AH Chapter 19: Poisonings

National Department of Health

Affordable Medicines Directorate
Essential Drugs Programme

Primary Healthcare Level Standard Treatment Guidelines – 2020-4 Review cycle
Adult Hospital Level Standard Treatment Guidelines – 2020-4 Review cycle

Evidence

Please access the National Essential Medicines List Committee (NEMLC) report for detailed evidence (including rationale, references and costings) informing decision-making on medicine addition, amendments and deletions:

NHI Website: https://www.health.gov.za/nhi-edp-stgs-eml
Knowledge Hub: www.knowledgehub.health.gov.za/e-library

Disclaimer

This presentation is an implementation tool and should be used alongside the most recently published STGs available on the Knowledge Hub. This information does not supersede or replace the STGs.

SCAN ME

AHL Chapter 19: Poisonings

Presentation Outline

1. Paracetamol Poisoning
2. Salicylate Poisoning
3. Ethanol for Toxic Alcohol Poisoning
4. Vitamin K for Anticoagulant Poisoning
5. Snake Bites
6. Other notable changes

Paracetamol Poisoning

AGREE 2 assessment of these updated guidelines scored a mean score of 5/7 (4/7 and 6/7 by respective reviewers). There is general overall agreement to recommend use of these guidelines in the South African setting, with modification.

The rigour of development of these guidelines, however was questioned. Level of Evidence: ***Low certainty***, ***strong recommendation***

The guidance defining repeated supratherapeutic ingestion (RSTI) toxic doses was updated, aligned with the updated guidelines for the management of paracetamol poisoning by Chiew et al (2020).

RSTI toxic doses are defined as:

- >200 mg/kg or 10 g (whichever is less) over a single 24-hour period.
- >300 mg/kg or 12 g (whichever is less) over a single 48-hour period.
- >60 mg/kg/day for more than 48 hours *and* patients have symptoms suggestive of liver injury.

Chiew AL, Reith D, Pomerleau A, Wong A, Isoardi KZ, Soderstrom J, Buckley NA. Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand. Med J Aust. 2020 Mar;212(4):175-183. https://pubmed.ncbi.nlm.nih.gov/31786822/

Paracetamol Poisoning

Amendments to STG: AHL Chapter 19

Take Note

Guidance for iatrogenic poisoning of paracetamol IV formulations was not included in the STG.
At the time of chapter review, paracetamol IV was not approved as an EML medicine.

AMENDED TO:
MEDICINE TREATMENT

N-acetylcysteine is the antidote of choice and should be given intravenously. Although it is more effective when given within 8 hours of ingestion of paracetamol, there may be benefit even if liver failure has developed. Histamine may be released, which mimics an allergic reaction. If this occurs and the patient is stable, infusion may continue at a slower rate under antihistamine cover. Stop the infusion if bronchospasm occurs.

N-acetylcysteine, IV:

- Initial infusion: 200 mg/kg in 500 mL dextrose, 5% over 4 hours.
- Second infusion: 100 mg/kg in 1000 mL dextrose, 5% over 16 hours.
- Any further N-acetylcysteine is given according to the second infusion regimen.

<u>If N-acetylcysteine IV formulation is unavailable:</u>
N-acetylcysteine, oral, 140 mg/kg immediately.

- Followed by 70 mg/kg 4 hourly, for up to seventeen doses.

Note:
As anaphylactoid reactions to N-acetylcysteine do occur, the loading dose should preferably be administered in a monitored area. Avoid giving oral N-acetylcysteine together with activated charcoal as systemic absorption and effect of N-acetylcysteine is reduced.

Further investigations and referral

» Blood tests such as renal function, clotting profile, serum glucose and acid/base status should only be done where clinically indicated.
» Patients who develop liver failure must be referred for further management and/or possible transplant.

