

Dapsone is a bacteriostatic antimicrobial that causes oxidative stress to haemoglobin, leading to methaemoglobinaemia and / or haemolysis

Toxicity / Risk Assessment

Dapsone metabolism leads to free radical induced RBC

damage + reticuloendothelial destruction via haemolysis

Dapsone's metabolites act as oxidizing agents to convert

haemoglobin to methaemoglobin (MetHb)

Dapsone can also induce sulphaemoglobinaemia (SulHb)

MetHb and haemolysis can occur separately or together

MetHb, SulHb and haemolysis all impede O₂ delivery

- Therapeutic doses of dapsone produce MetHb
- Clinically significant MetHb can occur up to 3 days post exposure and may be persistent, lasting for many days
- ½-life in OD up to 77 hours (30 hours in therapy)
- Children: 1 dapsone tablet may cause significant MetHb
Infants possess less ability to detoxify MetHb
- G6PD deficiency patients are more susceptible to MetHb
- Haemolysis generally occurs at doses > 200 mg per day
- Maculopathy and renal failure can occur as a secondary result of RBC fragmentation and microvascular occlusion*

Venous blood gas analysis is a reliable method of measuring MetHb fraction

Clinical Features

Dependent on the MetHb fraction and the compensatory response to reduced O₂-carrying capacity.

Pulse oximetry in the presence of MetHb is inaccurate & will usually reads 85-90% despite supplemental O₂

Severity of clinical effects increases with MetHb fraction, varying from no clinical symptoms to death:

- Cyanosis, tachycardia, tachypnoea, anxiety, confusion, seizures, acidosis, arrhythmias, CNS depression.

Heinz bodies on blood film is an early sign of haemolysis, which may lead to jaundice, hypoxaemia & shock

Management

Discontinuation of dapsone and monitoring of MetHb fraction % will be sufficient Rx in many cases

Provide oxygen. Consider AC 50 g (1 g/kg in children) within 2 hours of ingestion.

Enhanced elimination: Multi-dose activated charcoal is indicated if MetHb is present in cases of acute OD

Measure MetHb fraction % every 30-60 minutes until down trending, and to assess response to treatment.

Indications for antidotal Rx with methylene blue (see separate methylene blue guideline)

- MetHb fraction > 20%
- MetHb fraction > 10% AND symptomatic OR co-existing anaemia / chronic lung disease / cardiac failure
- Initial dose: 1-2 mg/kg (0.1-0.2 mL/kg of 1% solution) IV over 5 minutes, followed by a 20 mL saline flush
 - Measure MetHb fraction % every 30 minutes to assess response
 - A methylene blue infusion may be required for hours – days (long dapsone ½ life)
(commence methylene blue infusion at 0.25 mg/kg/hour and discuss with a toxicologist)

Other interventions in cases of severe toxicity (please discuss with clinical toxicologist)

Failure to respond to methylene blue Rx is an indication for exchange RBC transfusion