Malaria

Permission received from Partners In Health

Image retrieved from http://upload.wikimedia.org/wikipedia/commons/a/ae/Anopheles_albimanus_mosquito.jpg on Sep 1, 2012. Image is in the public domain.

Patrick Lee, MD, DTM&H

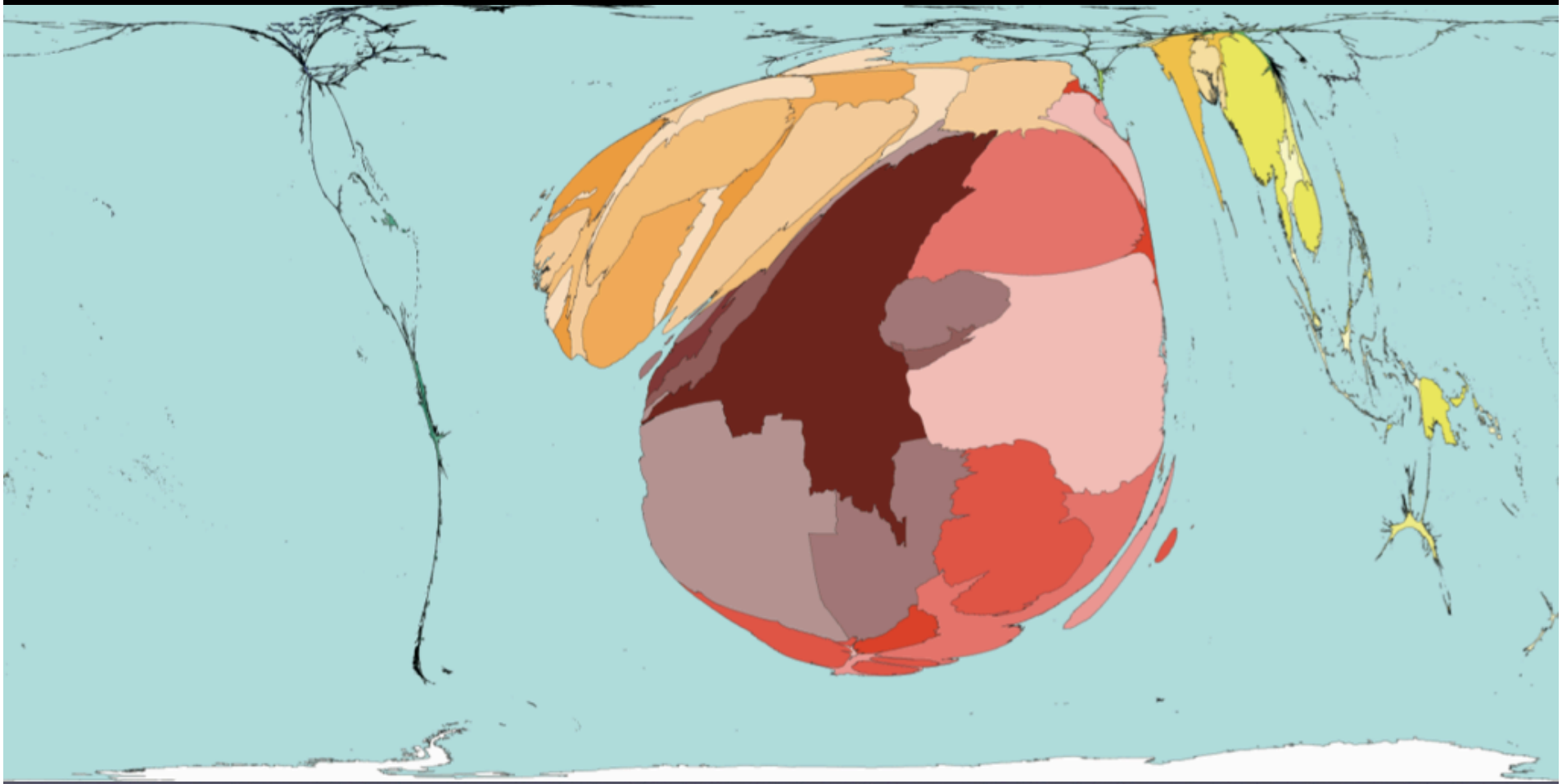
Clinical Topics in Global Health

