MEDECINS SANS FRONTIERES
ÄRZTE OHNE GRENZEN

PR Medical Protocol

Yellow Fever Case Management
OCG Protocol

DMED – OCG / 01.2013

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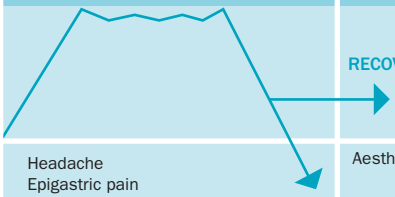
	Period of infection 3-6 days (viraemic)	Period of remission 2-24 hours	Period of intoxication 3-8 days	Convalescence 2-4 weeks
Fever				
Clinical features	Headache Myalgia Lumbosacral pain Nausea Malaise Prostration Dizziness Conjunctival injection Furred tongue, red at tip Bradycardia (Paget's sign)	Symptoms abate	Headache Epigastric pain Vomiting Prostration Malaise Jaundice Oliguria > anuria Tender liver Hypotension > shock Stupor > coma Hyothermia Haemorrhage Convulsions	Aesthenia
Laboratory features	Leukopenia Neutropenia AST > ALT Protenuria		Thrombocytopenia Leukocytosis AST > ALT protenuria Azotaemia Hyglycaemia Acidosis	
Infection and immunity	Viraemia		Antibody	Antibody

Table 1 Yellow fever phases.1

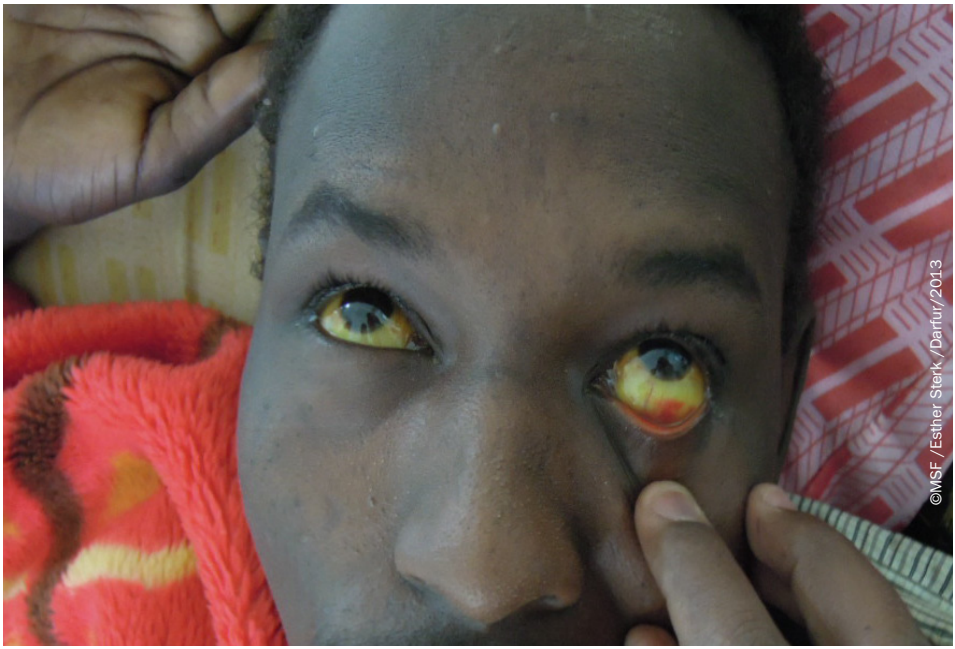
1. General Information

Yellow fever is a viral hemorrhagic fever with a variety of clinical presentations, from asymptomatic or flu-like symptoms to severe hemorrhagic illness with severe hepatitis, acute liver failure, liver encephalopathy, sepsis, bleeding, multiple organ failure (MOF) and shock. The disease has a viraemic period giving a mild disease during 3-6 days and then most of the patients get better. However, 15-25 % of the patients enters the second, toxic phase within 24 hours after initial remission and develop moderate to severe symptoms leading to a mortality of up to 80 % depending on the level of supportive care that can be provided.

1.1 Contagious period

Patients are contagious in the viraemic period which is 3-6 days after onset of disease. All patients suspected with yellow fever will need to stay 24 hours per day under a mosquito net. When 12the patient turns yellow (jaundice), he is normally not contagious anymore to mosquitoes.

