

## MANAGEMENT OF REACTIONS TO ANTIVENOM

See *Antivenom Reactions - Introduction* for a general account of this topic.

Pyrogenic, anaphylactic and anaphylactoid reactions may result in similar clinical manifestations and possibly result in death. These manifestations include:

urticaria	nausea	tachycardia
itching	vomiting	hypotension
fever	diarrhoea	bronchospasm
chills	abdominal cramps	angioedema
rigors		

If reactions manifest—



**Stop antivenom infusion temporarily and treat all reactions immediately**

The severity of reactions may vary from mild to severe – in all cases there is itching, urticaria and rigors;

**Mild reactions:** are limited to the skin (urticaria, erythema & angioedema), the blood pressure is normal;

**Moderate reactions:** include diaphoresis (profuse sweating), nausea, vomiting, light-headedness (presyncope), dyspnoea, stridor, wheeze (bronchospasm), chest/throat tightness, and abdominal pain;

**Severe reactions:** include hypotension, hypoxia, confusion, collapse, unconsciousness, and incontinence.

-- Brown SGA (2004)<sup>1</sup>

This classification may be useful for descriptive purposes but is not of practical use in treating reactions to antivenom.



### Treat reactions in the following steps:

(Condensed from WHO, 2016 pp. 131, 134 & 135: Sections 6.7.5 & 6.7.5.4<sup>2</sup>)

**Early anaphylactic reactions** - usually developing within minutes and up to 180 minutes after starting antivenom: itch, urticaria, dry cough, fever, nausea, vomiting, abdominal colic, diarrhoea and tachycardia; a minority developing severe life-threatening anaphylaxis (hypotension, bronchospasm and angio-oedema).

1. Adrenaline as soon as possible	<ul style="list-style-type: none"> <li>* Intramuscularly, into the upper lateral thigh Dose: 0.5 mg for adults, 0.01 mg/kg body weight for children.</li> <li>* Repeat every 5 - 10 mins if the reaction persists or the symptoms become worse.</li> </ul>
2. Additional treatment: If bronchospasm	<ul style="list-style-type: none"> <li>* Inhaled short-acting bronchodilator (salbutamol or terbutaline), ideally by oxygen-driven nebuliser.</li> <li>* Chlorpheniramine maleate by iv injection over a few minutes Dose: adults 10 mg, children 0.2 mg/kg.</li> <li>* Hydrocortisone can be given intravenously, but is unlikely to act for several hours Dose: adults 100 mg, children 2 mg/kg body weight.</li> </ul>
3. If unresponsive to intramuscular adrenaline: If shocked and hypotensive  Consider, if response is poor  If hypotension persists	<ul style="list-style-type: none"> <li>* Lay supine with legs elevated 45°.</li> <li>* Give intravenous volume replacement with 0.9% saline (1-2 litres rapidly in an adult).</li> <li>* iv adrenaline infusion*</li> <li>Dose: adults 1mg (1.0 ml) of 0.1% solution in 250 ml 5% dextrose or 0.9% saline) infused at the rate of 15-60 drops/min; the rate may be increased up to twice as fast if necessary depending on the response.</li> <li>* Dopamine infusion Dose: 400mg in 500ml 5% dextrose or 0.9% saline infused at 2–5 µ (micro) g/kg/min</li> </ul>
4. If patients remain dyspnoeic, with bronchospasm or angioedema:	<ul style="list-style-type: none"> <li>* Prop the patient up at 45°.</li> <li>* Give supplemental oxygen together with nebulised, inhaled or parenteral <math>\beta_2</math> agonist bronchodilator.</li> </ul>

#### \*Intravenous adrenaline is hazardous

#### Exercise extreme caution and administer the correct dose.

Monitor the blood pressure every 3 to 5 minutes: as the reaction resolves adrenaline requirements will fall, blood pressure will rise and the infusion rate will need to be reduced.<sup>3</sup>

After the patient has recovered from the early anaphylactic or pyrogenic reaction, the indications for antivenom therapy should be critically re-examined. If antivenom is still indicated, intravenous administration should be cautiously resumed until the total dose has been given.



The incidence of reactions reduces during the 2nd & 3rd doses of AV. However, late anaphylactic reactions can occur up to three hours after completion of AV administration and therefore monitoring for an adequate period following the end of antivenom infusion is mandatory.

**Pyrogenic reactions** - usually developing 1-2 hours after treatment.

Rigors, fever, vasodilatation and a fall in blood pressure.	<ul style="list-style-type: none"> <li>* Cool the patient physically - remove clothing, tepid sponge, fan.</li> <li>* Give an antipyretic - paracetamol by mouth or suppository.</li> <li>* Fluids by iv infusion if hypovolaemia.</li> </ul>
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**Treatment of late (serum sickness) reactions** - usually developing 1-12 days after treatment: fever, nausea, vomiting, diarrhoea, itching, recurrent urticaria, arthralgia, myalgia, lymphadenopathy, periarticular swellings, mononeuritis multiplex, proteinuria with immune complex nephritis and rarely encephalopathy.

<p>Patients who suffer early reactions that are treated with antihistamines and corticosteroids are less likely to develop late reactions.</p> <p>If symptoms develop:</p> <p>If failure to respond within 24-48 hours:</p>	<ul style="list-style-type: none"> <li>* A 5-day course of oral chlorpheniramine should be started Dose: adults 2 mg six hourly, children 0.25 mg/kg /day in divided doses.</li> <li>* Give a course of prednisolone Dose: adults 5 mg six hourly, children 0.7 mg/kg/day in divided doses for 5-7 days.</li> </ul>
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**References:**

1. Brown SGA (2004). Clinical features and severity grading of Anaphylaxis. *J Allergy Clin Immunol* 2004;**114**:371-6 available at doi:10.1016/j.jaci.2004.04.029
2. WHO (2016). Guidelines for the management of snake-bites, 2nd edition, World Health Organization 2016.
3. de Silva HA, Ryan NM, de Silva HJ (2015). Adverse reactions to snake antivenom, and their prevention and treatment. *Br J Clin Pharmacol*, 81:3, 446-452.