SOUTH AFRICAN ADULT HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 20: EMERGENCIES AND INJURIES
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2017 -2019)

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the chapter for emergencies and injuries.

A: NEW SECTIONS(S)/ SUBSECTION(S)

SECTION	CONDITION	MEDICINE MANAGEMENT	MEDICINE ADDED
20.2	**Post cardiac arrest**	Yes	• Dextrose 50%, IV • Sodium chloride 0.9%, IV • Parectamol, oral • Adrenaline (epinephrine), IV infusion
20.11.1.1	**Non-trauma related hypovolaemic shock**	Yes	• Sodium chloride 0.9%, IV
20.11.1.2	**Trauma related hypovolaemic shock**	Yes	• Oxygen • Crystalloids • Sodium chloride 0.9%, IV
20.10.1.2.1	**Massive transfusion**	Yes	• Lyophilised plasma • Tranexamic acid, IV

20.2 POST CARDIAC ARREST

The following STG was developed to provide guidance for management of care following successful cardiopulmonary resuscitation:

Description
Post cardiac arrest care starts following successful cardiopulmonary resuscitation. During this time the patient is vulnerable to several processes, including:

- the underlying disease condition or injury causing the cardiac arrest
- post cardiac arrest haemodynamic instability
- post cardiac arrest brain injury
- the sequelae of global ischaemia and reperfusion.

Care should be aimed at reversing or minimising the above processes to optimise the likelihood of neurologically intact survival.

General measures
The priorities of management post cardiac arrest include:

Determining the cause of cardiac arrest

- careful history and physical examination
- bedside tests such as 12-lead ECG, blood glucose, Hb, pulse oximetry, blood gases
- special investigations such as chest x-ray, eFAST, CT of the brain

Treating reversible conditions
This will be specific to the presentation and clinical findings.
Evidence of ST elevation myocardial infarction (STEMI) on ECG should prompt urgent treatment. See section 3.2.1: ST elevation myocardial infarction (STEMI).

Supportive care and prevention of complications
Airway

- Ensure that the airway is patent and protected.
- Endotracheal intubation may be required in patients that do not rapidly regain consciousness following return of spontaneous circulation.

Breathing

- Maintain oxygen saturation above 94%.
- Avoid hyperoxia by weaning the inspired oxygen concentration to the lowest percentage required to maintain the above saturation.
- Maintain $PaCO_2$ within normal range in ventilated patients where feasible.

Circulation

- Correct hypovolaemia if present, with judicious IV fluids (e.g. sodium chloride 0.9% or Ringer lactate).

» Monitor response to fluids: pulse rate, BP, urine output, skin perfusion, development of basal crepitations.
» If hypotension persists despite fluid resuscitation, in the absence of ongoing blood loss, commence inotropes. (e.g. adrenaline (epinephrine).
» Aim to maintain mean arterial blood pressure (MAP) above 65mmHg.
» If brain or spinal cord injury is suspected, it is reasonable to increase the target MAP to 80mmHg.

Neurological care
» Position head up 30 degrees.
» Monitor for seizures. Treat promptly and load with an anti-epileptic agent should seizures occur.

Blood glucose control
» Maintain blood glucose between 8 and 10 mmol/L and avoid hypoglycaemic episodes.

Temperature control
» Strictly avoid fever. Aim to control temperature below 36ºC in unconscious patients in the first 24 hours, using physical cooling methods e.g.: ice packs and fans, and antipyretics.

Deep vein prophylaxis
» Consider prophylaxis for venous thrombo-embolism, as required. See section 2.14 Venous thrombo-embolism.

Medical treatment

Hypoglycaemia
- Dextrose 50%, rapid IV injection, up to 50 mL.

Assess clinical status and finger prick glucose level over the next 5–10 minutes.

Hypovolaemia
- Sodium chloride 0.9%, IV.

Hypotension (after volume correction)
- Adrenaline (epinephrine), IV infusion, start at 0.1 mcg/kg/minute titrated according to the response.
  - Dilute 10 mg i.e. 10 ampoules of adrenaline 1:1 000 in 1 L sodium chloride 0.9%.
  - Infuse according to weight and clinical response.
  - Infusion rate: mL/hour:

mcg/kg/minute	Weight in kg						
	50	**60**	**70**	**80**	**90**	**100**	**110**
0.1	30	36	42	48	54	60	66
0.2	60	72	84	96	108	120	132
0.3	90	108	126	144	162	180	198
0.4	120	144	168	192	216	240	264
0.5	150	180	210	240	270	300	330
0.6	180	216	252	288	324	360	396
0.7	210	252	294	336	378	420	462
0.8	240	288	336	384	432	480	528
0.9	270	324	378	432	486	540	594
1	300	360	420	480	540	600	660

Seizures
Treat seizures in post cardiac arrest, similar to management of status epilepticus. See section 14.3.1: Status epilepticus.

Fever
- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4g in 24 hours.

Referral
» Following successful resuscitation cases should be discussed with a hospital with intensive care facilities for transfer.
» If evidence of myocardial infarction is present or if strongly suspected cases should be discussed with a cardiology service.

Hypoglycaemia

Dextrose 50% IV: *added*

Recommendation of rapid IV injection, up to 50 mL of dextrose 50% aligned with SEMDSA Guidelines.