March 1, 2012

Overview

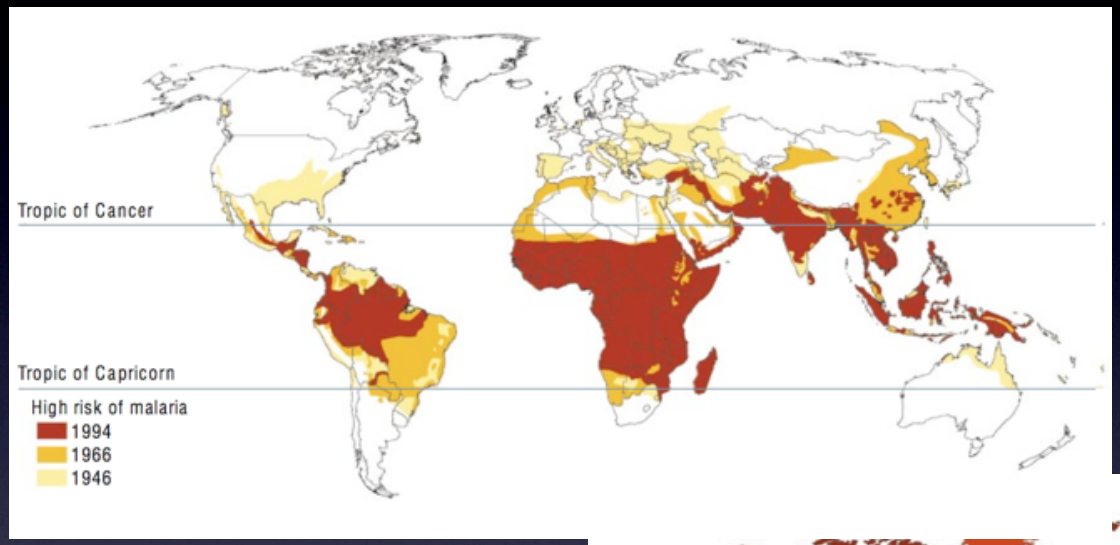
- Malaria – what's the big deal?
- Why is malaria so tenacious in Africa?
- What determines uncomplicated vs severe malaria?
- How do we diagnose malaria?
- How do we manage uncomplicated malaria?
- What about severe malaria?