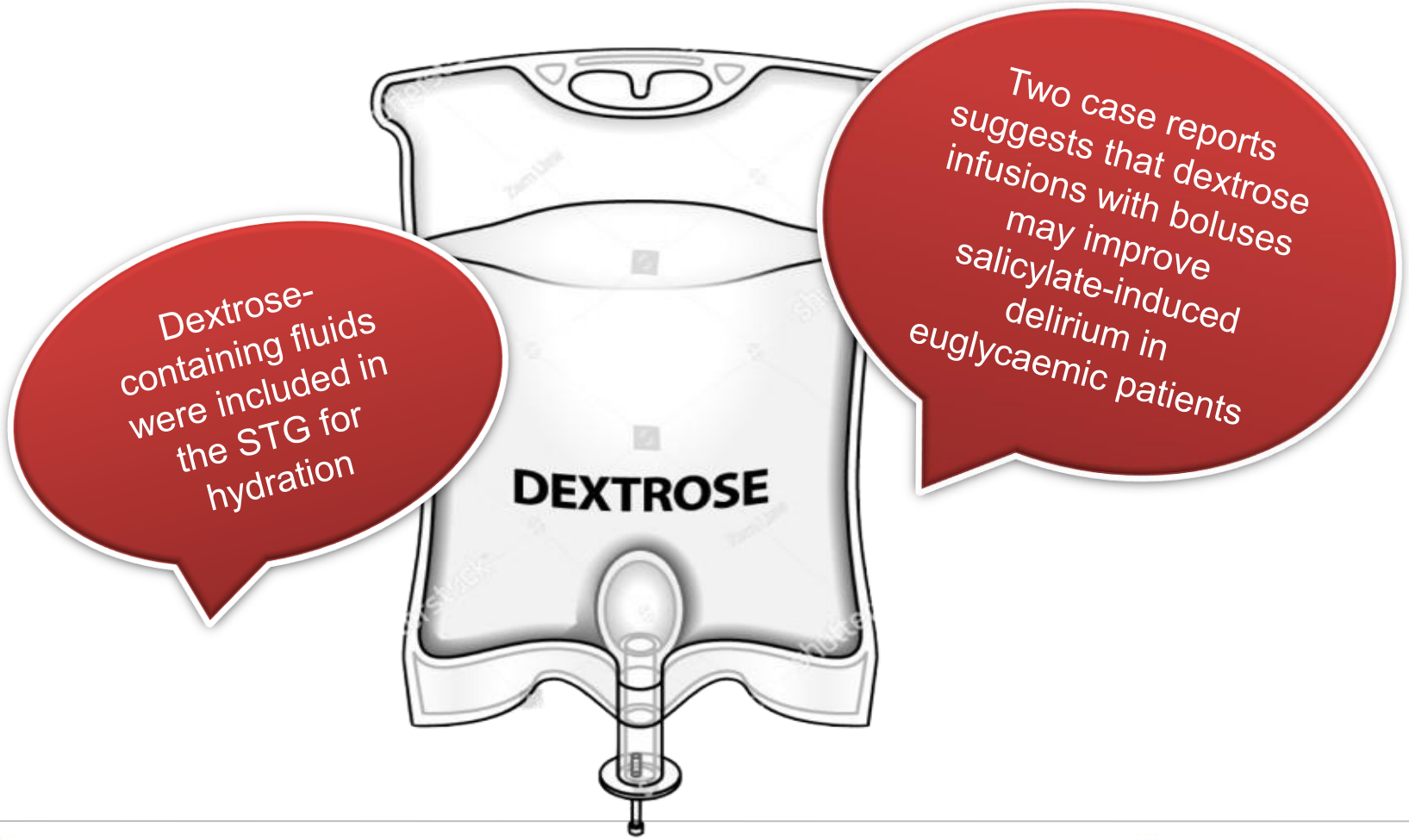
Paracetamol Poisoning

LoE:IIIa[xxiv]

Source: Daly FF, Fountain JS, Murray L, Graudins A, Buckley NA; Panel of Australian and New Zealand clinical toxicologists. Guidelines for the management of paracetamol poisoning in Australia and New Zealand-explanation and elaboration. A consensus statement from clinical toxicologists consulting to the Australasian poisons information centres. Med J Aust. 2008 Mar 3;188(5):296-301.

Figure 19.1: Paracetamol treatment nomogram. (Access the paracetamol nomogram tool on the EML Clinical Guide cellphone application).

Salicylate Poisoning



Kuzak N, Brubacher JR, Kennedy JR. Reversal of salicylate-induced euglycemic delirium with dextrose. Clin Toxicol (Phila). 2007 Jun-Aug;45(5):526-9. https://pubmed.ncbi.nlm.nih.gov/17503260/

Salicylate Poisoning

MEDICINE TREATMENT

- Salicylates delay gastric emptying, therefore activated charcoal may be effective for a longer period than usual.
- Whole bowel irrigation maybe useful for enteric-coated or modified-release preparations.