1 "Yellow fever: an update", Thomas P. Monath, in ***THE LANCET Infectious Diseases*** Vol 1 August 2001, p. 15.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2. Case Management and Treatment Challenges in Yellow Fever

There is no curative treatment for yellow fever. Supportive treatment should be provided according to symptoms and can significantly reduce mortality. There are 2 challenges in providing supportive medication to patients with yellow fever.

2.1 Hepatitis/liver failure

Yellow fever causes hepatitis and liver failure. The liver plays an important role in drug metabolism and in case of moderate or severe yellow fever the drug metabolism is hampered, making the possibilities for treatment with medication limited. Some drugs are more hepatotoxic than others and the balance should be made between the risks and benefits of administering medication to moderate and severe Yellow fever cases. Paracetamol and quinine should be avoided due to the risk of hepatotoxicity. The level of jaundice correlates with the grade of liver damage and the elevation of transaminase.

2.2 Bleeding tendency

The healthy liver synthesizes coagulation factors, but in liver failure this production of clotting factors is impaired. Severe yellow fever disease leads to liver failure induced coagulation factor deficit, coagulopathy, bleeding and DIC (Diffuse Intravascular Coagulation). The gastrointestinal tract is the most common site of bleeding. NSAIDS need to be avoided because of the risk of gastrointestinal bleeding and the anti-platelet effect (aspirin). Invasive procedures need to be reduced to the minimum to avoid inducing hemorrhage and only performed if considered essential. Urinary catheterisation is not recommended. However following urine output might be very important in critically ill patients to monitor shock, renal

failure and to guide fluid resuscitation. In this case urinary catheter can be place in patients without bleeding.Nasogastric tubes should only be placed as life saving procedure to avoid aspiration risk in vomiting patients with reduced consciousness, severe vomiting or in severe yellow fever patients with haematemesis. Intramuscular injections or intraosseous access need to be avoided, except if the IV route is not possible. The use of the anticoagulant heparin in case of DIC is not recommended.

2.3 Hospitalization

Not all patients need to be hospitalized. Yellow fever patients can be divided in 4 groups. Asymptomatic cases don't have symptoms and don't need treatment. Case management for mild, moderate and severe infections is different for each group.

- **Asymptomatic infections** > No hospitalization needed
- **Mild infections (viraemic period)** > No hospitalization needed
- **Moderate infections (toxic phase)** > Hospitalization
- **Severe infections (toxic phase)** > Hospitalization

2.4 Presumptive and prophylactic broad spectrum antibiotics treatment

It is advised to administer broad spectrum antibiotics to all suspected yellow fever patients with moderate or severe yellow fever disease.

First of all, yellow fever symptoms are similar to other endemic tropical diseases as dengue hemorrhagic fever, other viral hemorrhagic fevers, leptospirosis, severe malaria, acute/fulminant hepatitis, shigellosis and severe typhoid fever. Without laboratory results it is difficult to distinguish between these diseases and appropriate treatment for treatable diseases should not be delayed.

Secondly, yellow fever patients can have concomitant bacterial infections or a malaria infection that can interfere with their ability to build an immune response to the yellow fever infection.

Thirdly, severe yellow fever patients often develop secondary bacterial infections, like Gram negatives gastrointestinal infections or S.aureus and anaerobic bacterial pulmonary infections, often leading to sepsis.

Also often signs of infection are absent due to disturbed immune reaction. By providing antibiotics prophylaxis this risk of secondary infections can be reduced. Ceftriaxone IV is the recommended broad spectrum antibiotics to cover most of the bacterial infections and which is less dangerous to give in case of liver failure. Metronidazol IV should be added to the treatment of severe cases to minimize the growth of anaerobe and Gram negative bacteria (producing nitrogen) in the gut. The following antibiotics could only be considered if no Ceftriaxone is available, as they are potentially hepatotoxic: erythromycine, doxycycline, azithromycin, chloramphenicol, cloxacillin and cotrimoxazol.

2.5 Malaria rapid test (RDT)

All suspected yellow fever patients should be tested for malaria to rule out malaria as the cause of symptoms or as concomitant disease. In case of simple malaria, an ACT (DHA/PiP, ASSP or Coartem) should be given, however Amodiaquine should be avoided due to its liver toxicity. In case of severe malaria symptoms patients need to be treated preferably with artesunate IV. Quinine should be avoided viewing the potential liver toxicity in Yellow fever patients. If artesunate is not available, artemether IM is the treatment of choice however has the risk to provoke bleeding. Alternatively a full treatment with rectocaps artesunate during 7 days could be an option if artemether IM is not feasible due to bleeding.