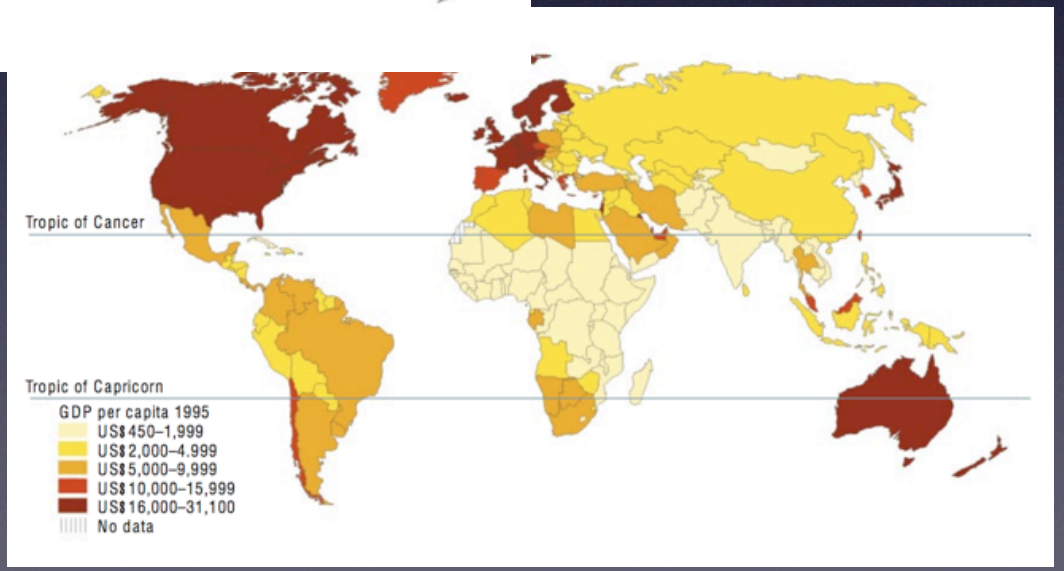
Malaria Deaths



A child dies from malaria every 30 seconds

Malaria, historically





Images retrieved from: http://www.nature.com/nature/journal/v415/n6872/full/415680a.html on July 1, 2012. Permission received from Nature.

Understanding the enemy

Image retrieved from http://upload.wikimedia.org/wikipedia/commons/a/ae/Anopheles_albimanus_mosquito.jpg on Sep 1, 2012. Image is in the public domain.

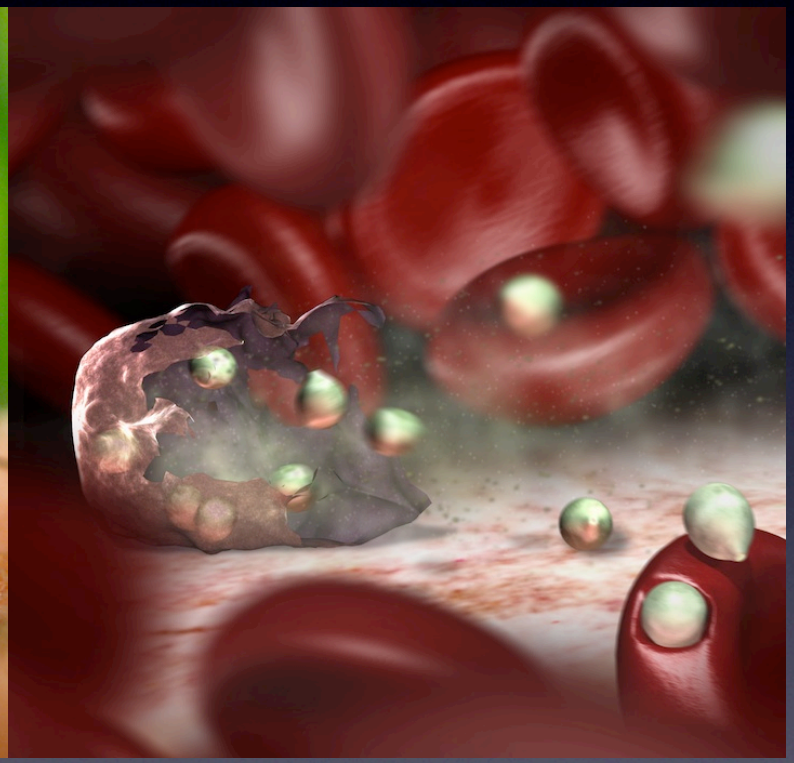


Image retrieved from http://www.abc.net.au/science/news/img/health/malaria_attack.jpg on Sept 1, 2012. Permission received from Drew Berry, The Walter and Eliza Hall Institute

Images retrieved from Sattler et al. *Malaria Journal* 2005 4:4 http://www.malariajournal.com/content/4/1/4 on Sept 1, 2012. Images are open access.

Photos by Patrick Lee. No permission needed.

On to the clinical...

Uncomplicated malaria

- Definition = symptomatic without organ dysfunction
- Occurs in semi-immune populations in endemic areas
- Non-specific febrile illness – can be associated with headache, nausea/vomiting, body aches, fatigue/malaise
- In an endemic area, any febrile illness should be considered as possible malaria

Severe malaria

- End-organ dysfunction, 15-20% mortality
- Generally occurs in non-immune populations
- WHO practical classification:
  - Neurological impairment (coma or prostration – inability to sit up or feed/drink)
  - Respiratory distress
  - Convulsions
  - Hgb < 5 g/dL
  - Persistent vomiting

What determines uncomplicated vs severe malaria?

