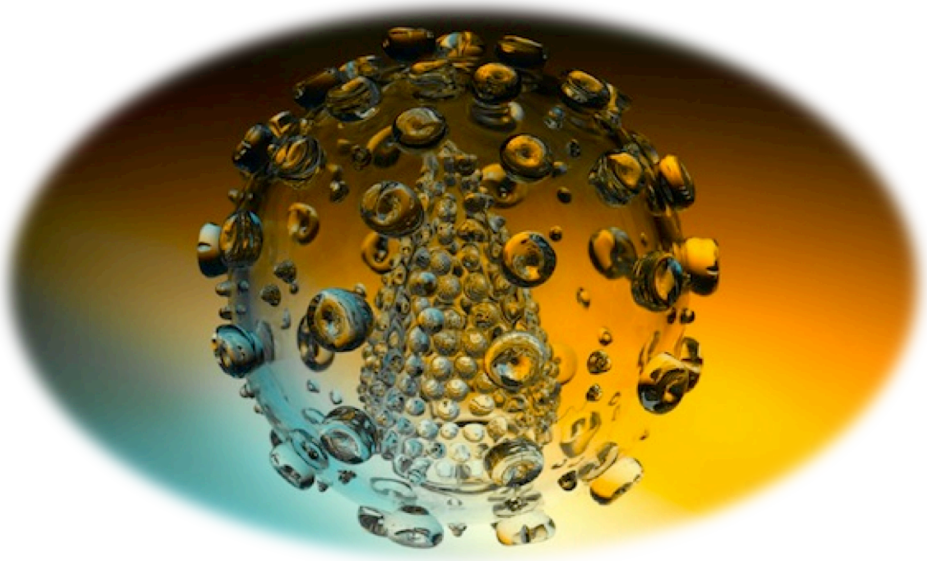
431
Microbiology Team

CNS BLOCK



Cerebral Malaria

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Species of malaria:

1. *Plasmodium falciparum:* malignant tertian malaria (most dangerous)
2. *Plasmodium vivax:* benign tertian malaria
3. *Plasmodium ovale:* benign tertian malaria
4. *Plasmodium malariae:* quartan malaria

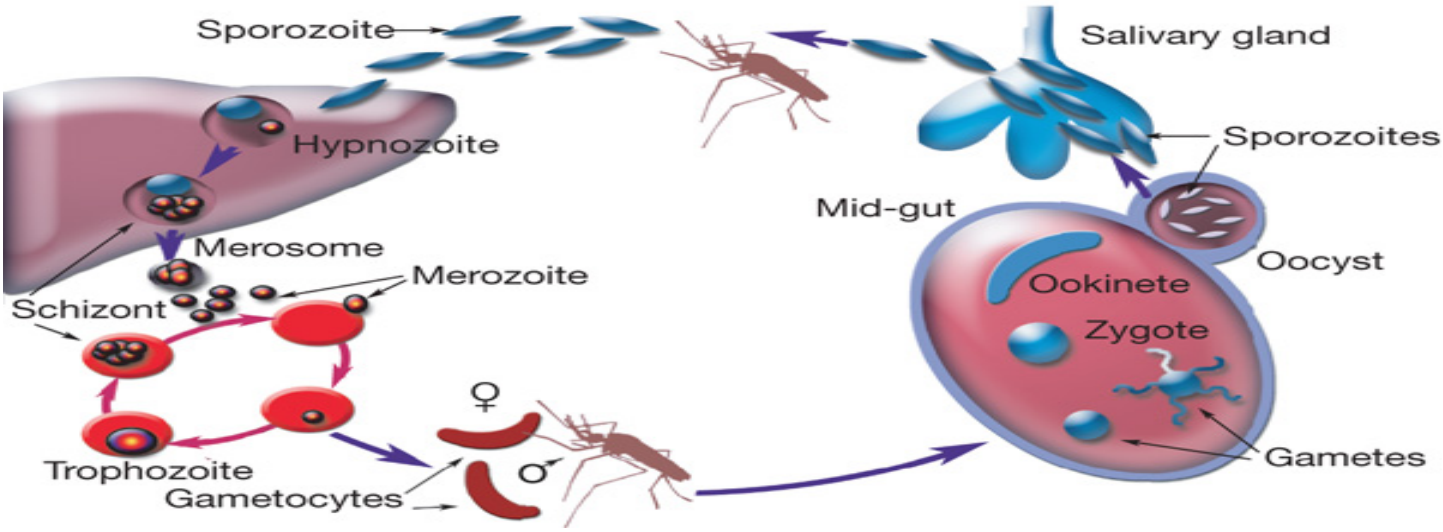
Tertian: occurs every 48 hours (every other day)

