), gram-negative diplococci, and protein concentration of 2073 mg/L (RR, 150–450 mg/L). The patient subsequently required intensive care admission for non-invasive ventilation and inotropic support. *Neisseria meningitidis* serotype C was detected in the CSF by polymerase chain reaction testing. The patient was discharged well except for mild headache and lethargy after 6 days. At 1-week review, she remained lethargic but was otherwise well. The rash was slowly resolving.

The second patient was a 51-year-old woman with fever and a 2-day history of progressive pain, swelling and erythema of the anterolateral area of the neck. The temperature was 38.5°C, heart rate 115 beats per min, and blood pressure 134/86 mmHg. There was no evidence of upper airway involvement. The anterior area of the neck and upper chest wall were swollen, erythematous, tender and warm. No fluid collections or masses were detected on ultrasound examination.

The patient was admitted to hospital with a diagnosis of cellulitis, and treatment was begun with intravenous flucloxacillin and metronidazole. After 17 hours, culture of blood taken on admission showed *N. meningitidis* serotype W135. Antibiotic treament was changed to ceftriaxone. After 5 days, the patient had mild residual inflammation and tenderness of the neck. She completed another week of treatment with oral amoxycillin.

Only 14 cases of *N. meningitidis* cellulitis have been published.[1-3] Seven cases involved children with periorbital cellulitis. In adults, three cases involved the face and neck, and four the limbs. *N. meningitidis* was isolated from blood (eight patients), conjunctival swabs (three), aspirates of the cellulitic areas (two) or CSF (one). There was one death: an elderly woman with bacteraemia and cellulitis of the face and neck.[2] As illustrated by our cases, the many guises of meningococcal disease continue to challenge clinicians.

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Professional development of registrars

Jagdishwar Singh

TO THE EDITOR: The CanMEDS 2000 report[1] and its 2005 revision[2] have emphasised that effectiveness as a medical specialist requires competencies in addition to clinical and medical expertise. These include being a communicator, collaborator, manager, health advocate, scholar and professional.

Building the non-clinical skills of doctors has been the focus of a professional development project in Australia that is targeting registrars. Junior doctors usually step up to the role of registrar in the 3rd year of their prevocational training. A national workshop convened by the Postgraduate Medical Council of Victoria in March 2004 agreed on a framework for the professional development of registrars, comprising the following 10 competencies: leadership; communication skills; supervision; mentoring; teamwork; self-awareness and empathy; time management; problem solving; professionalism and ethics; and safety and quality.[3]

To provide content for these competencies, a job-shadowing exercise involving two registrars at two different Victorian hospitals was undertaken in April 2005 to get a first-hand understanding of the roles of medical registrars as managers. The registrars were voluntary participants, and permission was obtained from all participants. I shadowed the two registrars during their entire 9-hour shifts. No major issues arose in relation to the shadowing process itself, and the consultants overseeing the two registrars were extremely accommodating in this process. The two observed registrars authenticated the veracity of the recorded observations. The observations from the job-shadowing exercise were clustered into competencies using the framework developed for the professional development of registrars discussed above. The Box summarises these observations and highlights the range of registrar interactions that are influenced by non-clinical competencies.

While the small number of registrars is an obvious limitation of the study, this job-shadowing exercise did demonstrate that managerial skills, knowledge and behaviour represent a significant component of the work of clinicians, especially as they move up the medical hierarchy. This assertion should not be misconstrued as suggesting that the clinical skills and knowledge become any less important. As noted in the 2005 CanMEDS framework, the medical expert role is the central role for doctors.

It is also worth noting here that some pilot professional development programs con-

Observations during job-shadowing of two registrars at two Victorian hospitals

Competency	Observed interactions
Supervision	• Reviewing patient treatment plans and test results and prescribing a course of action • Ensuring that procedures are followed • Coaching intern on test procedures, completion of patient records, etc • Giving ongoing feedback to intern • Delegating tasks to intern • Coordinating patient treatment with other units
Leadership	• Dealing with other health professionals, some of whom take directions from the registrar, as well others over whom there is no formal authority • Providing advice to intern and role modelling desired behaviour • Demonstrating the ability to respond quickly and with confidence • Involving subordinates and providing opportunities for them to participate in decision making • Using networking skills with other departments • Using negotiating skills in dealing with other departments, hospitals, etc
Communication skills	• Using communication skills with patients, intern, medical colleagues, other health care professionals, and service departments • Dealing with cross-cultural diversity issues with patients, their families, and staff • Using negotiating skills in dealing with other departments, hospitals, patients, and family members • Using recording skills to ensure treatment plans properly documented for others
Time management	• Prioritising patient list for ward rounds • The constant need to re-assess priorities during ward rounds, in light of time constraints • The ability to deal with constant interruptions from other colleagues, to provide necessary clarifications
Problem solving	• Making decisions on patients' continued treatment or discharge, and stipulating any follow-up action • Task contingency management skills to deal with patient treatment plans not proceeding as planned • Dealing with information gaps in patient historical records • Involving intern and other staff to assist in the decision-making process and raising issues with consultant
Professionalism and ethics	• Dealing with demarcation issues with other doctors and professionals • Role modelling professional behaviour to patients, staff, and the public • Balancing the interests of patients with hospital needs, without sacrificing patient trust • Obtaining patient consent for procedures
Teamwork	• Coordinating treatment plans with other doctors and health professionals • Sharing information and agreeing on treatment plans with allied health staff • Joint meeting with other colleagues to advise a patient and family members on surgical procedures and associated risks • Ability to work in both collaborative and individual modes during the day
Mentoring	• Providing advice to intern to be more assertive and confident when dealing with consultant
Self-awareness and empathy	• Patience and empathy in giving bad news to family • Dealing with patients who are aged or mentally or physically challenged
Safety and quality	• Knowledge and application of safe practices in relation to patient management • Ensuring that procedures are followed, such as obtaining consent, ordering of tests, etc • Reviewing records before dispensing treatment • Recording treatment plans and medications ◆