Level of Evidence: III Guidelines[1]

[1] The Society for Endocrinology, Metabolism and Diabetes of South Africa Type 2 Diabetes Guidelines Expert Committee. The 2017 SEMDSA Guideline for the Management of Type 2 Diabetes Guideline Committee. JEMDSA 2017; 21(1)(Supplement 1): S1-S196. http://www.jemdsa.co.za/index.php/JEMDSA/article/view/647/937

Hypovolaemia

Sodium chloride 0.9%, IV: *added*

Correction of hypovolaemia with judicious IV fluids aligned with Guidelines.

Level of Evidence: III Guidelines[2]

Blood glucose control

Blood glucose target: *added*

Guidance provided to maintain blood glucose between 8 and 10 mmol/L, as observational studies indicated that hyperglycaemia has worse outcomes[3] [4] and no additional benefit of tighter control and more likely to develop hypoglycaemia with use of lower target values.[5]

Level of Evidence: III Guidelines[6], Observational studies.

Fever

Paracetamol, oral: *added*

Fever associated with worse outcome post cardiac arrest[7] . No evidence for antipyretics, but consensus guidelines recommend in face of low risk[8].

Level of Evidence: III Guidelines

Stress ulcer prophylaxis

Proton pump inhibitor, oral: *not added*

In critically ill patients H2 blocker meta-analysis[9] indicated that proton pump inhibitors and antacids reduce overt gastrointestinal (GI) bleeding when compared to placebo or no prophylaxis. However, mortality rates in the intensive care unit were not decreased by stress ulcer prophylaxis.

Level of Evidence: I Meta-analysis

Deep vein thrombosis prophylaxis

Anticoagulants, IM: *added* (cross referenced to section 2.14 Venous thrombo-embolism).

Post-cardiac arrest patients are assumed to be high risk for DVT to immobility and acute illness.

Meta-analysis of 9 studies[10] showed that anticoagulation was effective in decreasing the risk of venous thrombo-embolism: During anticoagulant prophylaxis, patients had significant reductions in any pulmonary embolism (PE): ARR= 0.29%; NNT 345) and fatal PE: ARR= 0.25%; NNT 400); a non-significant reduction in symptomatic deep venous thrombosis (RR 0.47; 95% CI 0.22 to 1.00), and a non-significant increase in major bleeding (RR 1.32; 95% CI 0.73 to 2.37). Anticoagulant prophylaxis had no effect on all-cause mortality (RR 0.97; 95% CI, 0.79 to 1.19).

Level of Evidence: I Meta-analysis

[2] Clifton W. Callaway, Michael W. Donnino, Ericka L. Fink, Romergryko G. Geocadin, et al. 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 8: Post–Cardiac Arrest Care. Circulation. 2015;132:S465-S482.

[3] Longstreth WT Jr, Diehr P, Cobb LA, Hanson RW, Blair. Neurologic outcome and blood glucose levels during out-of-hospital cardiopulmonary resuscitation. Neurology. 1986 Sep;36(9):1186-91.

[4] Skrifvars MB, Pettilä V, Rosenberg PH, Castrén M. A multiple logistic regression analysis of in-hospital factors related to survival at six months in patients resuscitated from out-of-hospital ventricular fibrillation.Resuscitation. 2003 Dec;59(3):319-28

[5] Oksanen T, Skrifvars MB, Varpula T, Kuitunen A, Pettilä V, Nurmi J, Castrén M . Strict versus moderate glucose control after resuscitation from ventricular fibrillation. Intensive Care Med. 2007 Dec;33(12):2093-100. Epub 2007 Oct 11.

[6] Clifton W. Callaway, Michael W. Donnino, Ericka L. Fink, Romergryko G. Geocadin, Eyal Golan, Karl B. Kern, Marion Leary, William J. Meurer, Mary Ann Peberdy, Trevonne M. Thompson, Janice L. Zimmerman. 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 8: Post–Cardiac Arrest Care. Circulation. 2015;132:S465-S482

[7] Gebhardt K, Guyette FX, Doshi AA, Callaway CW, Rittenberger JC; Post Cardiac Arrest Service. Prevalence and effect of fever on outcome following resuscitation from cardiac arrest. Resuscitation. 2013;84:1062–1067.

[8] Nolan JP, Soar J, Cariou A, Cronberg T, Moulaert VR, Deakin CD, Bottiger BW, Friberg H, Sunde K, Sandroni C. European Resuscitation Council and European Society of Intensive Care Medicine Guidelines for Post-resuscitation Care 2015: Section 5 of the European Resuscitation Council Guidelines for Resuscitation 2015. Resuscitation. 2015 Oct;95:202-222

[9] Cook DJ, Witt LG, Cook RJ, Guyatt GH. Stress ulcer prophylaxis in the critically ill: a meta-analysis. Am J Med. 1991;91(5):519.

[10] Dentali F, Douketis JD, Gianni M, Lim W, Crowther MA. Meta-analysis: anticoagulant prophylaxis to prevent symptomatic venous thromboembolism in hospitalized medical patients. Ann Intern Med. 2007;146(4):278.

Seizures

Cross referenced to section 14.3.1: Status epilepticus. Aligned with guidelines[11] treating seizures postcardiac arrest in the same manner as status epilepticus**.**

Level of Evidence: III Guidelines

20.11.1.1 NON-TRAUMA RELATED HYPOVOLAEMIC SHOCK

Section 20.11.1 Hypovolaemic shock was further divided into two sub-sections i) Non-trauma related AND ii) Trauma-related shock (with massive blood transfusion protocol) to provide guidance for trauma healthcare workers in the emergency setting.