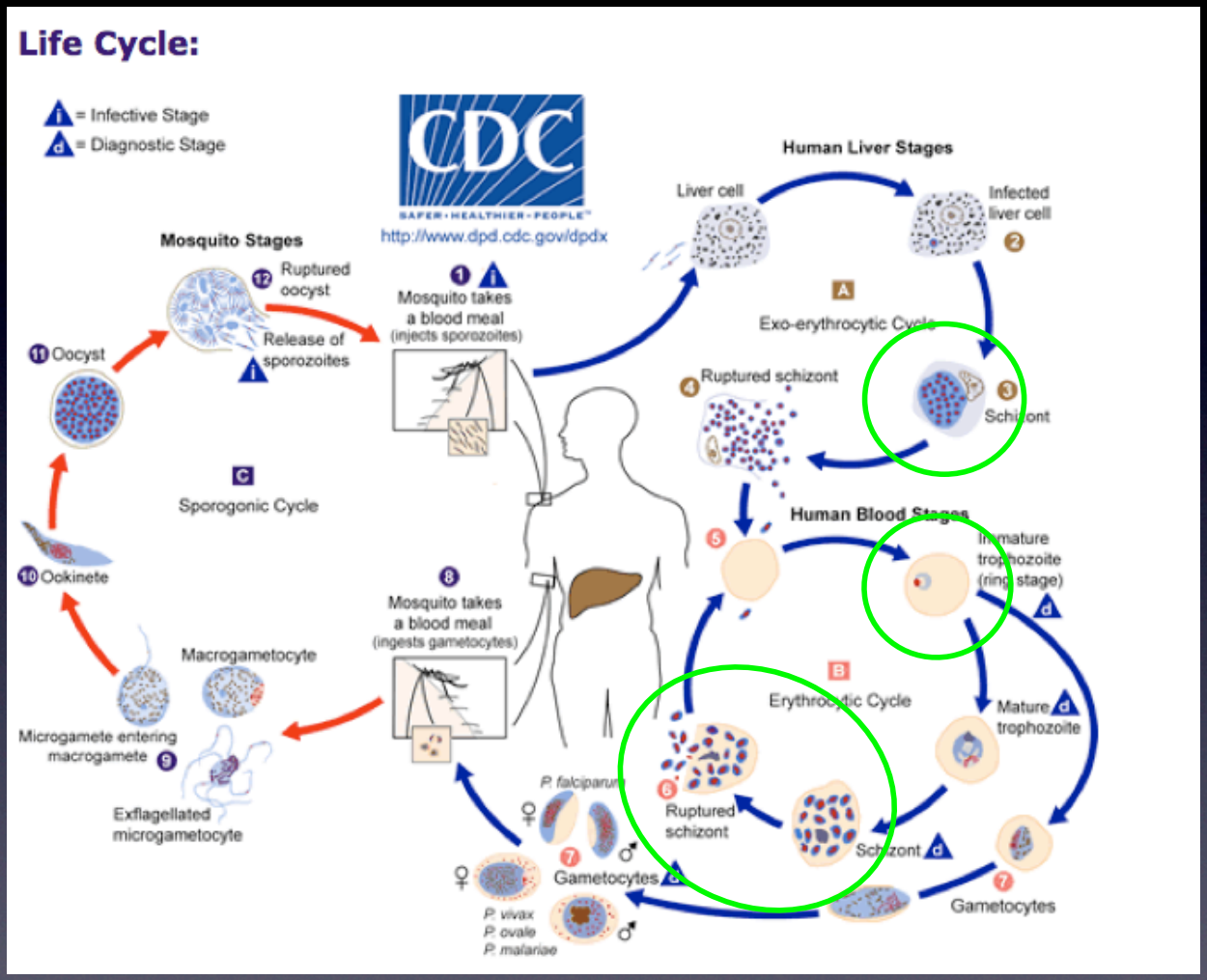


Image retrieved from http://www.cdc.gov/malaria/about/biology/index.html on July 1, 2012. Image is in the public domain.