Quartan: occurs every 72 hours

Quatidian: Occurs everyday

Malaria life cycle:

- Mainly transmitted by mosquitos → Sporozoites are injected and travel to the liver → they are released and invade red blood cells
- Pathogenicity occurs due to involvement of **red blood cells**



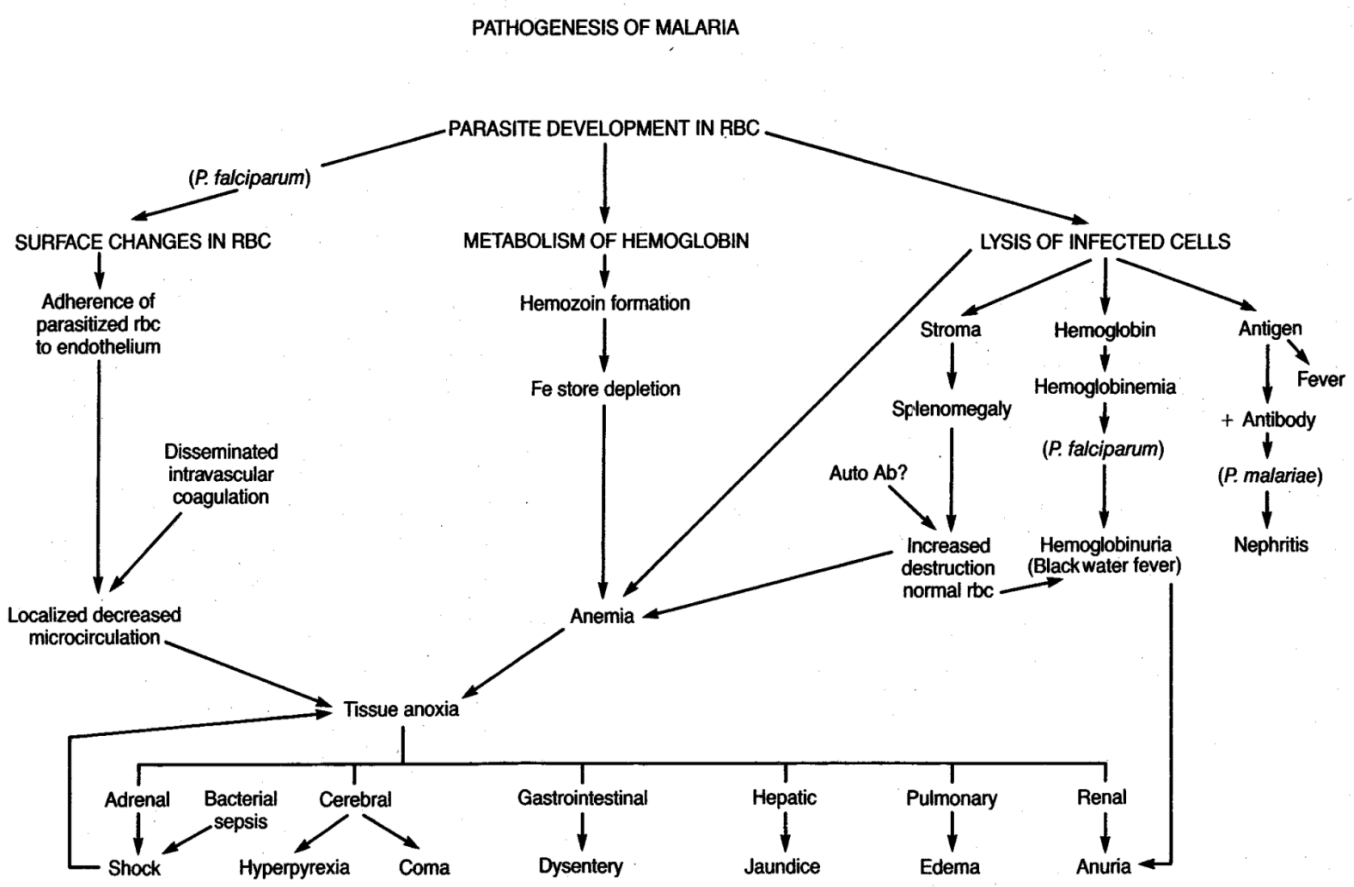
Malarial Paroxysms:

Clinical stages	*Plasmodium falciparum*	*Plasmodium vivax* ---------- *Plasmodium ovale*	*Plasmodium malariae*
Periodicity	Quotidian, tertian, irregular	48 hours, tertian	72 hours, quartan
Cold stage	• Feeling of intense cold • Vigorous shivering • Lasts 15-60 minutes		
Hot stage	• Intense heat • Dry burning skin • Throbbing headache • Lasts 2-6 hours		
Sweating stage	• Profuse sweating • Declining temperature • Exhausted and weak → sleep • Lasts 2-4 hours		

Pathogenesis of Malaria:

Due to two mechanisms:

- Anemia (due to lysis of RBC and metabolism of hB)
- Impairment of microcirculation (affect all organs):
  Due to abnormal surface of RBC it adheres to the endothelial surface of the blood capillaries which results in impairment of microcirculation



Uncomplicated Malaria:

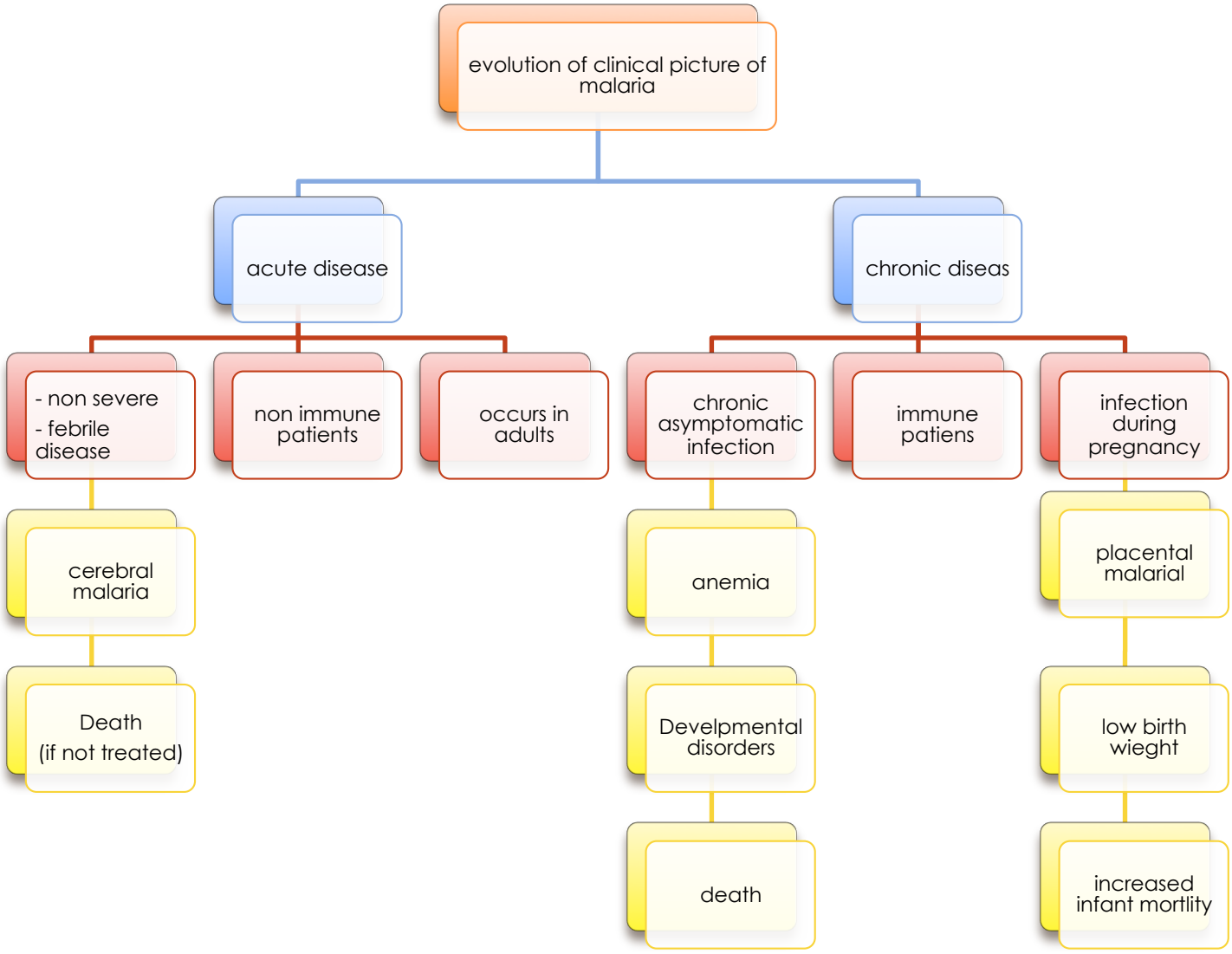
Symptomatic infection with malaria parasitemia **without** signs of severity or evidence of vital organ dysfunction