The following STG was added to the chapter:

Description

This happens when there is loss of intravascular fluid, e.g. severe diarrhoea and dehydration, haemorrhage or fluid shifts.

General measures

Control obvious bleeding with direct pressure.

Insert one or two large bore IV catheters; peripheral lines are adequate.

Medicine treatment

Non trauma related

- Sodium chloride 0.9%, IV, 1–2 L.

Monitor blood pressure, pulse and clinical response.

20.11.1.2 TRAUMA RELATED HYPOVOLAEMIC SHOCK

The following sub-section was added to the chapter:

Description

Shock is inadequate perfusion of the vital organs. Clinically this may manifest with hypotension, tachycardia, weak pulses, clammy skin, pallor, altered mental state, poor urine output and elevated lactate.

The presence of shock in a patient with bleeding indicates that a significant volume of blood has already been lost.

The common traumatic sites of blood loss include the chest, abdomen, pelvis, long bone fractures and vascular injuries.

Major non-traumatic bleeds include gastrointestinal haemorrhage, ruptured ectopic pregnancy and obstetric haemorrhage.

General measures

Control bleeding. Techniques may include:

» Direct, sustained pressure over the bleeding point.

» Use of tourniquets in exsanguinating limb haemorrhage, e.g. manual BP cuff or specialized tourniquet while awaiting transfer to theatre. (Do not use for longer than 6 hours).

» Tamponade techniques e.g. inflated Foley catheter in neck, axilla or femoral wounds.

Obtain large bore IV access, preferably two lines.

Prevent hypothermia.

Send blood sample to blood bank as early as possible for blood type and screening. Notify blood bank of possible massive transfusion.

Medicine treatment

- Oxygen if hypoxaemic.

Trauma related

- Sodium chloride 0.9%, IV.

<u>Consider blood products If more than 1 litre of crystalloid is needed, consider blood products:</u>

» In cases of major bleeding, limit crystalloid volumes to less than 1.5 litres in total where possible. Replace acute blood loss with blood and blood products.

» Emergency blood should be used in unstable patients and when there will be significant delay in obtaining cross-matched blood from a blood bank.

» Rh typing is advised when possible.

– Type O Rh negative blood should be reserved for women of childbearing age that are Rh negative or Rh status unknown.

– Type O Rh positive blood may be given to Rh positive women of childbearing age, females > 50 years of age or males regardless of Rh status.

After 2 units of emergency blood, consider activation of massive transfusion protocol. See section 20.10.1.2.1: Massive transfusion.

[11] Clifton W. Callaway, Michael W. Donnino, Ericka L. Fink, Romergryko G. Geocadin, Eyal Golan, Karl B. Kern, Marion Leary, William J. Meurer, Mary Ann Peberdy, Trevonne M. Thompson, Janice L. Zimmerman. 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 8: Post–Cardiac Arrest Care. Circulation. 2015;132:S465-S482.

20.11.1.2.1 MASSIVE TRANSFUSION

There are no national guidelines for massive blood transfusion, and the South African National Blood Services likewise does not have a protocol. Standardised protocol, aligned with massive blood transfusion protocol from Groote Schuur Hospital (with permission) was included in the chapter.

Description

A massive transfusion is the replacement of a patient's blood volume or 10 units over a 24-hour period, or replacement of half of that volume over 4 hours.

General measures

Actively treat and prevent hypothermia.

When it is anticipated that large volumes of blood will be required, the replacement of platelets and clotting factors in addition to red blood cells is needed to prevent coagulopathy.

This may be implemented by following an empiric ratio, i.e. 1 unit of red blood cells to 1 unit of fresh frozen plasma to 1 unit of platelets, or by measuring haematological parameters (INR, platelets, Hb, fibrinogen, viscoelastical haemostatic assay) and supplementing the individual components as appropriate.

Medicine treatment

Facilities without access to a blood bank:

- Lyophilised plasma, IV.
  - 1 unit for each unit of emergency blood transfused.

Arrange urgent transfer to a centre with blood bank and specialist services.

Facilities with access to a blood bank:

» Ensure that the blood bank receives an appropriate specimen as soon as the possible need for transfusion is identified.

» Notify the blood bank as soon as possible of the need for a massive transfusion and request a massive transfusion pack.

A massive transfusion pack will typically consist of:

- Red blood cells (RBCs), 6 units.

AND

- Fresh frozen plasma (FFP), 6 units - thawed when requested.

AND

- Platelets, 1 mega-unit (normally 6 pooled donor units).
  - Aim to transfuse the above products in a 1:1:1 ratio, or as guided by laboratory parameters.
  - Send specimens for FBC and INR and continue to monitor.

Expedite definitive control of bleeding:

- Tranexamic acid, IV, 1 g, infused over 10 minutes.
  - Followed with IV infusion, 1 g, over 8 hours.
  - Benefit is greatest if initiated in the 1st hour. Initiation beyond 3 hours of tranexamic acid may be harmful.

If patient responds initially and subsequently deteriorate, there may be an ongoing occult haemorrhage. If no response occurs, consider:

» Occult exsanguinating haemorrhage: intra-abdominal, retroperitoneal and intrapleural.

» Non-hypovolaemic shock: tension pneumothorax, myocardial contusion, cardiac tamponade or myocardial infarct.