LoE:IIIb[xxix]

<u>For mild toxicity:</u>

» Rehydrate and correct hypovolaemia with dextrose-containing fluids.
  - Add dextrose 50%, 100mL to every litre of balanced crystalloid solution (e.g. ringers lactate) or sodium chloride 0.9%, and administer by IV infusion. LoE:IIIb[xxx]
  - During preparation of the infusion fluid, ensure the equivalent volume of rehydration fluid (e.g. 100mL) is removed from the bag before adding the total dextrose 50% volume (e.g. 100mL).
  - The rate and duration of IV fluids should be guided by clinical assessment of fluid balance. LoE:IVb

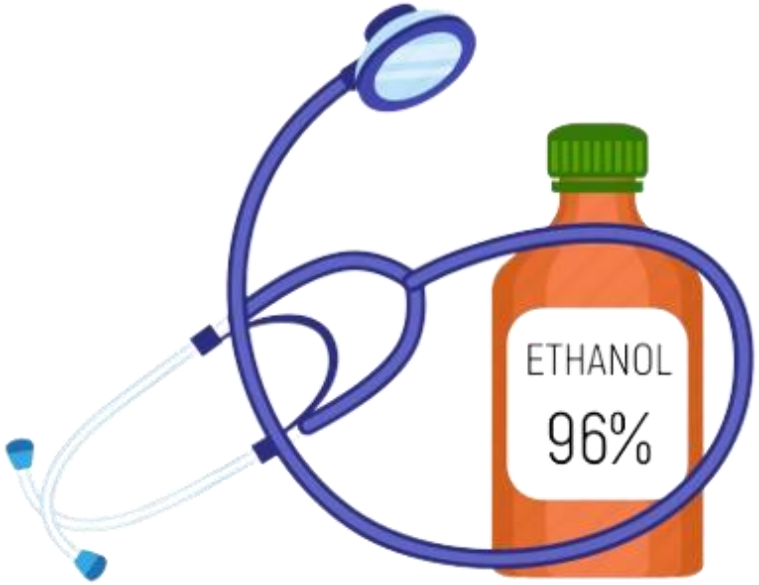
<u>In patients with moderate to severe toxicity and/or acidosis:</u>

- Sodium bicarbonate 8.4%, IV, 1–2 mL/kg over 30 minutes to manage acidosis. LoE:IIIb[xxxi]
- Simultaneously fluid resuscitate with sodium bicarbonate 8.4%, 150mL added to dextrose 5%, 1L and administer by IV infusion to correct hypovolaemia.
  - During preparation of the infusion fluid, ensure the equivalent volume of dextrose 5% (i.e. 150 mL) is removed from the bag before adding the total sodium bicarbonate 8.4% volume of 150 mL.
  - Continue a maintenance infusion at 150 – 200 mL/hour, targeting a urine output of 2mL/kg/hour.
  - Titrate the sodium bicarbonate maintenance infusion to a urinary pH of 7.5 – 8.5 and blood pH of 7.45 – 7.5.
  - Monitor for and correct hypokalaemia. LoE:IVb

REFERRAL

» Discuss with specialist and consider ICU admission
» Where acidosis does not respond to sodium bicarbonate, refer for haemodialysis. LoE:IIIa[xxxii]

Ethanol for Toxic Alcohol Poisoning



Errors were detected in the Adult Hospital Level STGs and EML, 2019 regarding ethanol doses in this clinical setting. An erratum to address this was subsequently circulated by NDoH.

Subsequent to the erratum, comments were received that the guidance on the dilution and administration of ethanol was not clear.

Following a pilot of several alternatives, the guidance was amended for improved clarity *(see next slide)*

NEMLC would like to encourage ongoing comment/suggestions from clinicians to improve clarity and eliminate any ambiguity with interpreting the STG.

Ethanol for Toxic Alcohol Poisoning

Amendments to STG: AHL Chapter 19

MEDICINE TREATMENT

Ethanol

Indications: LoE:Ivb[ix]

History of ingestion, plus any two of the following criteria:

- Arterial pH <7.3
- Serum bicarbonate <20 mmol/L
- Presence of urinary oxalate crystals (ethylene glycol only) or visual disturbances (methanol only)

Preparation and administration of ethanol:

Step 1: Prepare an ethanol 20% solution:

If using Ethanol 96% BP, oral,

- Add 1 part ethanol 96% to 4 parts juice or water e.g. 250 mL of ethanol 96% with 1000mL water or juice to give a total volume of 1250 mL ethanol 20%.

If using Ethanol 40% v/v (gin, whiskey, vodka), oral

- Add 1 part ethanol 40% to 1 part juice or water e.g. dilute 500mL of ethanol 40% with 500mL water or juice to give a total volume of 1000mL ethanol 20%.
- **Note:** Spirit liquor products in South Africa are frequently bottled at 43% v/v. These can be used interchangeably.

Step 2: Administer a loading dose:

- Ethanol 20% (the solution prepared in Step 1), oral, 4 mL/kg over 15-30 minutes.

