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Department:
Health
REPUBLIC OF SOUTH AFRICA

SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 21: EMERGENCIES AND INJURIES
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020)

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the emergencies and injuries chapter.
Note: The PHC emergencies chapter has been updated to align to previous NEMLC recommendations as well as the recent NEMLC-approved Adult Hospital Level STGs and EML, 2019 edition.

MEDICINE AMENDMENTS

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED
21.3.1.4 Snakebites	Polyvalent antivenom	Amended (indications for use)
21.3.3 Exposure to poisonous substances	Activated charcoal, oral	Amended (Indications, contra-indications and directions for use)
-Organophosphate poisoning	Protective equipment for staff	Added
	Atropine, IV/IM	Amended (bolus IV dose and treatment protocol)
-Paracetamol poisoning	N-acetylcysteine, oral	Added (if referral is delayed)
21.3.6.1 Post exposure Prophylaxis, occupational	Tenofovir + lamivudine + dolutegravir, oral	Added
21.3.6.2 Post exposure Prophylaxis, rape and sexual assault **21.3.6.3 Post exposure Prophylaxis, inadvertent non-occupational**	Tenofovir + emtricitabine + atazanavir/ritonavir or lopinavir/ritonavir	Amended (Indication: for WOCP, pregnant <6 weeks gestation and intolerant to DTG)

21.3.1.4 SNAKEBITES

Polyvalent antivenom: *Indications for use amended*

Indications amended for cytotoxic, neurotoxic bites and where snake is unidentified.
Text amendment guided by expert opinion[1] [2] to:

Criteria for antivenom administration
» Signs of neurotoxicity.
» Positively identified puff adder, Gaboon adder, Mozambique spitting cobra or rinkhals bites AND evidence of progressive severe cytotoxicity.
» Unidentified snakebites and evidence of progressive severe cytotoxicity envenomation i.e.:
- swelling of whole hand or foot within 1 hour
- swelling to the knee or elbow in less than 6 hours
- swelling of the whole limb in less than 12 hours
- swelling progression > 2.5cm per hour
- a threatened airway due to swelling
- evidence of complication e.g. compartment syndrome

21.3.3 EXPOSURE TO POISONOUS SUBSTANCES

Evidence for drug decontamination *(activated charcoal)* is limited and of very low methodological quality. The Toxicology Societies and Centres recommended that "Single dose activated charcoal should not be given routinely; it may be of benefit when given early (within 1 hour, possibly 2 hours), in cases where potentially large amount ingested,

[1] Wood D, Sartorius B, Hift R. Snakebite in NE South Africa: clinical characteristics and risks for severity. S Afr Fam Prac 2016; 58(2):62-67. https://www.tandfonline.com/doi/full/10.1080/20786190.2015.1120934
[2] Wood, Sartorius, Hift. Classifying snakebite in South Africa: validating a scoring system. S Afr Med J 2017;107(1):46-51. https://www.ncbi.nlm.nih.gov/pubmed/28112091

of a substance that is absorbed by charcoal."

Activated charcoal, oral: *indication, contra-indications and directions for use amended*
Refer to Adult Hospital Level medicine review for activated charcoal in poisonings (March 2019):

Activated charcoal for Poisonings_Adul

http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/286-hospital-level-adults

Recommendation: Based on this review, the Adult Hospital Level Committeerecommended that single dose activated charcoal (SDAC) should not be given routinely, but recommended for administration within one to two hours of ingestion of a potentially toxic amount of a poison known to be adsorbed by charcoal, in patients with an intact airway (i.e. awake and co-operative patients or with a protected airway). For substances that delay gastric emptying or modified-release preparations, there may be a longer time interval in which to administer SDAC if required.
Rationale: Single dose activated charcoal may be of benefit when given early (within 1 hour), where potentially toxic amounts of poison has been ingested. However, there is insufficient data to support or exclude use after one hour of ingestion, but considered pragmatic to recommend use within 1-2 hours of ingestion of toxin. Despite the uncertainty of the clinically meaningful benefit of activated charcoal in poisonings, volunteer studies of healthy individuals showed reduced absorption of ingested poisons when single dose activated charcoal was administered within an hour. Risk-benefit assessment and recommendation aligned with standard practice, recommending use only in patients with an intact or protected airway.