How do we diagnose malaria?

MALARIA DIAGNOSIS

- Prompt parasitological confirmation by microscopy or alternatively by RDTs is recommended in all patients suspected of malaria before treatment is started.
- Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible.

WHO Malaria Treatment Guidelines, 2010

Uncomplicated malaria – clinical diagnosis

- Use confirmatory dx whenever possible
- In some settings, resource limitations / time constraints may make parasitological dx impractical
- Use pretest probability to help
- If risk is low, use degree of exposure, h/o fever in past 3 days, no other features of severe disease
- If risk is high, use fever in previous 24hrs and/or presence of anemia (esp pallor of palms in children)

Uncomplicated malaria – confirmatory diagnosis

- Preferred to clinical dx whenever possible
- 2 options:
  - Light microscopy
  - Rapid diagnostic tests (RDTs)

Light microscopy

- Low cost
- High sensitivity / specificity when staff are appropriately trained
- Requires trained technologist and ongoing quality assurance
- May be more cost-effective where case load is high

Photo by Patrick Lee. No permission needed.

Rapid diagnostic tests

- Easy to use (can train community health workers)
- More expensive (though prices are coming down)
- Variable sensitivity/specificity
- Vulnerable to high temperatures and humidity

How do we manage uncomplicated malaria?

"Much of the world's symptomatic malaria is treated in peripheral health centers or remote villages, where facilities are limited. The aim is therefore to provide simple and straightforward treatment recommendations based on sound evidence that can be applied effectively in most settings."

– WHO Malaria Treatment Guidelines, 2006

Uncomplicated malaria – treatment

- Objective – cure the infection (prevent progression, prevent transmission)
- Secondary goal – reduce resistance
- Artemesinin – clears parasites very rapidly (10,000-fold per asexual cycle); effective against all 4 species of malaria
- Control fevers

Uncomplicated malaria – treatment

TREATMENT OF UNCOMPLICATED *P. FALCIPARUM* MALARIA

- Artemisinin-based combination therapies (ACTs) are the recommended treatments for uncomplicated *P. falciparum* malaria.
- The following ACTs are recommended:
  - artemether plus lumefantrine, artesunate plus amodiaquine, artesunate plus mefloquine, and artesunate plus sulfadoxine-pyrimethamine.
- The choice of ACT in a country or region will be based on the level of resistance of the partner medicine in the combination.
- Artemisinin and its derivatives should not be used as monotherapy.
- Second-line antimalarial treatment:
  - alternative ACT known to be effective in the region;
  - artesunate plus tetracycline or doxycycline or clindamycin; any of these combinations to be given for 7 days;
  - quinine plus tetracycline or doxycycline or clindamycin; any of these combinations should be given for 7 days.

WHO Malaria Treatment Guidelines, 2010

What about pregnant women?

Summary of recommendations on the treatment of uncomplicated falciparum malaria in pregnancy

RECOMMENDATIONS	LEVEL OF EVIDENCE
First trimester: quinine + clindamycin[a] to be given for 7 days. ACT should be used if it is the only effective treatment available.	O, E
Second and third trimesters: ACT known to be effective in the country/region or artesunate + clindamycin to be given for 7 days or quinine + clindamycin to be given for 7 days.	O, E

[a] If clindamycin is unavailable or unaffordable, then the monotherapy should be given.

What about young children?

Summary of recommendations on treatment of uncomplicated falciparum malaria in infants and young children

RECOMMENDATIONS	LEVEL OF EVIDENCE
The acutely ill child requires careful clinical monitoring as they may deteriorate rapidly.	E
ACTs should be used as first-line treatment for infants and young children.	T, O, E
Referral to a health centre or hospital is indicated for young children who cannot swallow antimalarials reliably.	E

"Ultimately, effective treatment needs to be available at the community or household level in such a way that there is no financial or physical barrier to access."

