Methotrexate

Toxicity following single acute ingestion is unlikely to occur. Repeated supra-therapeutic exposure can lead to life-threatening multi-organ toxicity.

Toxicity / Risk Assessment

Acute single ingestion and *normal* renal function:

- Very unlikely to develop any clinical toxicity if ingested dose < 1000 mg (5 mg/kg in paediatric patients)
- Gastrointestinal absorption of methotrexate is a limited following a single dose (low bioavailability)

Acute single ingestion + ↓ renal function (eGFR<45):

- Increased risk of developing clinical toxicity
- Renal pathway responsible for 80% of elimination

Repeated ingestion, *regardless* of renal function:

- Methotrexate is normally given as a single weekly dose
- Risk of clinical toxicity if:

  Dose taken for 3 consecutive days or greater

  Dose taken BD for 2 days or greater

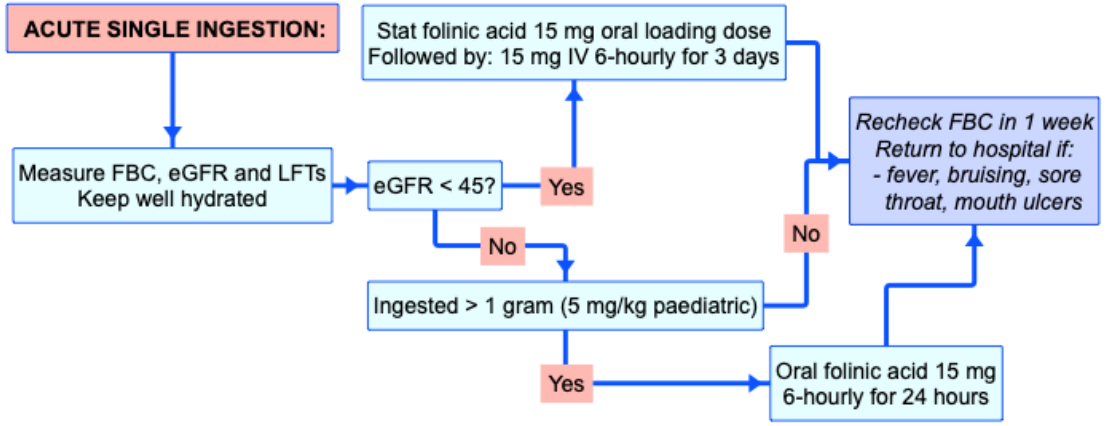
<u>Clinical features:</u>

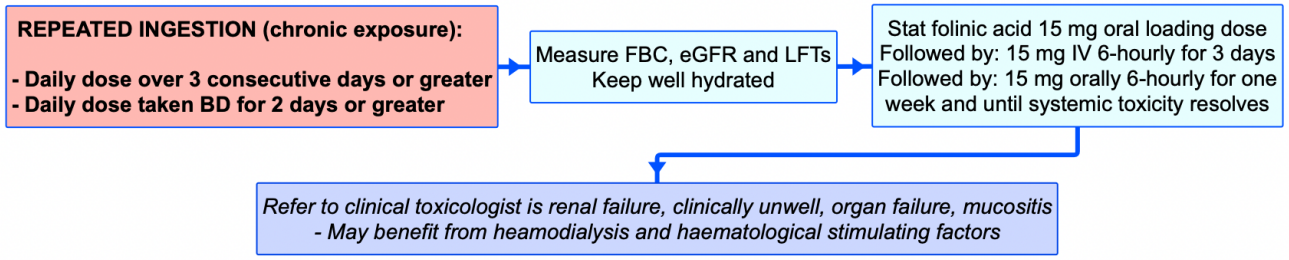
- Initially asymptomatic
- Clinical features develop over following days and reflect a reduction in cell replication:
- *Stomatitis, nausea, vomiting, diarrhea, anaemia, renal and hepatic failure*

Management

Methotrexate concentrations are not useful in guiding management, and should not be measured

Antidote: Folinic acid given PO / IM / IV (Note: the antidote is **not *folic acid*)**





Paediatric ingestions:

- Significant ingestions are rare
- Single ingestions < 5 mg/kg are benign (refer larger ingestions to clinical toxicologist)