Level of Evidence: III Pharmacokinetic studies, Case reports, Expert opinion[3]
Of note is that the European Toxicology society's (EAPCCT) position statement is currently under review; to prolong the time period for administration of single dose activated charcoal (still to be published, but presented at the recent Annual Congress).

STG text was amended to align with the Adult Hospital Level STGs and EML, 2019 - *from:*

- ~~Activated charcoal.~~
  - ~~Only if the patient is fully conscious and able to maintain their airway and if ingestion was within the previous hour prior to presentation.~~
  - ~~Children: 1 g/kg mixed as a slurry with water. See dosing table, pg 23.1.~~
  - ~~Adults: 50–100 g mixed as a slurry with water.~~
  - ~~Add water to charcoal and not vice versa.~~
  - ~~Do not administer orally if the level of consciousness is reduced.~~

» ~~Activated charcoal should not be given in the case of:~~
- ~~volatile hydrocarbon poisoning, e.g. paraffin, petrol~~
- ~~corrosive poisons, e.g. acids, alkalis, potassium permanganate~~
- ~~camphor and other convulsants~~
- ~~metals, e.g. iron, lithium etc.~~
- ~~all alcohols~~
- ~~paracetamol overdose where oral acetylcysteine will be given~~

» ~~Protect the airway:~~
- ~~Place in lateral position if decreased level of consciousness.~~

[3] Activated charcoal (single dose): Chyka PA, Seger D; American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position statement: single-dose activated charcoal. J Toxicol Clin Toxicol 1997;35(7):721-41. https://www.ncbi.nlm.nih.gov/pubmed/15822758
Activated charcoal (single dose): Rosenberg J, Benowitz NL, Pond S. Pharmacokinetics of drug overdose. Clin Pharmacokinet 1981; 6:161– 192. https://www.ncbi.nlm.nih.gov/pubmed/7016383
Activated charcoal (single dose): Yeates PJA, Thomas SHL. Effectiveness of delayed activated charcoal administration in simulated paracetamol (acetaminophen) overdose. Br J Clin Pharmacol 2000; 49:11–14. https://www.ncbi.nlm.nih.gov/pubmed/7016383
Activated charcoal (single dose): Laine K, Kivisto¨ KT, Pelttari S, Neuvonen PJ. The effect of activated charcoal on the absorption of fluoxetine, with special reference to delayed charcoal administration. Pharmacol Toxicol 1996; 79:270– 273. https://www.ncbi.nlm.nih.gov/pubmed/8936562
Activated charcoal (single dose): Laine K, Kivisto¨ KT, Neuvonen PJ. Effect of delayed administration of activated charcoal on the absorption of conventional and slow-release verapamil. J Toxicol Clin Toxicol 1997; 35:263–268. https://www.ncbi.nlm.nih.gov/pubmed/9140320
Activated charcoal (single dose): Laine K, Kivisto¨ KT, Ojala-Karlsson P, Neuvonen PJ. Effect of activated charcoal on the pharmacokinetics of pholcodine, with special reference to delayed charcoal ingestion. Ther Drug Monit 1997; 19:46– 50. https://www.ncbi.nlm.nih.gov/pubmed/9029746
Activated charcoal (single dose): Green R, Grierson R, Sitar DS, Tenenbein M. How long after drug ingestion is activated charcoal still effective? J Toxicol Clin Toxicol 2001; 39:601– 605. https://www.ncbi.nlm.nih.gov/pubmed/11762668

» ~~Identify the poison and keep a sample of the poison or container.~~
» ~~Contact the nearest hospital or Poisons Information Helpline for advice.~~

To:

- Activated charcoal.
  - Administer only when the airway is protected (i.e. patient is fully awake and cooperative or intubated with a depressed level of consciousness).
  - Administer within 1 hour of ingestion of toxin, unless poison is a substance that delays gastric emptying.
  - Children: 1 g/kg mixed as a slurry with water. See dosing table, pg 23.1.
  - Adults: 50 g (36 level medicine measures) diluted in 100 mL water.
  - When mixing, add a small amount of water to charcoal in a container.
  - Cap and shake container to make a slurry and then dilute further.