Level of Evidence: III Guidelines

NEMLC MEETING OF 27 SEPTEMBER 2018:

The NEMLC recommended that for facilities with access to a blood bank, lyophilised plasma should be recommended as an alternative option to fresh frozen plasma, as it is a more convenient and a more affordable option to fresh frozen plasma (Refer to the Adult Hospital Level costing analysis comparing FFP to FDP. www.health.gov.za)

Chapter layout

Amended to delineate management according to:

- Cardiac arrest – cardiopulmonary resuscitation
- Medical emergencies
- Trauma and injury

To assist the healthcare worker in the trauma setting, the following sections were added to the chapter with cross referral to relevant STGs in other chapters in the Adult Hospital Level and Primary Health Care Level STGs and EML: 20.13 Acute kidney injury, 20.14 Bites and stings; 20.2 Injuries; 20.3 Cardiac dysrhythmias; 20.4 Acute coronary syndromes; 20.5 Asthma, acute; 20.9 Diabetic emergencies; 20.12 Status epilepticus; 20.13 Acute kidney injury; 20.14 Bites and stings; 20.16 Exposure to poisonous substances; 20.17 Eye injuries; 20.18 Post exposure prophylaxis; 20.19 Soft tissue injuries; 20.20 Sprains and strains.

B: MEDICINE AMENDMENTS

SECTION	MEDICINE	ADDED/DELETED/AMENDED
Cardiac arrest – cardiopulmonary resuscitation	Cardiac arrest algorithm	Amended
20.1 Cardiac arrest adults	Adrenaline (epinephrine)	Directions for use amended (route of administration)
	Amiodarone, IV	Directions for use amended
20.6 Angioedema	Adrenaline (epinephrine), IM	Deleted (indicated for anaphylaxis)
- If urticaria and/or itch present (no imminent airway compromise)	Hydrocortisone, IV	Amended
	Promethazine, IV	Added
	Cetirizine, oral	Retained
- Severe ACE-inhibitor induced angioedema with threatened airway:	Lyophilised plasma	Amended to first line option
	Fresh frozen plasma	Amended to second line option
20.7 Anaphylaxis/ anaphylactic shock	Adrenaline (epinephrine), IV infusion	Added
	H_2-antagonists	Not added
	Glucagon	Not added
	Ringer lactate, IV	Not added
	Sodium chloride 0.9%, IV	Retained
- If urticaria and/or itch present (no imminent airway compromise)	Promethazine, IV	Added
	Cetirizine, oral	Retained
20.8 Delirium with perceptual disturbances *- Agitated and acutely disturbed patient:*	Haloperidol, IM	Added (moved from mental healthcare chapter); haloperidol dosing amended
	Lorazepam, IM	
	Clonazepam, IM	
	Diazepam, IV	
20.10 Pulmonary oedema, acute	Furosemide, IV	Direction for use amended
	Nitrates, SL/IV	Direction for use amended
20.11 Hypovolaemic shock	Tourniquets	Restriction of use deleted
20.11.2.1 Neurogenic shock	Ringer lactate, IV	Not added
	Sodium chloride 0.9%, IV	Added
20.11.2.2 Septic shock *- Perform a fluid challenge for hypotension*:	Sodium chloride 0.9%, IV	Retained as the primary resuscitation fluid for all indications
	Balanced solutions, IV	Recommended as a therapeutic class for appropriate patients, including critically ill patients presenting with hyperchloraemia, previous renal replacement therapy
	Ringer lactate, IV	Recommended as the example of therapeutic class (listed in STG)
	Balsol, IV	Added as a therapeutic alternative
	Plasmalyte B, IV	Added as a therapeutic alternative
20.11.3 Cardiogenic shock	Ringer lactate, IV	Not added
	Sodium chloride 0.9%, IV	Added
20.15 Burns *- local wound care*	Povidone iodine, topical	Not added
	Silver sulfadiazine, topical	Deleted
	Mupirocin, topical	Not added
	Nano-crystalline dressings	Not added
	Melaleuca alternifolia	Not added

CARDIAC ARREST – CARDIOPULMONARY RESUSCITATION

Cardiac arrest algorithm: *amended*

Adapted version of the Resuscitation Council of South Africa (RCSA) cardiac arrest algorithm (with permission), aligned with the text in the STG included in the STG. Early defibrillation and electrical cardioversion are recommended as the mainstay of treatment in the emergency setting.

Level of Evidence: III Guidelines, Standard practice

20.1 CARDIAC ARREST, ADULTS

Airway and breathing: International Liaison Committee on Resuscitation (ILCOR) recommends C-A-B approach (compressions, airway, breathing) as circulation is critical in CPR. Evidence shows that starting CPR sequence with compressions (rather than maintenance of airway and breathing - the A-B-C approach) decreases the time to

commencement of chest compression[12] [13] [14].

Adrenaline (epinephrine): *directions for use amended*
If no IV line is available, recommended route of administration amended from "endotracheal" to "intraosseous" aligned with RCSA algorithm for cardiac arrest, 2015.
Level of Evidence: III Guidelines

Amiodarone, IV: *directions for use amended*
Aligned with 2015 International Liaison Committee on Resuscitation Guidelines[15] *(recommended amiodarone/lidocaine in adults with shock refractory ventricular fibrillation/pulseless ventricular tachycardia (VF/pVT) (weak recommendation, low quality evidence of 1999[16]))* and Resuscitation Council of South Africa – Advanced Cardiac Arrest Algorithm, 2015.

