ANTIVENOM THERAPY

Antivenom therapy should be commenced as soon as possible following the detection of systemic envenoming. Polyvalent antivenoms of Indian manufacture are used in Sri Lanka, produced using the venoms of Indian snakes—cobra, Russel's viper, common krait and saw-scaled viper. Their use against the venoms of Sri Lanka snakes should be confined to bites by the cobra, Russell's viper, kraits, and the saw-scaled viper. There is no benefit of antivenom therapy for bites of hump-nosed pit viper—even if severe local swelling is present—green pit-viper and seasnakes; envenoming by these snakes should be managed as described in the relevant articles.

Antivenom should NOT be administered for local envenoming EXCEPT for cobra bites. It may be given for local envenoming if half the limb is involved, or in ascending swelling, in other snake bites.

Reactions following antivenom administration - either early (within a few hours) or late (5 days or more) - are common. As many as 81% of recipients of antivenom incur a reaction, and as many as 43% were severe reactions (Ariaratnam et al, 2001, de Silva et al, 2016).

It is never too late to give antivenom provided the indications are present: systemic envenoming.
Give for local envenoming alone in cobra bites
and
only if extensive in bites of other snakes

Premedication

In view of the high incidence of reactions to the antivenom currently available, premedication with low-dose adrenaline, given just before the commencement of antivenom to prevent or reduce reactions is recommended. However, early detection and vigorous treatment of anaphylaxis continues to be very important.

For adults with no co-morbidities the dose of adrenaline is 0.25 mg subcutaneously (0.25 ml of 1:1000 solution)

The dose for children is 0.005 ml/kg body weight of 1:1000 solution subcutaneously

- WHO Guidelines 2016, p. 134

"Use of histamine anti-H1 and anti-H2 blockers, corticosteroid, and the rate of intravenous infusion of antivenom (between 10 and 120 minutes), do not affect the incidence or severity of early antivenom reactions"

- (WHO Guidelines 2016: de Silva et al, 2011; Isbister et al, 2012).

Antivenom administration

Antivenom is administered intravenously in both adults and children, after suitable dilution with normal saline. The antivenom dose in children is the same as for adults, as the venom dose would have been the same. But the volume of diluent needs to be adjusted to match the smaller body volume - see the article *Snakebite in Children*. Each vial of antivenom is supplied by the manufacturer together with a 10 ml ampoule of water for reconstituting prior to use. The total dose to be administered (usually stated as the number of ampoules or *reconstituted* volume) should be made up to a total volume of 500 ml with normal saline and infused over a period of one hour.

Antivenom dose

100-200 ml (10-20 ampoules) or more of Indian polyspecific antivenom in 400 ml of normal saline infused intravenously over one hour.
The dose of antivenom depends on the severity of envenoming—in acute, severe coagulopathy following Russell's viper bites 30 ampoules should be given as the first dose.

In **cobra and krait bites** usually **one** antivenom dose (10 ampoules) is sufficient.

In **Russell's viper bites** the first antivenom dose of 20-30 ampoules may be **repeated** in 6 hours in a dose of 10 ampoules if coagulopathy persists.

The endpoint of antivenom therapy is reversal of coagulopathy as determined by serial performance of the 20WBCT. Do not continue antivenom administration for persistent neurotoxicity, provided the coagulopathy has been reversed. In viper bites, monitor the efficacy of antivenom by repeatedly performing the 20WBCT at the bedside. Initially before the start of antivenom therapy. Repeat in 6 hours following antivenom infusion. If the blood does not clot in 20 minutes, repeat antivenom infusion (10 ampoules) and perform 20WBCT 6 hours later.

Continue the cycle till the blood clots.

CAUTION

Observe the patient carefully for signs of anaphylaxis

MONITOR

Pulse, blood pressure and respiration and observe for the appearance of a rash

Have adrenaline available at the bedside

TREAT ANAPHYLACTIC REACTIONS IMMEDIATELY

ANAPHYLACTIC REACTIONS

"The treatment of anaphylactic reactions to antivenom involves pharmacologic and non-pharmacologic interventions. Non-pharmacologic measures include temporarily stopping the antivenom infusion, airway management and fluid resuscitation. The mainstay of pharmacologic management is adrenaline given intramuscularly, which pharmacokinetic studies have shown to be superior to subcutaneous administration."