Step 3: Continue with maintenance doses:

- Ethanol 20% (the solution prepared in Step 1), oral:
  - Non-drinker: 0.5 mL/kg/hour
  - Chronic drinker: 1 mL/kg/hour

WORKED EXAMPLES

For a 60kg patient who is a non-drinker:
Loading dose: 240 ml of the ethanol 20% solution orally over 15-30 minutes.
Maintenance dose: 30 mL per hour orally of the ethanol 20% solution.

For a 60kg patient who is a chronic drinker:
Loading dose: 240 ml of the ethanol 20% solution orally over 15-30 minutes.
Maintenance dose: 60 mL per hour orally of the ethanol 20% solution.

CAUTION

Locally available commercial ethanol products are not approved for IV administration and should not be administered via this route.

- Maintain ethanol levels of 1–1.3 g/L (100–130 mg/dL).
- Where ethylene glycol, methanol (see Section 19.17.3: Methanol poisoning), and ethanol levels are not available for monitoring purposes, titrate the ethanol rate of administration according to improvement in metabolic acidosis and signs of systemic toxicity.
- Increase the dose of ethanol if the patient is receiving concomitant haemodialysis.
- Several days of ethanol therapy may be required until clinical condition improves.
- Alcoholic beverages are sometimes labelled as "percentage proof". Alcohol proof values are double the alcohol percentage (volume/volume) values. i.e. an 80 proof alcohol would be 40% (v/v).

LoE:IVb[xi]

Vitamin K for Anticoagulant Poisoning

Guidance on the use of vitamin K, oral or IV, for the management of warfarin and superwarfarin (rodenticide) poisoning was amended.

Vitamin K is not given prophylactically, but only if the patient is actively bleeding or the INR > 4.

It is preferably given orally, for those IV formulations on tender, it is advised against dilution, so should be administered undiluted as a slow IV bolus injection.

As treatment with vitamin K may be prolonged for Superwarfarin poisoning, consultation with a Poisons Information Centre or haematologist was added.

Vitamin K for Anticoagulant Poisoning

Amendments to STG: AHL Chapter 19

MEDICINE TREATMENT

Do NOT give vitamin K_1 prophylactically. It is only indicated when there is active bleeding or a specifically raised INR (INR > 4).

Active bleeding:

R58 + (T45.5 + X44.99/X64.99/Y14.99)

- Lyophilised plasma, IV, 15 mL/kg.

OR

LoE:IIIa[lxxi]

- Fresh Frozen Plasma, IV, 15 mL/kg.

AND

- Vitamin K_1, IV, 10 mg
  - Administer as a slow IV injection.
  - Do not dilute or mix with other injectables.

For patients on long term vitamin K antagonist anticoagulants, e.g. warfarin:

- Temporarily discontinue anticoagulant therapy.
- Decrease Vitamin K dose by half, i.e. Vitamin K1, IV, 5 mg. Administer as a slow IV injection.

LoE:IV

No bleeding but INR is raised (INR > 4):

Note: If Vitamin K_1 is only available as a parenteral preparation, administer the same preparation orally as this is safest in anticoagulant poisoning.

Patients NOT on long-term therapeutic anticoagulants and INR > 4.0:

- Vitamin K_1, oral, 10-20 mg.
  - Check INR at least 12 hours after vitamin K_1 has been administered. Repeated doses should be guided by further INR (or PT) measurements every 4-6 hours until the patient is stable, and thereafter, every 24 hours. INR (or PT) levels may take 3-4 days to normalise.

Patients on long-term vitamin K antagonist anticoagulant drugs (e.g. warfarin therapy):

If INR 5-8:

- Temporarily discontinue any anticoagulant treatment.

If INR > 8:

- Vitamin K_1, oral, 0.5 – 1.0 mg (one tenth of the normal dose).
  - A repeat dose may be given 12-24 hrs later if the INR remains ≥ 8.

Note:

LoE:IVb[lxxii]

- These patients are complex and require management in consultation with a haematologist.
- Patients with prosthetic heart valves receiving high-dose vitamin K have a higher risk for increased resistance to warfarin and development of thromboembolism. Treat as above but monitor INR frequently to prevent overcorrection. Treat in consultation with a specialist.
- For patients on other anticoagulant therapies, additional antagonists may be required.
- In all patients on therapeutic warfarin, a major overdose or bleeding episode should prompt careful review of the need for anticoagulation.
- Warfarin should be re-started once the INR is in the therapeutic range if it is still indicated.
- In patients with superwarfarin toxicity, treatment with vitamin K_1 may need to be prolonged for several months as superwarfarins are very long acting. Discuss with the Poisons Information Centre or haematologist for advice on dosing and duration of treatment.