However, recent meta-analyses[17] [18] suggest that there is uncertainty about the efficacy of antiarrhythmics in cardiac arrest to improve rates of return of spontaneous circulation, survival to hospital discharge or neurological outcomes when compared to placebo. Conflicting outcomes for survival to hospital admission was reported for use of antiarrhythmics in advanced life support: McLeod et al, 2017 showed that amiodarone (RR 1.18; 95% CI: 1.08 to 1.30) was associated with a statistically significant increase in survival to hospital admission, whilst Chowdury et al, 2017 showed that amiodarone had no significant effect on survival to admission (OR=1.33; 95% CI 0.91 to 1.97; I^2 = 92%; p=0.14).

The Adult Hospital Level Committee was of the opinion that antiarrhythmics failed to show improvements regarding clinical meaningful survival questions and suggests the need for re-evaluating antiarrhythmics' place in cardiopulmonary resuscitation. Bystander initiated CPR and time to arrival of emergency services and defibrillators are more relevant and harms associated with amiodarone needs consideration.
The Adult Hospital Level Committee requests that NEMLC guide on this recommendation.
Level of Evidence: I Meta-analyses, low quality RCT, Guidelines

20.6 ANGIOEDEMA

Adrenaline (epinephrine), IM: *deleted*
More relevant to anaphylaxis – section 20.1.2, and the following text was inserted in a box for emphasis:

In cases where angioedema is part of anaphylaxis, treat as anaphylaxis. See section 20.1.2: Anaphylaxis/Anaphylactic shock.

If urticaria and/or itch present (no imminent airway compromise):
Hydrocortisone, IV: *amended*
Promethazine, IV: *added*
Cetirizine, oral: *retained*
Standard practice to administer antihistamines for histamine-mediated angioedema, whilst corticosteroids used for severe disease.
Level of Evidence: III Expert opinion

[12] Lubrano R, Cecchetti C, Bellelli E, Gentile I, Loayza Levano H, Orsini F, Bertazzoni G, Messi G, Rugolotto S, Pirozzi N, Elli M. Comparison of times of intervention during pediatric CPR maneuvers using ABC and CAB sequences: a randomized trial. Resuscitation. 2012;83:1473–1477.
[13] Marsch S, Tschan F, Semmer NK, Zobrist R, Hunziker PR, Hunziker S. ABC versus CAB for cardiopulmonary resuscitation: a prospective, ran- domized simulator-based trial. Swiss Med Wkly. 2013;143:w13856.
[14] Sekiguchi H, Kondo Y, Kukita I. Verification of changes in the time taken to initiate chest compressions according to modified basic life support guidelines. Am J Emerg Med. 2013;31:1248–1250.
[15] Morrison LJ, Deakin CD, Morley PT, Callaway CW, Kerber RE, Kronick SL, Lavonas EJ, Link MS, Neumar RW, Otto CW, Parr M, Shuster M, Sunde K, Peberdy MA, Tang W, Hoek TL, Böttiger BW, Drajer S, Lim SH, Nolan JP; Advanced Life Support Chapter Collaborators. Part 8: Advanced life support: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation. 2010 Oct 19;122(16 Suppl 2):S345-421. https://www.ncbi.nlm.nih.gov/pubmed/20956256
[16] Kudenchuk PJ, Cobb LA, Copass MK, Cummins RO, Doherty AM, Fahrenbruch CE, Hallstrom AP, Murray WA, Olsufka M, Walsh T. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. N Engl J Med. 1999 Sep 16;341(12):871-8. https://www.ncbi.nlm.nih.gov/pubmed/10486418
[17] McLeod SL, Brignardello-Petersen R, Worster A, You J, Iansavichene A, Guyatt G, Cheskes S. Comparative effectiveness of antiarrhythmics for out-of-hospital cardiac arrest: A systematic review and network meta-analysis. Resuscitation. 2017 Dec;121:90-97. https://www.ncbi.nlm.nih.gov/pubmed/29037886
[18] Chowdhury A, Fernandes B, Melhuish TM, White LD. Antiarrhythmics in Cardiac Arrest: A Systematic Review and Meta-Analysis. Heart Lung Circ. 2018 Mar;27(3):280-290. https://www.ncbi.nlm.nih.gov/pubmed/28988724

Severe ACE-inhibitor induced angioedema with threatened airway

Lyophilised plasma: *amended to first line option*

Fresh frozen plasma: *amended to second line option*

Lyophilised plasma recommended as the preferred treatment, based on cost[19] [20] and pragmatic implications (including storage at room temperature, longer shelf-life, infection control, etc)

Level of Evidence: III Expert opinion

20.7 ANAPHYLAXIS/ANAPHYLACTIC SHOCK

Adrenaline (epinephrine), infusion: *added*

In cases of persistent hypotension or where multiple repeat doses of bolus doses of adrenalin (epinephrine) is required, adrenaline (epinephrine) infusion be recommended.

The following text was added, aligned with management in neurogenic shock.

In cases of persistent hypotension or where multiple repeat doses are required:

- Adrenaline (epinephrine), IV infusion, start at 0.05 mcg/kg/minute titrated according to the response.
  - Dilute 10 mg i.e. 10 ampoules of adrenaline 1:1 000 in 1 L sodium chloride 0.9%.
  - Infuse according to weight and clinical response.
  - Infusion rate: mL/hour:

mcg/kg/minute	Weight in kg						
	50	60	70	80	90	100	110
0.05	15	18	21	24	27	30	33
0.1	30	36	42	48	54	60	66
0.2	60	72	84	96	108	120	132
0.3	90	108	126	144	162	180	198
0.4	120	144	168	192	216	240	264
0.5	150	180	210	240	270	300	330
0.6	180	216	252	288	324	360	396
0.7	210	252	294	336	378	420	462
0.8	240	288	336	384	432	480	528
0.9	270	324	378	432	486	540	594
1	300	360	420	480	540	600	660

Level of Evidence: III Expert opinion

H_2-antagonists: *not added*

Glucagon: *not added*

H_2-antagonists and glucagon, though recommended on the RCSA algorithm, are not included in the secondary level EML for anaphylaxis.