Charcoal may be useful if these poisons are taken in toxic dose	Poisons where charcoal is ineffective and should not be given
» carbamazepine, barbiturates, phenytoin » dapsone, quinine » theophylline » salicylates » mushroom poisoning (Amanita phalloides) » slow release preparations » digoxin » beta-blockers » NSAIDs	» ethanol, methanol, ethylene glycol » brake fluid » petroleum products (e.g. petrol or paraffin) » iron salts » lead, mercury, arsenic » lithium » strong acids or alkalis » other corrosive agents (e.g. household detergents)

Protect the airway:
» Place in lateral position if decreased level of consciousness.
» Identify the poison and keep a sample of the poison or container.
» Contact the nearest hospital or Poisons Information Helpline or nearest hospital for advice.

Organophosphate poisoning

General measures

Protective equipment for staff: *recommendation added*

Recommended by Guidelines based on reports of healthcare workers exposed to body fluids from a patients poisoned with organophosphates.

Level of Evidence: III Guidelines[4], Case reports[5] [6]

Medicine treatment

Atropine, IV: *bolus IV dose and treatment protocol amended*

Aligned with guidelines to provide clear guidance on dosing and monitoring of response to atropine treatment – restricted to IV bolus dosing for primary level of care.

Level of Evidence: III Guidelines[7]

N-acetylcysteine, oral: *added*

Where referral to access parenteral formulation is delayed, oral N-acetylcysteine (NAC) recommended as a safe alternative. Oral NAC dosing regimen as follows:

If N-acetylcysteine, when referral is delayed:

[4] Little M, Murray L; Poison Information Centres of New South Wales, Western Australia, Queensland, New Zealand, and the Australian Capital Territory. Consensus statement: risk of nosocomial organophosphate poisoning in emergency departments. Emerg Med Australas. 2004 Oct-Dec;16(5-6):456-8. https://www.ncbi.nlm.nih.gov/pubmed/15537409

[5] Centers for Disease Control and Prevention (CDC). Nosocomial poisoning associated with emergency department treatment of organophosphate toxicity--Georgia, 2000. MMWR Morb Mortal Wkly Rep. 2001 Jan 5;49(51-52):1156-8. https://www.ncbi.nlm.nih.gov/pubmed/11198947

[6] Stacey R, Morfey D, Payne S. Secondary contamination in organophosphate poisoning: analysis of an incident. QJM. 2004 Feb;97(2):75-80. https://www.ncbi.nlm.nih.gov/pubmed/14747621

[7] Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. Lancet. 2008 Feb 16;371(9612):597-607. https://www.ncbi.nlm.nih.gov/pubmed/17706760

Eddleston M, Dawson A, Karalliedde L, Dissanayake W, Hittarage A, Azher S, Buckley NA. Early management after self-poisoning with an organophosphorus or carbamate pesticide - a treatment protocol for junior doctors. Crit Care. 2004 Dec;8(6):R391-7. https://www.ncbi.nlm.nih.gov/pubmed/15566582

- N-acetylcysteine, oral, 140 mg/kg, followed by 70 mg/kg 4-hourly for seventeen doses**.**

Note: Avoid giving activated charcoal if giving N-acetylcysteine orally as it will reduce the systemic absorption and thus negate the effect of oral N-acetylcysteine.

Level of Evidence: III Observational studies[8] [9] [10]

21.3.6.1 POST-EXPOSURE PROPHYLAXIS, OCCUPATIONAL *and* **21.3.6.2 NON-OCCUPATIONAL POST EXPOSURE PROPHYLAXIS , SEXUAL ASSAULT** *and* **21.3.6.3 NON OCCUPATIONAL POST EXPOSURE PROPHYLAXIS , INADVERTENT EXPOSURE**

Tenofovir + lamivudine + dolutegravir, oral: *added*
Tenofovir + emtricitabine + atazanavir/ritonavir or lopinavir/ritonavir: *retained and indication amended (WOCP, pregnant <6 weeks gestation and intolerant to DTG)*

Ford et al (2015) systematic review of very low quality data[11], assessed safety and efficacy of 2- vs 3- based ART regimens for PEP (occupational and non-occupational. Efficacy of various PEP regimens could not be determined, but PEP completion rates were report to be highest for the TDF-based regimens (>71.1%) vs AZT-based regimen (59.1%); and discontinuation due to ADRs reported to be lowest for the TDF+FTC+RAL regimen (1.9%). Authors suggest use of co-formulated TDF with 3TC/FTC as backbone with third ARV selection dependent on availability and resources (RAL recommended in the context of high-income settings).