* Mostly fever attacks

Complicated (Severe) Malaria:

Symptomatic malaria in patients with ***P. falciparum* asexual parasitaemia** with one or more of the following complications:

- **Cerebral malaria** (unrousable coma, not caused by other issues) Most series
- **Generalized convulsions** (more than 2 episodes within 24 hours)
- Severe normocytic anemia
- **Hypoglycemia** Very common
- Metabolic acidosis with respiratory distress
- Fluid and electrolyte disturbances
- **Acute renal failure** *(urine <400 ml/24 h in adults; 12 ml/kg/24 h in children)*
- **Acute pulmonary edema** and adult respiratory distress syndrome
- Abnormal bleeding
- Jaundice
- Hemoglobinuria
- Circulatory collapse, shock, septicemia (algid malaria)
- **Hyperparasitaemia** *≥10% in non-immune; ≥20% in semi-immune (Semi-immune is a patient that lives in an area where P. falciparum is widely spread)*



Notes*

Acute disease: the patient never got affected before. Example: in areas where there is no transmission of the disease

Chronic disease: the patient had recurrent attacks of malaria. Example: endemic areas as in Africa

An immune person can transfer the disease to a non-immune person via transfusions. When an immune person comes to an area where there is no infection and donates blood and a recipient who has never gotten malaria is transfused with that blood immediately gets infected

Clinical signs of severe malaria

prostration	•inabitlity to sit unassistid in a child normal able to do so •in infants inability to breast feed
impaired consciousness	•based on blantyre coma scale (<2 cerebral malaria) •coma may be difficult to distinguish from imparied consciousnes following convulsions
respiratory distress	•deep breathing with increased chest amplitude excrusion •tachypnea •in severe cases decreased rate of breathing
high fever	•increase convulsions and coma •abnormal bleeding •jaundice and pulmonary edema (more common inadults than children

Clinical triage:

If you see a child:

1. Fitting (having a convulsion)
2. Is prostrated
3. Has respiratory distress

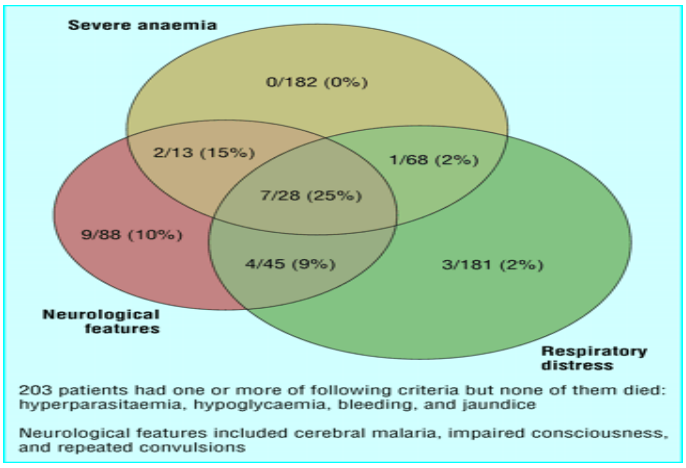
They MUST be brought to the top of the queue for immediate assessment and treatment

Causes of death in severe malaria

Immune patients - Children (Areas of high transmission)	**Non-Immune patients - Adults (Areas of low transmission)**
Cerebral malaria	Cerebral Malaria
Malarial Anemia	Acute renal insufficiency
Metabolic acidosis	Pulmonary edema
	Disseminated intravascular coagulation

Note*

Mortality rate increase with if there is more than one or more of the clinical syndromes present in the patient

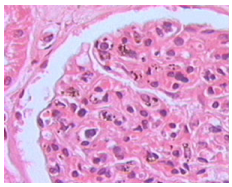


Clinical Syndromes in Severe malaria:

- **Anemia:** Due to:

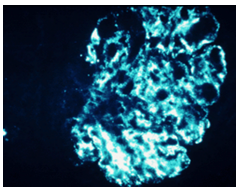
1- Increased destruction of normal erythrocytes by erthro-phagocytosis (particularly in the spleen)
2- Impaired production of new erythrocytes in the bone marrow

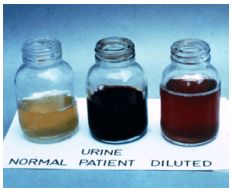
- **Acute renal insufficiency:**



Proteinuria:

1- Found in 20% of the cases
2- Acute glomerulonephritis is usually transient and disappears after antimalarial treatment and appropriate fluid replacement
3- Some patients may progress to acute renal failure (by acute tubular necrosis)
4- Proteinuria and acute glomerulonephritis is due to sequestration of parasites in the glomerulus
5- Immunofluorescent evidence of immune complex deposition in quartan malarial nephropathy
6- **Black water fever**: is a combination of severe intravascular hemolysis, hemoglobinuria, and renal failure.