Promethazine, IV: *added*

Cetirizine, oral: *retained*

Promethazine, IV: added, aligned with RCSA algorithm and for consistency with PHC STGs and EML, 2018.

Paucity of good quality RCT evidence for promethazine, IV for management of anaphylaxis. [21] Despite adrenaline being the mainstay of treatment, administering antihistamines was standard practice and is included in anaphylaxis treatment algorithms internationally.

Recommendation: Promethazine, IV be retained in the treatment protocol for anaphylaxis and consideration for a single dose of cetirizine (non-sedating antihistamine).

Rationale: General consensus that early administration of adrenaline is the mainstay of therapy and is associated with survival. However, administration of antihistamines is standard practice and included in treatment algorithms internationally. Case reports indicate use of antihistamines in this setting.

Level of Evidence: III Guidelines, Case reports[22], Standard of Care[23]

[19] South African National Blood Service State Price list 2018/9: Fresh Frozen plasma, 280 mL (1unit) = R 1 494,49

[20] Contract circular RT285-2019: Lyophilised plasma, 200 mL (1 unit) = R 1 141.90

21 Sheikh A, ten Broek Vm, Brown SG, Simons FE. H1-antihistamines for the treatment of anaphylaxis with and without shock. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD006160. https://www.ncbi.nlm.nih.gov/pubmed/17253584

22 Fernando SL, Broadfoot AJ. Ondansetron anaphylaxis: a case report and protocol for skin testing. Br J Anaesth. 2009 Feb;102(2):285-6. https://www.ncbi.nlm.nih.gov/pubmed/19151059

Ringer lactate, IV: *not added*
Sodium chloride 0.9%, IV: *retained*
Refer to the Ringer Lactate medicine review and discussion thereof, below.

20.8 DELIRIUM WITH PERCEPTUAL DISTURBANCES

Delirium STG was moved from the mental healthcare chapter to the emergencies chapter.

Sub-heading of this section was amended from:
"***Delirium with aggressive disruptive behaviour*"**
To
"***Delirium with perceptual disturbances***"
Rationale: Aligned with the new DSM 5 (*APA 2014)* definition, which shifts the definition of delirium to that of an attentional abnormality with perceptual disturbances (instead of a problem of altered consciousness).
Level of Evidence: III Guidelines

Management was delineated to provide guidance for:
i) Severe aggression and disruptive behavior
ii) Agitated and acutely disturbed patient

i) For management for severe aggression and disruptive behaviour:
Cross reference was added to section 15.1: Aggressive disruptive behaviour in adults.

ii) For agitated and acutely disturbed patient:
Haloperidol, IM: *added (moved from mental health care chapter); and dosing amended*
Lorazepam, IM: *added (moved from mental health care chapter)*
Clonazepam, IM: *added (moved from mental health care chapter)*
Diazepam, IV: *added (moved from mental health care chapter)*

Lower doses of haloperidol, IM recommended for delirium with perceptual disturbances, aligned with Guidelines:

Haloperidol, IM, ~~5~~ 0.5-1 mg.
- This can be repeated in 60 minutes, if required and then 4 hourly to a maximum dose of 10 mg within 24 hours.
- ~~Maximum dose: 10 mg within 24 hours.~~
- Monitor vital signs and beware of acute dystonia and neuroleptic malignant syndrome.
- Dosing may vary according to clinical circumstances, e.g. lower doses in the elderly or where HIV infection or HIV-related dementia is known or suspected.

Level of Evidence: III Guidelines

Evidence review:
Nikooie et al, 2019: A recently published meta-analysis of RCTs and observational studies[24] shows that the current evidence does not support the **routine use** of antipsychotics to treat delirium in adult inpatients.

Cochrane reviews: Systematic reviews for antipsychotics in the terminally ill patient[25], hospitalised non-ICU patients[26] and critically ill patients[27] showed that evidence was insufficient and of low methodological quality to support or refute the use of antipsychotics in patients with delirium with perceptual disturbances.

[23] Resuscitation Council of South Africa, Emergency Management of Anaphylaxis Guidelines, 2015. https://resus.co.za/anaphylaxis/
[24] Nikooie R, Neufeld KJ, Oh ES, Wilson LM, Zhang A, Robinson KA, Needham DM. Antipsychotics for Treating Delirium in Hospitalized Adults: A Systematic Review. Ann Intern Med. 2019 Sep 3. https://www.ncbi.nlm.nih.gov/pubmed/31476770
[25] Finucane AM, Jones L, Leurent B, Sampson EL, Stone P, Tookman A, Candy B. Drug therapy for delirium in terminally ill adults. Cochrane Database Syst Rev. 2020 Jan 21;1:CD004770. https://www.ncbi.nlm.nih.gov/pubmed/31960954
[26] Burry L, Mehta S, Perreault MM, Luxenberg JS, Siddiqi N, Hutton B, Fergusson DA, Bell C, Rose L. Antipsychotics for treatment of delirium in hospitalised non-ICU patients. Cochrane Database Syst Rev. 2018 Jun 18;6:CD005594. https://www.ncbi.nlm.nih.gov/pubmed/29920656
[27] Burry L, Hutton B, Williamson DR, Mehta S, Adhikari NK, Cheng W, Ely EW, Egerod I, Fergusson DA, Rose L. Pharmacological interventions for the treatment of delirium in critically ill adults. Cochrane Database Syst Rev. 2019 Sep 3;9:CD011749. https://www.ncbi.nlm.nih.gov/pubmed/31479532

NICE Guidelines: Clinical Guideline[28] for the prevention, diagnosis and management of delirium recommends (where verbal and non-verbal de-escalation techniques have been ineffective/inappropriate) short-term (≤1 week) haloperidol initiated at the lowest clinically appropriate dose with cautious titration according to symptoms.