Dolutegravir: Open-label, single-arm, non-randomized study assessed the safety and tolerability of a single PEP regimen, TDF+FTC+DTG, in men who have sex with men[12].
Recommendation: TDF with 3TC/FTC be recommended as PEP backbone with 3rd ARV, DTG; except in pregnant women <6 weeks gestation where alternative option protease inhibitor to be considered.
Rationale: There is limited evidence of efficacy for integrase strand transfer inhibitors as prevention of HIV prophylaxis treatment. DTG is preferred in a number of guideline[13] [14], due to the higher barrier to resistance, daily dosing and better tolerability; noting that completion of treatment contributes to the effectiveness of PEP therapy. The risk of NTDs associated with DTG precludes use of DTG-based regimen in WOCP and pregnant women < 6 weeks gestation[15].
Level of Evidence: III Observational studies

[8] Yarema MC, Johnson DW, Berlin RJ, Sivilotti ML, Nettel-Aguirre A, Brant RF, Spyker DA, Bailey B, Chalut D, Lee JS, Plint AC, Purssell RA, Rutledge T, Seviour CA, Stiell IG, Thompson M, Tyberg J, Dart RC, Rumack BH. Comparison of the 20-hour intravenous and 72-hour oral acetylcysteine protocols for the treatment of acute acetaminophen poisoning. Ann Emerg Med. 2009 Oct;54(4):606-14. https://www.ncbi.nlm.nih.gov/pubmed/19556028
[9] Williamson K, Wahl MS, Mycyk MB. Direct comparison of 20-hour IV, 36-hour oral, and 72-hour oral acetylcysteine for treatment of acute acetaminophen poisoning. Am J Ther. 2013 Jan;20(1):37-40. https://www.ncbi.nlm.nih.gov/pubmed/23299230
[10] Rumack and Bateman. Acetaminophen and acetylcysteine dose and duration: past, present and future. Clin Toxicol (Phila) 2012;50(2):91-98. https://www.ncbi.nlm.nih.gov/pubmed/22320209
[11] Ford N, Shubber Z, Calmy A, Irvine C, Rapparini C, Ajose O, et al. Choice of antiretroviral drugs for postexposure prophylaxis for adults and adolescents: A systematic review. Clinical Infectious Diseases. 2015;60 Suppl 3:S170–6. https://www.ncbi.nlm.nih.gov/pubmed/25972499
[12] McAllister JW, Towns JM, McNulty A, Pierce AB, Foster R, Richardson R, et al. Dolutegravir with tenofovir disoproxil fumarate-emtricitabine as HIV postexposure prophylaxis in gay and bisexual men. AIDS. 2017;31(9):1291–5. https://www.ncbi.nlm.nih.gov/pubmed/28301425
[13] Goldschmidt RH. CDC Releases Updated Guidelines for Postexposure Prophylaxis After Sexual, Injection Drug, or Other Nonoccupational Exposures to HIV. Am Fam Physician. 2016 Sep 1;94(5):392-3. https://www.ncbi.nlm.nih.gov/pubmed/27583430
[14] Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. CMAJ. 2018 Jun 25;190(25):E782. https://www.ncbi.nlm.nih.gov/pubmed/29941442
[15] Zash R, Holmes L, Diseko M, Jacobson DL, Brummel S, Mayondi G, Isaacson A, Davey S, Mabuta J, Mmalane M, Gaolathe T, Essex M, Lockman S, Makhema J, Shapiro RL. Neural-Tube Defects and Antiretroviral Treatment Regimens in Botswana. N Engl J Med. 2019 Aug 29;381(9):827-840. https://www.ncbi.nlm.nih.gov/pubmed/31329379