– WHO Malaria Treatment Guidelines, 2006

Severe malaria

- End-organ dysfunction, 15-20% mortality
- Generally occurs in non-immune populations
- WHO practical classification:
  - Neurological impairment (coma or prostration – inability to sit up or feed/drink)
  - Respiratory distress
  - Convulsions
  - Hgb < 5 g/dL
  - Persistent vomiting

TREATMENT OF SEVERE MALARIA

- Severe malaria is a medical emergency. After rapid clinical assessment and confirmation of the diagnosis, full doses of parenteral antimalarial treatment should be started without delay with whichever effective antimalarial is first available.
- For adults, artesunate IV or IM:
  - quinine is an acceptable alternative if parenteral artesunate is not available.
- For children (especially in the malaria endemic areas of Africa) the following antimalarial medicines are recommended as there is insufficient evidence to recommend any of these antimalarial medicines over another:
  - artesunate IV or IM;
  - quinine (IV infusion or divided IM injection);
  - artemether IM (should only be used if none of the alternatives are available as its absorption may be erratic).
- Give parenteral antimalarials in the treatment of severe malaria for a minimum of 24 h, once started (irrespective of the patient's ability to tolerate oral medication earlier) and, thereafter, complete treatment by giving a complete course of:
  - an ACT;
  - artesunate plus clindamycin or doxycycline;
  - quinine plus clindamycin or doxycycline.
- If complete treatment of severe malaria is not possible, patients should be given pre-referral treatment and referred immediately to an appropriate facility for further treatment. The following are options for pre-referral treatment : rectal artesunate, quinine IM, artesunate IM, artemether IM.

WHO Malaria Treatment Guidelines, 2010

Cerebral malaria

- Common in children and adults with severe malaria; 10-30% case fatality
- Up to 80% of children with coma suffer from seizures at some point
- Coma may result from hypoglycemia, seizures, or directly from severe malaria (sequestration?)

Severe anemia

- Hgb <5 in children or <7 in pregnant women
- Presents with fever / pallor / weakness / breathlessness
- Results from direct destruction of infected RBCs *and* destruction of non-infected RBCs in spleen and liver
- In absence of other signs of severe malaria, carries a relatively good prognosis

Table 7. Immediate clinical management of severe manifestations and complications of falciparum malaria

Manifestation/complication	Immediate management[a]
Coma (cerebral malaria)	Maintain airway, place patient on his or her side, exclude other treatable causes of coma (e.g. hypoglycaemia, bacterial meningitis); avoid harmful ancillary treatment such as corticosteroids, heparin and adrenaline; intubate if necessary.
Hyperpyrexia	Administer tepid sponging, fanning, cooling blanket and antipyretic drugs.
Convulsions	Maintain airways; treat promptly with intravenous or rectal diazepam or intramuscular paraldehyde.
Hypoglycaemia (blood glucose concentration of <2.2 mmol/l; <40 mg/100ml)	Check blood glucose, correct hypoglycaemia and maintain with glucose-containing infusion.
Severe anaemia (haemoglobin <5 g/100ml or packed cell volume <15%)	Transfuse with screened fresh whole blood

Table 7. Immediate clinical management of severe manifestations and complications of falciparum malaria

Acute pulmonary oedema[b]	Prop patient up at an angle of 45°, give oxygen, give a diuretic, stop intravenous fluids, intubate and add positive end-expiratory pressure/continuous positive airway pressure in life-threatening hypoxaemia.
Acute renal failure	Exclude pre-renal causes, check fluid balance and urinary sodium; if in established renal failure add haemofiltration or haemodialysis, or if unavailable, peritoneal dialysis. The benefits of diuretics/dopamine in acute renal failure are not proven.
Spontaneous bleeding and coagulopathy	Transfuse with screened fresh whole blood (cryoprecipitate, fresh frozen plasma and platelets if available); give vitamin K injection.
Metabolic acidosis	Exclude or treat hypoglycaemia, hypovolaemia and septicaemia. If severe add haemofiltration or haemodialysis.
Shock	Suspect septicaemia, take blood for cultures; give parenteral antimicrobials, correct haemodynamic disturbances.

Thank you!