Maudsley et al[29]: Guidelines recommend haloperidol IM, at a dose of 0.5–1 mg, observe for 30–60 minutes and repeat if necessary.

20.10 PULMONARY OEDEMA, ACUTE

Furosemide, IV: *direction for use amended*
Nitrates, SL/IV: *directions for use amended*
The Adult Hospital Level Committee acknowledged the NEMLC recommendation (made at the meeting of 2 November 2017)[30] where acute pulmonary oedema be managed with diuretics and nitrates rather than initial management with nitrates only, as most patients present with oedema in South Africa. However, the Adult Hospital Committee recommends that the STG also provide guidance for cases where there is no overload.
Recommendation: Management has been delineated to provide guidance when:

- Fluid overload present – initiate treatment with diuretics.
- No fluid overload is present – initiate treatment with nitrates.

Level of Evidence: III Expert opinion

20.11 HYPOVOLAEMIC SHOCK

Tourniquet: Guideline recommend that tourniquet time should be limited and tourniquets should be removed when definitive care is available. When correctly used, the complication rate from tourniquet use is exceedingly low[31].
Recommendation: Text, "*Do not use tourniquets*" was deleted, aligned with guidelines.
Level of Evidence: III Guidelines

20.11.2.1 NEUROGENIC SHOCK

Sodium chloride 0.9%, IV: *added*
Ringer lactate, IV: *not added*
Refer to the Ringer Lactate medicine review and discussion thereof, below.

The following text was added, based on standard practice:

Administer crystalloid in titrated boluses up to 1 litre.

Level of Evidence: III Expert opinion

20.11.2.2 SEPTIC SHOCK

Fluid challenge for hypotension
Sodium chloride 0.9%, IV: *retained as the primary resuscitation fluid for all indications*
Balanced solutions, IV: *recommended as a therapeutic class for appropriate patients, including critically ill patients presenting with hyperchloraemia, previous renal replacement therapy*
Ringer lactate, IV: recommended as the example of therapeutic class (listed in STG)
Balsol, IV: *added as a therapeutic alternative*
Plasmalyte B, IV: *added as a therapeutic alternative*

Refer to the Ringer Lactate medicine review and discussion thereof, below.

[28] NICE. Clinical guideline: Delirium: prevention, diagnosis and management, 28 July 2010. www.nice.org.uk/guidance/cg103
[29] Taylor, David; Paton, Carol; Kapur, Shitij. The Maudsley Prescribing Guidelines, Twelfth Edition. London: CRC Press; 2015
[30] NEMLC minutes of the meeting: 2 November 2017.
[31] Fox N, Rajani RR, Bokhari F, Chiu WC, Kerwin A, Seamon MJ, Skarupa D, Frykberg E; Eastern Association for the Surgery of Trauma. Evaluation and management of penetrating lower extremity arterial trauma: an Eastern Association for the Surgery of Trauma practice management guideline. J Trauma Acute Care Surg. 2012 Nov;73(5 Suppl 4):S315-20. https://www.ncbi.nlm.nih.gov/pubmed/23114487

NEMLC had recommended at the meeting of 26 September 2019 that the STG text updated to:

Perform a fluid challenge for hypotension:

- Sodium chloride 0.9%, 500 mL boluses over 30 minutes, whilst monitoring clinical response until 30 mL/kg has been achieved.
  - Assess blood pressure and pulse rate response. Response is defined by a good urine output (> 0.5 mL/kg/hour) and adequate cerebral perfusion rather than an absolute blood pressure value.

Balanced solutions may be appropriate in some patients (i.e. presentation with hyponatraemia, previous renal placement therapy):

- Balanced solution, e.g.:
- Ringers lactate, 500 mL boluses over 30 minutes, whilst monitoring clinical response until 30 mL/kg has been achieved.
  - Assess blood pressure and pulse rate response. Response is defined by a good urine output (> 0.5 mL/kg/hour) and adequate cerebral perfusion rather than an absolute blood pressure value.

20.11.3 CARDIOGENIC SHOCK

Fluid challenge

Sodium chloride 0.9%, IV: *added*

Ringer lactate, IV: *not added*

Refer to the Ringer Lactate medicine review and discussion thereof, below.

20.15 BURNS

Local Wound Care

Povidone iodine, topical*: not added*

Silver sulfadiazine, topical: *deleted*

Mupirocin, topical: *not added*

Nano-crystalline dressings: *not added*

Melaleuca alternifolia: *not added*

Evidence of efficacy: Limited evidence for use of topical antibiotics and antiseptics for prevention of wound infection. No available evidence could be found for mupirocin.