2.6 IV fluids

Patients going into the toxic phase are at risk to go into relative hypovolemic shock caused by peripheral vasodilatation and capillary hyper-permeability. IV fluids should be given standard to moderate yellow fever patients not able to drink correctly and to all severe cases to prevent electrolyte disturbances, hypovolaemia and renal failure. Circulatory monitoring (pulse, peripheral circulation and temperature, capillary refill, blood pressure, respiratory rate and urinary output are essential to detect changes and to be able to treat reactively.

2.7 Acute liver failure and liver encephalopathy

A normal functioning liver produces coagulation factors, immune factors, bile, proteins, stores glycogen, performs gluconeogenesis and metabolizes and detoxifies medication and substances formed in the body during the digestive process. In liver failure, the production and metabolization capacity are not functioning anymore, leading to bleeding, infections and electrolyte and metabolic disturbances as hypoglycaemia, hypokaliemia and metabolic acidosis. Bilirubine is building up in the blood causing jaundice. Toxic substances as ammonia are accumulating and may penetrate the blood-brain barrier and affect the central nervous system, leading to liver encephalopathy, a life-threatening disease often complicated by cerebral edema causing elevated intracranial pressure and brainstem herniation. Treatment of acute liver failure and liver encephalopathy is symptomatic and focused on prevention of complications. Environment for patients with hepatic encephalopathy should be quiet, with minimal sensory stimulation: avoidance of light and noise.

The use of oral enteral lactulose, an indigestible disaccharide, is under discussion. When stupor is caused by high ammonia levels as is the case in liver encephalopathy, than lactulose could be beneficiary as it reduces ammonia levels. In patients with gastrointestinal bleeding and a dysfunctional liver, ammonia levels can increase quickly due to the digestion of blood leading to high protein and thus ammonia levels. However, the differential diagnostics of pathologies provoking alteration of consciousness is large. If the stupor is caused by hypoglycaemia, shock, hypothermia, etc, than administration of lactulose is not useful and could even be harmful due to the risk of aspiration in patients with altered level of consciousness. In case other pathologies causing stupor are excluded and liver encephalopathy is the most probable diagnosis for the altered consciousness, the recommended dose for lactulose dose is 30 ml per os or per nasogastric tube 2 or 3 times per day for adults.

2.8 Hypoglycaemia

Patients with liver failure are at risk of hypoglycaemia due to impaired gluconeogenenis and depletion of hepatic glycogen stores. For severe yellow fever cases it is recommended to ensure a continuous Ringers Lactate/Glucose 5% drip. Take

out 100 ml of RL from 1 liter of RL and add 100 ml of G50% to obtain a continuous RL/5% Glucose perfusion for adults and children during the period with severe symptoms. In addition regular glucose measurements need to be performed and glucose bolus needs to be given reactively in case of detected hypoglycaemia.

2.9 Vomiting

Metoclopramide IV can be used to reduce vomiting in case of severe non-bloody vomiting. If the patient is vomiting blood, metoclopramide should NOT be given because the blood and formed blood clots in the gastrointestinal tract need to be able to get out of the body to reduce nausea, the risk of paralytic ileus and the ammonia levels after digestion of the proteins.

2.10 Prevention of bleeding, reduction of bleeding tendency and in case of active bleeding

Vitamin K deficiency may contribute to the coagulopathy of acute liver failure in a substantial minority of patients. Empirically vitamin K 10 mg IV/day for 3 days could be administered preventively in moderate and severe patients to reduce bleeding tendency, and in case of active bleeding. However, good monitoring should be provided by the health staff. In case of active bleeding, blood transfusion should be provided to correct haemoglobine levels, shock, and to replace lost coagulation factors.

2.11 Gastric pain, prevention of ulcer and prevention of gastric bleeding

Omeprazol or Ranitidine is recommended in all moderate and severe cases to reduce gastric pains, to diminish the risk of ulcer and gastric bleeding. However half dosages are recommended in cases of severe liver impairment.

2.12 Oxygen

Critically ill patients, especially the ones with circulatory disturbances, may benefit from oxygen supplementation. If available, all patients with severe yellow fever should receive oxygen (2 liters/minute with nasal prongs or 5 liters/minute with mask).