"Antihistamines and corticosteroids are no longer recommended for the treatment of anaphylaxis"

(de Silva HA et al, 2015; Simons FE et al, 2011 & 2013)

The WHO Guidelines 2016 clearly states that the mainstay of treatment of anaphylaxis following antivenom administration is intramuscular administration of adrenaline (of 0.5 mg for adults, 0.01 mg/kg body weight for children). It goes on to say that additional treatment can be given in the following circumstances:

- If bronchospasm is present inhaled salbutamol or terbutaline, and
- Chlorpheniramine maleate (adults 10 mg, children 0.2 mg/kg by intravenous injection over a few minutes).
- Intravenous hydrocortisone (adults 100 mg, children 2 mg/kg body weight) can be given, but it is unlikely to act for several hours.

Patients who remain shocked and hypotensive should be laid supine with their legs elevated and given intravenous volume replacement with 0.9% saline (1-2 litres rapidly in an adult). Intravenous epinephrine (adrenaline) infusion should be considered [adult dose 1mg (1.0 ml) of 0.1% solution in 250 ml 5% dextrose or 0.9% saline.

OTHER ANTIVENOM REACTIONS

Anaphylaxis is one of three possible types of reactions seen following antivenom administration. Competency in identifying them and responding appropriately is an essential part of the management of a snakebite victim. The following section has been compiled with material taken from the WHO Guidelines, 2016, pages 131 & 134, sections 6.7.5 & 6.7.5.4 and outlines treatment strategies.

Reactions following antivenom administration can take three forms:

1. **Early anaphylactic reactions**: usually within minutes and up to 180 minutes after starting antivenom. The patient begins to itch (often over the scalp) and develops urticaria, dry cough, fever, nausea, vomiting, abdominal colic, diarrhoea and tachycardia. A minority of these patients may develop severe life-threatening anaphylaxis: hypotension, bronchospasm and angio-oedema.

2. **Pyrogenic (endotoxin) reactions**: usually develop 1-2 hours after treatment. Symptoms include shaking chills (rigors), fever, vasodilatation and a fall in blood pressure. Febrile convulsions may be precipitated in children. These reactions are caused by pyrogen contamination during the manufacturing process. They are commonly reported.

3. **Late (serum sickness type) reactions**: developing 1-12 (mean 7) days after treatment. Clinical features include fever, nausea, vomiting, diarrhoea, itching, recurrent urticaria, arthralgia, myalgia, lymphadenopathy, periarticular swellings, mononeuritis multiplex, proteinuria with immune complex nephritis and rarely encephalopathy. Patients who suffer early reactions that are treated with antihistamines and corticosteroid are less likely to develop late reactions.

Treatment of Reactions

Anaphylactic reactions: Epinephrine (adrenaline) is given intramuscularly (ideally into the upper lateral thigh) in an initial dose of 0.5 mg for adults, 0.01 mg/kg body weight for children. Patients who remain shocked and hypotensive should be laid supine with their legs elevated and given intravenous volume replacement with 0.9% saline (1-2 litres rapidly in an adult). Intravenous epinephrine (adrenaline) infusion should be considered [adult dose 1mg (1.0 ml) of 0.1% solution in 250 ml 5% dextrose or 0.9% saline - (i.e., 4 µ (micro) g/ml concentration) - infused at 1–4 µ (micro) g/minute (15–60 drops/min using a microdropper burette chamber), increasing to maximum 10 µ (micro) g/min] and, in patients who remain hypotensive, a vasopressor agent such as dopamine [dose 400mg in 500ml 5% dextrose or 0.9% saline infused at 2–5 µ (micro) g/kg/min].

Patients who remain dyspnoeic, with bronchospasm or angioedema, should be propped up at 45 degrees and given supplemental oxygen by any available route together with optimal nebulised/inhaled and/or parenteral bronchodilator (β2 agonist) (Kemp & Kemp, 2014).

Pyrogenic reactions: the patient must be cooled physically (remove clothing, tepid sponging with fanning) and given an antipyretic (e.g., paracetamol by mouth or suppository).

Intravenous fluids should be given to correct hypovolaemia. Patients who also exhibit features of anaphylaxis should be given adrenaline as well (see above).

Treatment of late (serum sickness) reactions: Late (serum sickness) reactions may respond to a 5-day course of oral antihistamine. Patients who fail to respond within 24-48 hours should be given a 5-day course of prednisolone.

Doses: Chlorphenamine: adults 2 mg six hourly, children 0.25 mg/kg /day in divided doses. Prednisolone: adults 5 mg six hourly, children 0.7 mg/kg/day in divided doses for 5-7 Days

[See the **Quick Reference Guide** to Management of Antivenom Reactions for a simplified treatment algorithm]

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