Silver sulfadiazine: Cochrane review[32] showed that silver silver sulfadiazine was associated with a statistically significant increase in burn wound infection vs. dressings/skin substitute (OR = 1.87; 95% CI: 1.09 to 3.19, I^2 = 0%). Though, RCTs were at high, or unclear, risk of bias. Silver sulfadiazine was also associated with significantly longer length of hospital stay vs dressings/skin substitute (MD = 2.11 days; 95% CI: 1.93 to 2.28).

Povidone iodine: Cochrane review[33] showed that there is probably no difference in infection rates between an iodine-based treatment vs moist exposed burn ointment (moderate certainty evidence) – Mean time to healing for wounds treated with povidone iodine vs chlorhexidine: MD - 2.21 days, 95% CI 0.34 to 4.08.

Nano-crystalline dressings: Cochrane review showed that, "There is moderate certainty evidence that, on average, burns treated with nanocrystalline silver dressings probably have a slightly shorter mean time to healing than those treated with Vaseline gauze (difference in means -3.49 days, 95%CI -4.46 to -2.52; I^2 = 0%; 2 studies, n=204), but low certainty evidence that there may be little or no difference in numbers of healing events at 14 days between burns treated with silver xenograft or paraffin gauze (RR 1.13, 95% CI 0.59 to 2.16 1 study; n=32)".

Melaleuca alternifolia: No available evidence could be sourced for cooling burns with Melaleuca alternifolia (tea tree oil) for the first 12 hours. There is also the associated risk of hypothermia for large burn wounds, if this is practiced.

[32] Barajas-Nava LA, López-Alcalde J, Roqué i Figuls M, Solà I, Bonfill Cosp X. Antibiotic prophylaxis for preventing burn wound infection. Cochrane Database Syst Rev. 2013 Jun 6;(6):CD008738. https://www.ncbi.nlm.nih.gov/pubmed/23740764

[33] Norman G, Christie J, Liu Z, Westby MJ, Jefferies JM, Hudson T, Edwards J, Mohapatra DP, Hassan IA, Dumville JC. Antiseptics for burns. Cochrane Database Syst Rev. 2017 Jul 12;7:CD011821. https://www.ncbi.nlm.nih.gov/pubmed/28700086

Recommendations:

- Silver sulfadiazine, topical for prevention of wound infections be deleted.
- Povidone iodine, topical not be added for management of infections in burns.
- Nano-crystalline dressings not be recommended for management of burns.
- Mupirocin, topical not be recommended for management of burns.
- Melaleuca alternifolia, not be recommended for cooling of burns.

Rationale: No available evidence of efficacy could be retrieved from the published literature for mupirocin, topical. Cochrane reviews shows that silver sulfadiazone is associated with a statistically significant increase in burn wound infection and length of hospital stay vs. dressings/skin substitute; that povidone-iodine showed no difference in infection rates vs moist exposed burn ointment (i.e. chlorhexidine) and that nano-crystalline dressings were comparable to paraffin gauze with regards to healing events. No available evidence could be sourced for cooling of burns with *Melaleuca alternifolia (*tea tree oil).

Level of Evidence: II Systematic review of low to moderate quality RCTs

The following text was added to the STG:

» Keep the wound clean and dress with sterile dressings.

RINGER LACTATE MEDICINE REVIEW

Sodium chloride 0.9%, IV: *retained as the primary resuscitation fluid for all indications*
Balanced solutions, IV: *recommended as a therapeutic class for appropriate patients, including critically ill patients presenting with hyperchloraemia, previous renal replacement therapy*
Ringer lactate, IV: recommended as the example of therapeutic class (listed in STG)
Balsol, IV: *added as a therapeutic alternative*
Plasmalyte B, IV: *added as a therapeutic alternative*

Background: In the previous Adult Hospital Level review cycle, available RCT evidence in the published literature was reviewed suggesting that Ringer lactate was not superior to sodium chloride 0.9%. Sodium chloride 0.9%, IV was then recommended based on price. (Refer to the medicine review: Ringer lactate for Resuscitation in patients with hypovolaemia, October 2015).

Ringer Lactate for resuscitation in Adu

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

The medicine review has subsequently been updated – refer to the updated medicine review: Ringer lactate for Resuscitation in adults with hypovolaemia, November 2019):

Ringer Lactate for resuscitation in Adu

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

Recommendations

- Based on this evidence review, the National Essential Medicines List Committee *(Ref: Minutes of the NEMLC meeting of 26 September 2019)* reccomends that normal saline should be the primary resuscitation fluid (including for septic shock).
  Rationale: Meta-analyses showed that among critically ill patients receiving crystalloid fluid therapy, use of a balanced crystalloid compared with normal saline did not reduce the mortality, risk of severe AKI or RRT use rate. Evidence is limited regarding the effects of hyperchloraemic acidosis on hard clinical outcomes.

Level of Evidence: I Systematic reviews and meta-analyses [10, 14]

- A caveat be included that balanced solutions (Ringers Lactate, balsol/ Plasmalyte) may be appropriate in some patients.
  Rationale: Limited evidence (including RCT sub-analysis) shows that balanced solutions may be appropriate in certain patients (including critically ill patients presenting with hyperchloraemia, previous renal replacement therapy).

Level of Evidence: III RCT Sub-analysis[12], Disease-oriented RCTs of low methodological quality[15]

Report prepared by TD Leong: Secretariat to the Adult Hospital Level Committee (2017-2020)
- ***Note:*** *Information was sourced from NEMLC ratified minutes and NEMLC-approved documents.*