2.13 Renal failure

Due to systemic and intra-renal haemodynamic changes and liver failure in yellow fever patients, there is a high risk of developing renal failure. Treatment of acute renal failure in development settings where no dialysis is available, is extremely difficult, so focus should be on preventive measures. Arterial perfusion needs to be maintained by adequate volemia, prevention of infections, avoidance of hypovolemic shock, and avoiding nephrotoxic medications. Good volemia needs to be achieved by continuous maintenance fluids for severe cases and circulatory monitoring is essential to be able to correct circulatory inbalances asap. A bolus of Furosemide IV (1 mg/kg) can be given to enhance diuresis BUT should only be administered if volemia and perfusion are restored.

2.14 Corticosteroids

The so-called cytokine storm plays a role in the physiopathology of Multiple Organ Failure and septic shock. Avoiding or reducing the cytokine release could be of benefit for patients with yellow fever, however this assumption is not evidence based. The administration of methylprednisolone stress dose of 200-300 mg/day is recommended by experts for the management of septic shock and could in theory have a beneficiary effect on yellow fever patients, however studies are needed to demonstrate the impact. At the moment of writing corticosteroids are NOT recommended in the case management of yellow fever.

2.15 Itching

Calamine lotion could be given to alleviate itching induced by high bilirubine levels.

3. Case Management of Mild Yellow Fever Cases

Patients with mild yellow fever infection don't need to be hospitalized and can be treated at home by family members if in reach of a health care setting. Bednets need to be given.

Symptoms	Low grade fever or no fever. General malaise. Headache. Muscle and/or back pain. Conjunctival injection. Furred tongue – red at tip. Bradycardia relative to fever. Nausea. Loss of appetite.
Mortality	Almost 0%.
Laboratory test	RDT should be performed if feasible. Urine should be checked for proteinuria, if +++ patient should be hospitalized as moderate case.
Treatment at home	Bed net: 24 hours/day during the acute and febrile illness. Fever: tapid sponging. NO NSAIDS or PARACETAMOL. Hydration: water and ORS. Multivitamins. Antibiotics: NO presumptive or prophylactic antibiotics are needed.

Paracetamol at cumulative dose may cause hepatotoxicity in yellow fever patients. It is advised NOT to give paracetamol at house hold level, due to the potential risk of excessive and uncontrolled paracetamol use in case of fever or pain. Mild yellow fever patients normally have only low grade fever that could be lowered by tapid sponging. Paracetamol is not a life-saving drug and the advantages don't way out the potential harmful effect on the patient.

The majority of the patients presenting mild symptoms will be cured after a few days. However, after a short remission of 2-24 hours (see Table 1) 15-25% of these patients will develop moderate or severe symptoms. The patient, family members and if available Community Health Workers need to be sensitized for alarm signs, indicating that the patient is entering the toxic phase and developing moderate or severe symptoms. In case the patient is presenting one or more of these alarm signs, the patient needs to be taken to the health structure ASAP where immediate access to aggressive and proactive symptomatic case management will increase the chances of survival for the patient. The patient will need to be treated as a moderate or severe yellow fever case depending on the symptoms, (see Chapter 4. Case management of moderate yellow fever cases and Chapter 5. Case management of severe yellow fever cases).

Alarm signs	High temperature (39,0° or above) or chills. Jaundice. Vomiting. Decreasing urine output. Not able to drink or eat. Reduced consciousness or convulsions. No improvement within 5 days after onset of disease. Proteinuria. Bleeding: at skin level (petechiae, purpurae) or at mucosal level (nose bleeding, haematemesis, haematuria, bloody stools, etc.).

4. Case Management of Moderate Yellow Fever Cases

Patients with moderate yellow fever infection need to be hospitalized. They have started with mild symptoms but show now symptoms in between mild and severe potentially fatal disease and entered the toxic phase. Part of the moderate patients will get cured with the below mentioned standard supportive treatment without developing severe symptoms. Fore some other patients, the condition will worsen quickly and patients will become more and more toxic and develop severe symptoms.

Patients with moderate infection need to be given supportive and preventive symptomatic treatment listed below. Close monitoring is needed to be able to react fast with supportive case management in case of deterioration of patient's condition in order to increase patients' survival chances. When patients with moderate infection develop symptoms of severity, they need to be treated as severe yellow fever patient (see next Chapter 5. Case management of severe yellow fever cases).