ducted recently as part of the registrar project show that registrars welcome training that enhances their non-clinical skills, especially when provided professionally in an environment conducive to learning.

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Effective shade structures

Kay R Coppa and John S Greenwood

To the Editor: We were pleased to read Turnbull and Parisi's short piece on the effectiveness of shade structures, highlighting the challenges of ensuring adequate and effective shade protection, particularly in children's settings.[1] Cancer councils in various states have long recognised these challenges and provided assistance to those who design or manage facilities for children, in the form of training workshops, resources and guidelines.

Epidemiological evidence indicates that childhood exposure to ultraviolet (UV) radiation is a strong determinant of risk of melanoma but there is also evidence of its contribution to the development of non-melanocytic skin cancer.[2,3] It is estimated that living in Australia for the first 15 years of life contributes about two-thirds of the lifetime risk of melanoma of a lifelong resident.[4] Sun exposure in childhood, especially that leading to sunburn, is the main environmental determinant of the number of melanocytic naevi. An individual's number of naevi is the strongest measurable predictor (after age and ethnicity) of risk of melanoma.[5]

Our publication, *Under Cover*, referred to by Turnbull and Parisi, is one such resource, developed as a comprehensive reference tool for anyone involved in shade planning and design in New South Wales and has been adapted for use in other states by state cancer councils.[6]

Turnbull and Parisi comment that *Under Cover* provides inappropriate advice regarding the use of deciduous trees, as solar UV radiation levels can be hazardous during winter in subtropical Queensland. As might be expected, the NSW edition of *Under Cover* does not address winter solar protection issues in northern Queensland.

We note that the "requirements for effective shade" cited by Turnbull and Parisi are identical to those prescribed in *Under Cover*.

For those interested in determining when UV protection is required throughout the year in different locations, an interactive shade planning software program will be available shortly at <www.webshade.com.au>. In it, ShadeCalendar recommends what type of shade would be most appropriate for comfort and solar protection in different months of the year. The Bureau of Meteorology now issues the SunSmart UV Alert when the UV Index is forecast to reach 3 or above, highlighting when sun protection is required (www.bom.gov.au/products/uvindex_national.shtml). The SunSmart UV Alert is reported in most newspaper, television and radio weather forecasts across Australia.

Shade is only one of a range of sun protection strategies recommended by the Cancer Council. With Australia having the highest skin cancer rates in the world, general practitioners play a pivotal role in providing sun protection counselling advice to parents of children aged 1–13 years.[7] The Cancer Council NSW recommends a range of sun protection measures including UV avoidance during the peak UV times (10:00–14:00 or 11:00–15:00 during daylight saving time), shade, clothing, hats, sunglasses and use of sun protection factor 30+ broad spectrum, water resistant sunscreen.

Competing interests

John Greenwood owns shares in, and is a Director of, WebShade Pty Ltd.

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Chronic heart failure: time to optimise methods of diagnosis in the community

Heather H Buchan, Susan M Phillips, Lynn M Weekes, Judith M Mackson, Andrew N Boyden and Andrew M Tonkin

To the Editor: Investigators in the recent Canberra Heart Study[1] highlighted the importance of improving the detection of heart failure in the community, given the high proportion of people with preclinical disease. The accompanying editorial[2] expressed concern about the lack of major Australian initiatives that focus on the prevention and treatment of this disease.

We fully endorse the authors' view that under-recognition and under-treatment of heart failure is an important national issue. While we support their call for sustained and adequately funded programs, we feel it is important to note that there *are* initiatives under way to attempt to improve the situation. The National Prescribing Service, the National Heart Foundation of Australia and the National Institute of Clinical Studies joined forces in 2004 to improve the diagnosis and management of heart failure in primary care. A national program, undertaken in partnership with 45 divisions of general practice, began in October 2004 and will conclude in early 2006.[3]

Nationally, the program provided newsletter materials to all general practitioners, pharmacists and physicians.[4] In participating divisions, educational outreach visits and interactive small group meetings involved over 1600 GPs and local specialists in discus-

sions of the role of echocardiography in diagnosis, and pharmacological and lifestyle management issues. Patient education materials were also widely disseminated.[5] Outcomes of this large-scale quality improvement program are currently being evaluated, and results are expected to be available in early 2007.

Other groups have also recognised heart failure as an important issue — for example, it is one of the featured conditions in the Department of Veterans' Affairs Medicines Advice and Therapeutics Education Services program.[6]

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