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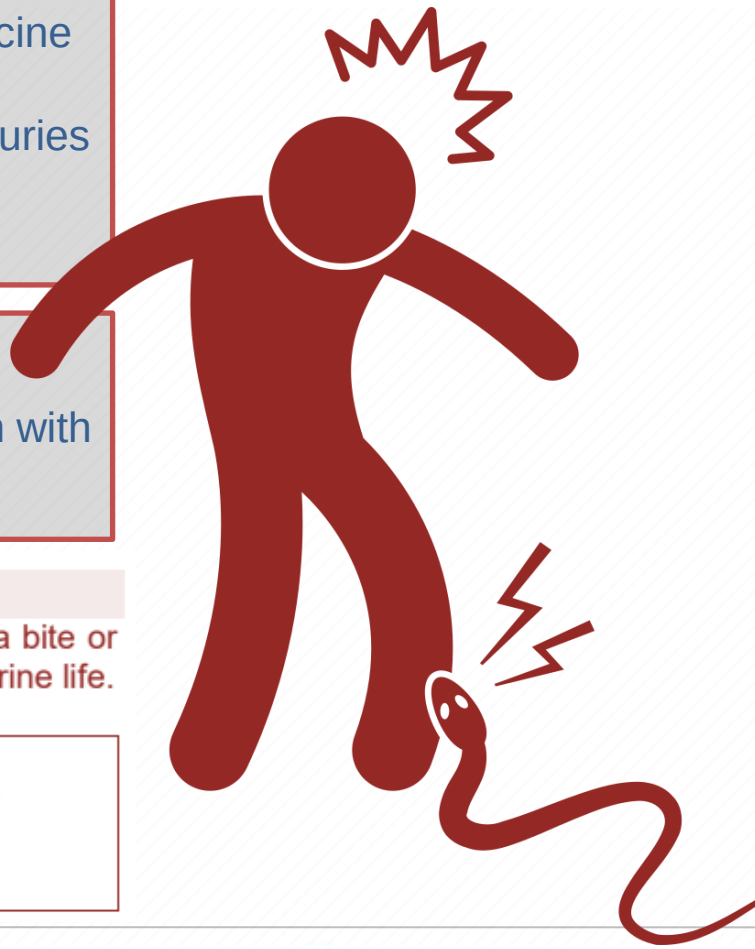
Snake bites

Guidance for the administration of tetanus toxoid vaccine has been added to align with the PHC Chp 13: Immunisation and PHC Chp 21: Emergencies and Injuries chapters, i.e. tetanus vaccination indicated if not previously immunised within the last 5 years.

Contact details for procurement of snake, spider and scorpion antivenom has been updated in consultation with the SAVP and Poisons information Centre.



ENVENOMATION

Envenomation is an instance of poisoning by venom resulting from a bite or sting from an animal such as a snake, spider, scorpion, insect, or marine life.

South African Vaccine Producers (SAVP): For procurement of Snake/spider/scorpion antivenom: Email: benita.mouton@nhls.ac.za	Office hours: (011) 386 6062/6063/6078 After hours 071 680 9897

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Other notable changes

Iron Poisoning:

Deferoxamine (desferrioxamine) - IM administration: *Added*

- Deferoxamine (desferrioxamine) is registered for both IM and IV administration, and can be used in clinical practice particularly for low risk patients.
- The literature supports both IM and IV administration, except for patients in cardiogenic shock when IV administration is preferred.
- The inclusion of the IM route of administration will empower clinicians, particularly when IV access is not readily available.
- IM administration will also avert the insertion of unnecessary IV lines.

Calcium Channel Blocker and Beta Blocker Poisoning:

High-dose Insulin Euglycaemic Therapy (HIET): *Not added*

- The Committee noted that the evidence on the use of HIET as a first line therapy for the management of calcium channel blocker and/or beta blocker poisoning is evolving although much of this is limited to observational studies.
- Following extensive deliberation by the ERC and NEMLC, it was agreed that HIET not be included in the AH Chp 19: Poisonings chapter, as patients receiving HIET require management in a High Care/ICU setting.
- The use of HIET for managing calcium channel blocker and/or beta blocker poisoning to be considered for prioritisation during the next review cycle as part of the AH Chp 23 Critical Care review.

Contact details

Poisons Centre: www.afritox.co.za

Poisons Information Helpline (national number) 0861 555 777

Thank You!!