Symptoms	High fever (39°). Ill looking. Prostration. Congested face and conjunctivae. Mild jaundice. Bradycardia relative to fever.
Mortality	5-10%.
Hospitalization	Isolation. If jaundice, no bed net during daytime needed . Close monitoring: T, pulse rate, blood pressure, peripheral circulation, capillary refill, respiratory rate, 02 saturation, fluid input and output, level of consciousness, signs of severity.

Lab tests	RDT on admission. Check for haemoglobine, neutropenia, leucopenia, thrombocytopenia, electrolytes disorders, hypoglycaemia, elevated transaminases, prolonged PT (bleeding time), blood lactate, urea, creatinine, urine dipstick for proteinuria and haematuria.
Treatment	Fever: tapid sponging in case of fever. NO NSAIDS or Paracetamol Hydration: oral hydration with water and ORS or IV hydration with RL maintenance dose: 2-3 liters of RL/24hrs for adults if no intake. Antibiotics: IV Cephtriaxone. ***Adults:*** 2 gr once daily for 5 days. ***Children:*** 100 mg/kg once daily for 5 days. Ulcer prevention: ***Adults:*** Omeprazol 20 mg PO once daily in the morning, or Ranitidine 300 mg once daily. ***Children:*** Omeprazol 0,4 mg/kg PO once daily in morning. Vitamin K: 10 mg IV/day for 3 days. Glucose measurement: If hypoglycaemic: bolus of glucose. ***Adults:*** 1 ml/kg G50% IV slowly. ***Children:*** 5 ml/kg G10% IV slowly. Multivitamins.
Signs of severity	Vomiting, deep jaundice, hypothermia, bleeding, oliguria/anuria, delerium/convulsions/coma, shock.

5. Case Management of Severe Yellow Fever Cases

Patients with severe yellow fever infection are in the toxic phase, which is lasting 4-8 days. Severe infections often lead to impaired coagulation with bleeding, single or multi-organ failure (kidneys, liver, heart and spleen), hypoglycaemia, hypovolemic shock, secondary bacterial infections, aspiration pneumonia, and cardiac arrhythmia. Treatment recommendations are standard for all severe cases and are based on supportive treatment for the different organ failures and prevention of complications.

Symptoms	Fast deterioration. Fever 39°. Very sick patient. Severe vomiting. Bradycardia relative to fever. Deep jaundice. Congestion of face and conjunctivae.
Mortality	Delirium and coma. Hemorrhagic symptoms: epistaxis,
Hospitalization	haematemesis (explosive vomiting of black vomit), melena, hematuria, gingival bleeding, etc. Oliguria, then anuria caused by kidney failure due to intravascular hypovolemia. 50-80% depending on level of supportive care available. If possible ICU. Isolation. If jaundiced, no bed net needed during day time. Close monitoring: T, pulse rate, peripheral circulation, capillary refill, blood pressure, O2 saturation, respiratory rate, fluid input, output, level of consciousness. If reduced consciousness: elevate head end of patients' bed to 30°. Prevent bed sores by turning patient every 2 hours.

Lab tests	RDT on admission. Check for anemia, neutropenia, leucopenia, thrombocytopenia, electrolytes disorders, hypoglycaemia, elevated transaminases, prolonged PT, blood lactate, urea, creatinine, urine dipstick for proteinuria and haematuria. Perform blood grouping and look for potential blood donors.
Treatment	Fever: tapid sponging. NO NSAIDS or Paracetamol. Hydration: IV hydration, 2-3 liters of RL/G5% continuous per 24hr. See above for preparation. Use Intra-osseous needle when no IV access. Fluid balance: intake, output. Antibiotics: ***Adults:*** Ceftriaxone: IV 2 gr once daily 5 -10 days + Metronidazol IV 500mg 8 hourly 5 – 10 days. ***Children:*** Ceftriaxone 100mg/kg once daily 5-10 days + Metronidazole IV Children 10mg/kg 8 hourly. Glucose measurement: If hypoglycaemic: reactive bolus of glucose. ***Adults:*** 1ml/kg G50% IV slowly. ***Children:*** 5ml/kg G10% IV slowly. Nasogastric tube: Put big bore NG tube to prevent aspiration and gastric distension to allow drainage. Do not perform suction. Vitamin K: 10mg IV/day for 3 days. Metoclopramide: In case of severe non-bloody vomiting. ***Adults:*** 10mg IV every 8 hrs. ***Children:*** 2-5mg IV every 8 hrs. Ulcer prevention: IV Omeprazol. ***Adults:*** 20mg/day once daily. ***Children:*** 0-4mg/kg/day once daily. Oxygen: 2 liters/min with nasal prongs or 5 liters/min with mask.

