

Aphasia in a farmer after viper bite

Sir—J M Polo and colleagues (June 22, p 2164)¹ report aphasia in a farmer after he was bitten on the left thumb by a viper. He developed swelling and ecchymosis of the corresponding limb. He reported to hospital within 2 h of being bitten, and his status was an absolute indication for immediate administration of polyvalent antivenom, according to WHO recommendations, to avoid the systemic effects of venom.² However, delayed administration of antivenom or waiting until he had systemic manifestations—ie, a 6 h wait—resulted in systemic envenoming.

We work in a rural area and have reported various poisonous snake bites.³ Between June, 2001, and May, 2002, six people were admitted to hospital for viper bite (four *Echis carinatus*, one Pit viper, one Russell's viper). The time lapse between bite and admission was 2.5, 1.0, 1.25, 4.5, 1.5, and 1.5 h, respectively. All patients brought the killed snakes to the hospital for identification.

Every patient developed progressive local oedema extending beyond the bitten segment of the limb, with ecchymosis. All were given polyvalent antivenom without test dose, preceded by subcutaneous adrenalin as prophylaxis against anaphylaxis to the antivenom.² Each patient recovered within 48 h without development of systemic manifestations.

A male farmer aged 32 years was bitten on the dorsum of his right hand by a Russell's viper while harvesting grass. He felt giddy and experienced severe pain at the site of the bite. Swelling developed rapidly with bleeding from the fang marks. He reported to hospital within 1.5 h. On arrival, his blood pressure was 80/60 mm Hg. He developed rapid progressive swelling with ecchymosis over the bitten limb, and enlarged tender lymph nodes in right axilla. His head was placed in a low position, intravenous crystalloid solution was administered, and 4 mL blood was drawn into a clean glass test tube for coagulation testing.² His blood did not clot for 20 min and remained incoagulable. We gave the patient ten vials of polyvalent antivenom in 200 mL dextrose over 60 min. Oedema lessened gradually over 48 h. His blood clotted within 10 min after 6 h of administration of antivenom. We gave him penicillin for wound infection and tetanus immunisation; he did not have diabetes.

Early administration of antivenom if the indication is clear² can

prevent development of venom-induced thrombus and subsequent development of disseminated intravascular coagulation.^{3,4} The delayed administration of antivenom to Polo and colleagues' patient resulted in systemic envenoming; the patient kept his head turned to the left, which suggests that he was pointing the lesion at left cerebral cortex.⁵ Timely administration of appropriate and adequate quantity of polyvalent antivenom is more beneficial^{2,3} than waiting.

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- 2 Warrell DA. WHO/SEARO guidelines for the clinical management of snake bites in the southeast asian region. *Southeast Asian J Trop Med Public Health* 1999; **30** (suppl): 1–84.
- 3 Bawaskar HS, Bawaskar PH. Profile of snake bite envenoming in western Maharashtra, India. *Trans R Soc Trop Med Hyg* 2002; **96**: 79–84.
- 4 Cardoso JLC, Fan HW, Franca FOS, et al. Randomized comparative trial of three antivenoms in the treatment of envenoming by lance-headed viper (*Bothrops jararaca*) in São Paulo, Brazil. *Q J Med* 1993; **86**: 315–25.
- 5 Horton JC. Disorder of the eye. In: Brunald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, eds. *Harrison principles of internal medicine*; 15th edn. New York: McGraw-Hill, 2002: 164–77.

Drug resistance and influenza pandemics

Sir—Nikolaos Stilianakis and colleagues (May 25, p 1862)¹ discuss the issue of drug resistance and influenza pandemics.

They state that amantadine is associated with substantial toxic effects when used in the elderly and renally impaired. This belief is based on use of doses higher than those recommended in the UK, where the standard dose is 100 mg daily, and lower in the elderly and renally impaired. If elderly people receive half the daily dose of otherwise healthy adults, the nature and rate of side-effects are similar.² Side-effects associated with the standard UK dose are generally mild and transient.

The usefulness of amantadine for the control of influenza in residential homes is recognised in Canada, where outbreak-control protocols are in operation that detail the dose regimens for people with various levels of renal function.

Stilianakis and colleagues further state that amantadine at the lower dose of the

UK and Japan is not established as effective against pandemic strains of influenza A. Effective treatment is impossible to show for something that has not yet happened. However, all isolates of the H9N2 and H5N1 potential pandemic viruses that have been tested by the UK Public Health Laboratory Service have been susceptible to amantadine. Furthermore, whether neuraminidase inhibitors, at any dose, will be effective against such strains is unknown.

High levels of resistant virus have been isolated only when amantadine has been used for the management of influenza in closed communities such as residential homes. Surveys of isolates from the community have shown only low levels of resistance. In the UK, the Public Health Laboratory Service has been screening for resistant influenza A isolates held in their laboratories. In a preliminary report on around 1500 isolates, the frequency of resistance was 1.5%.³ The high level of resistance that is quoted when amantadine is used in closed communities might be biased. If amantadine successfully controls an influenza outbreak in such a facility, isolates will probably not be collected for characterisation. Even when resistant virus has been isolated in residential facilities, amantadine has a net positive benefit.⁴

Since amantadine was approved for treatment of influenza A in Japan in 1998, a third of individuals with symptomatic influenza during outbreaks are estimated to have been treated with amantadine. Despite this approval, no widespread circulation in the community of amantadine resistant viruses is reported.

It is incorrect to state that amantadine has not reduced the incidence of the secondary complications of influenza. Amantadine has lowered the incidence of such complications in individuals who are otherwise healthy, elderly, or at high risk. In combination with vaccination, amantadine used for treatment of outbreak control reduces the risk of secondary complications, including hospital admissions and death in the elderly. Treatment with amantadine has also lowered the rate of progression to pneumonia in immunocompromised patients in hospital.⁵

Any restrictions on the use of amantadine would therefore lessen its therapeutic value.

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- 1 Stilianakis NI, Perelson AS, Hayden FG. Drug resistance and influenza pandemics. *Lancet* 2002; **359**: 1863–64.