6. Treatment of Complications of Yellow Fever

6.1 Treatment of severe bleeding

Severe yellow fever patients can start bleeding due to coagulopathy, reduced levels of coagulation factors and DIC. Bleeding is most often from the gastrointestinal tract with sometimes explosive frequent haematemesis. Patients with severe active bleeding need to receive whole blood transfusion to replace lost coagulation factors, to correct Hb levels and can help in correcting hypovolemic shock. The Haemoglobine drop is often delayed in case of active bleeding, so blood transfusion needs to be started regardless of the initial haemoglobine level.

The total amount of blood that needs to be transfused has to replace the estimated total blood loss and the ongoing bleeding. A minor epistaxis doesn't require blood transfusion, but bleeding from several orifices or massive hematemesis or melena requires replacement of the blood volume. As long as there is active bleeding, blood transfusion needs to continue. Drip speed depends on total lost blood volume, signs of shock and bleeding speed.

a. Ensure the screening tests are done for donors.
b. Perform the bedside blood match.
c. Estimate total blood loss volume and blood loss speed.
d. Insert a second IV line for the blood transfusion, preferably with a large lumen canula. The initial IV line will be used for Ringer lactate and as injection site for medication.
e. Do WHOLE blood transfusion.
f. Blood transfusion may be repeated depending on the estimated amount of blood loss, in case of continuous active bleeding and when Haemoglobine < 8 g/dl.
g. No Furosemide should be given during the blood transfusion.

Continous monitoring for bleeding patients, check:

- Haemoglobine level: if < 8g/dl continue to give blood transfusion until Hb > 8 g/dl
- Signs of hypovolemic shock (see below): if in shock, blood

transfusion might help to correct the shock when given at maximum drip speed, together with RL perfusion

- Active bleeding: as long as there is active bleeding, blood transfusion needs to continue. After correction of the initial total blood loss, the drip speed can be adapted to the speed of active continuing blood loss.

6.2 Hypovolemic shock

Patients with severe yellow fever infection are at risk to go into relative hypovolemic shock caused by peripheral vasodilatation and capillary hyperpermeability. As symptoms of shock and hypoglycaemia are quite similar and the risk to develop hypoglycaemia in a yellow fever patient is high, always check for hypoglycaemia.

a. First the patient need to get out of shock by rapid Ringer Lactate infusions, then treatment should be continued by a slower drip speed of 70 ml/kg RL (See Table 2).

If patients start bleeding, blood transfusion can be started simultaneously and can also be used as shock treatment by a maximum flow rate.

Symptoms	Altered consciousness. Lethargy, confusion. Hypotension. Weak, fast pulse. Cold peripheries with poor capillary refill (> 2 sec.).
Treatment	Rapid IV fluids replacement. Check for hypoglycaemia. Place urine catheter (only when there are no bleeding signs). Elevate legs.

b. Remark: In case of shock in yellow fever patients, cristalloids (RL or normal saline) should be used. Colloids should be banned as it may affect blood clotting and evidence of superiority of colloids over cristalloids is lacking in patients with shock.

6.2.1 Perfusion for adults and children in case of signs of shock

- 20 ml/kg in 10-15 min, then reassess, if no improvement repeat 20 ml/kg in 10-15 min (several times if needed) until improvement.
- When out of shock, continue with:
  – 70 ml/kg in 5 hrs for children < 12 months.
  – 70 ml/kg in 2h30 for children > 12 months and adults.

Table 2. Drip speed for shock treatment
Paediatric set = drip speed/min x 3

AGE	WEIGHT	20 ML/KG IN 10-15 MIN		70 ML/KG IN 5 HR	
		TOTAL VOLUME	DRIP SPEED	TOTAL VOLUME	DRIP SPEED
Newborn	3 kg	60 ml	Open	200 ml	1 dr/4 sec
	4 kg	80 ml	Open	280 ml	1 dr/4 sec
	5 kg	100 ml	Open	350 ml	1 dr/3 sec
6 months	6 kg	120 ml	Open	400 ml	1 dr/2 sec
	7 kg	140 ml	Open	500 ml	1 dr/2 sec
9 months	8 kg	160 ml	Open	560 ml	1 dr/2 sec
1 year	9 kg	180 ml	Open	630 ml	1 drops/sec
	10 kg	200 ml	Open	700 ml	1 drops/sec
	11 kg	220 ml	Open	770 ml	2 drops/sec
2 years	12 kg	240 ml	Open	840 ml	2 drops/sec
	13 kg	260 ml	Open	910 ml	2 drops/sec
	14 kg	280 ml	Open	980 ml	2 drops/sec
5 years	15 kg	300 ml	Open	1050 ml	2 drops/sec
	16 kg	320 ml	Open	1120 ml	3 drops/sec
	17 kg	340 ml	Open	1190 ml	3 drops/sec
	18 kg	360 ml	Open	1260 ml	3 drops/sec
	19 kg	380 ml	Open	1330 ml	3 drops/sec
9 years	20 kg	400 ml	Open	1400 ml	3 drops/sec
	21 kg	420 ml	Open	1470 ml	3 drops/sec
	22 kg	440 ml	Open	1540 ml	3 drops/sec
	23 kg	460 ml	Open	1610 ml	4 drops/sec
	24 kg	480 ml	Open	1680 ml	4 drops/sec
	25 kg	500 ml	Open	1750 ml	4 drops/sec
15 years	30 kg	600 ml	Open	2100 ml	4 drops/sec
Adult	40 kg	800 ml	Open	2800 ml	4 drops/sec
	60 kg	1200 ml	Open	4200 ml	4 drops/sec

6.3 Convulsions

6.3.1 Treatable causes in case of suspected yellow fever patients

- Hypoglycaemia.
- Hyperthermia.

6.3.2 Symptomatic treatment

- Check glucose level and treat if hypoglycaemic with glucose 50% booster.
  Adult: 1 ml/kg G50% IV slowly.
  Children: 5 ml/kg G10% IV slowly.
- Tapid sponging if febrile.
- If no improvement: Diazepam.
  Reduce the recommended standard dose by half.
  Adult: 5 mg rectally or by slow IV.
  Children: 0,3 mg/kg rectally or 0,2 mg/kg by slow IV.

6.4 Acute liver failure

6.4.1 Signs

- Encephalopathy: lethargy, delirium, psychiatric symptoms, ataxia, tremor, incontinence.
- Hypoglycaemia.
- Bleeding.
- Flapping tremor.

6.4.2 Symptomatic treatment

- Prevent hypotension and hypoglycaemia by providing a continous RL/G5% drip (maintenance dose) and give reactive glucose 50% boluses.
- Put nasogastric tube to prevent aspiration.
- Avoid central nervous system depressant drugs.
- Reduce protein intake to 0,5 to 0,7 g/kg/day during the first 10 days after failure onset to avoid the high ammonia levels.
- Avoid light and noise for patients with hepatic encephalopathy. Environment should be quiet with minimal sensory stimulation.
- In case of liver encephalopathy: give lactulose 30 ml per os or per nasogastric tube 2 or 3 times per day for adults.

6.5 Renal failure

6.5.1 Signs

- Oliguria (< 15 ml urine/hr or < 500 ml/24 hr) or anuria.
- Confusion.
- Hyperkaliemie (cardiac arytthmia).

- Glucose level fluctuations.
- Metabolic acidosis (hyperventilation).
- Raised urea and creatinine.

6.5.2 Symptomatic treatment

- Avoidance of hypotension : continuous IV fluids (maintenance dose).
- After ensuring good volaemia (including good peripheral circulation and capillary refill < 2 sec.) and no improvement in urine output: Furosemide.
  Adults and children: 0,5-1 mg/kg/injection.
- Close follow up of urinary output. Urine catheter can be placed for monitoring if no bleeding.

6.6 Hypokalemia

6.6.1 Signs

- Muscle cramps.
- Severe abdominal distension (meteorism).
- Respiratory distress.
- Irregular pulse.
- Palpitations.

6.6.2 Treatment

- ORS if able to take orally.
- Potassium IV.
  Adult: 3 ampoules of 10 % KCl (equivalent to 40 mmol or 3 gram) in a litre of RL and give over 4 hours. The infusion can be repeated once during the day, if necessary (do not give more than 6 gram/day).
  Children: 0,5 ml/kg of 10 % KCl (equivalent to 0,67 mmol/kg or 50 mg/kg) mixed in 10 ml/kg of RL, give over 4 hours. The infusion can be repeated once during the day, if necessary (do not give more than 1 ml/kg/day).

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