Cerebral Malaria

Definition:

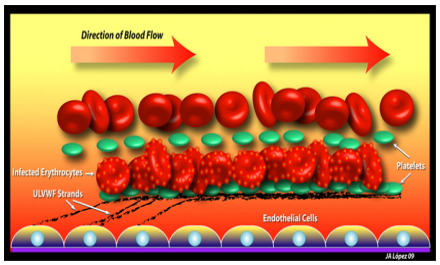
- Severe falciparum malaria with coma (persisting for more than 30 minutes) after a seizure is considered to be cerebral malaria.
- After other etiologies have been excluded (febrile convulsions, hypoglycemia, sedative drugs, viral, bacterial or fungal meningoencephalopathies and septicemia)

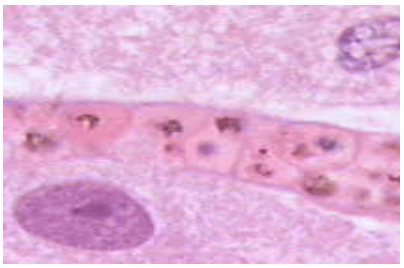
Note* with the case of febrile convulsions patients could lose consciousness for less time

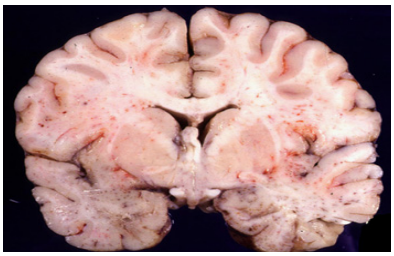
Blantyre Coma scale is to be read for information only (added on last page)

Pathogenesis:

- Affected RBC adhere to endothelial lining due to their surface changes so they cause blood flow blockage
- Small hemorrhages (petechial hemorrhages) in the capillaries







Clinical picture:

- Increased intracranial pressure in majority of children (contributes to fatal outcome)
- Hypoglycemia (presenting feature, less common in adults)
- Main clinical presentation is in the muscle tone:
  - Either flaccid "**broken neck syndrome**"
  - Hypertonic "**opisthotonus**" (resembling tetanus)
- Grinding of the teeth "bruxism"
- Convulsions before or after the onset of coma
- Disconjugate gaze (optic axes are not parallel in vertical and horizontal planes)
- Decerberate rigidity (lost cerebral function) due to complication by hypoglycemia
- Retinal hemorrhage

It is important to exclude other conditions with similar features:

- Hypoglycemia: important to detect in child with impaired consciousness
- Meningitis: Lumbar puncture to exclude meningitis.
  - Concurent bacterial meningitis was found in 4% of children with cerebral malaria
  - If lumbar puncture not possible patient **should be treated for meningitis**

Treatment

General Management of cerebral malaria:

There should be extensive nursing care

- Insert a urethral catheter
- Insert a nasogastric tube and aspirate stomach contents
- Keep an accurate record of fluid intake and output
- Monitor level of consciousness
- Treat convulsions using either **Diazepam** or **Paraldehyde**

*adjunctive management on the last page (for information only)

Consciousness	***Impaired consciousness***	***No impaired consciousness***
	Supportive Care	Treatment of complications
Drug route	Parentrally	Orally (if possible)
Anti-Malarial Drugs	Artemether Artesunate (Drug of choice) Quinine	

Evolution of cerebral malaria

- Cerebral Malaria carries mortality around 20% in adults and 15% in children.
- Residual deficits are unusual in adults (<3%).
- About 10% of the children (particularly those with recurrent hypoglycemia, severe anemia, repeated seizures and deep coma), who survive cerebral malaria may have persistent neurological deficits.

Summary:

- Pathogenicity occurs due to involvement of RBCs

- if we cant exclude meningitis using lumbar puncture, we start treament for both

- Clinical signs of severe malaria: Prostration, impaired consciousness, respiratory distress, high fever.

- P. Falciparum is the most infectious because it affects RBCs of all ages (mentioned by the doctor)

- Most common complication and cause of death in malaria is **cerebral malaria**

- CSF in malaria is clear (unlike meningitis)

Species:

1. ***Plasmodium falciparum***: malignant tertian malaria (most dangerous)
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Tertian: occurs every 48 hours (every other day)

Quartan: occurs every 72 hours

Quatidian: Occurs everyday

Pathogenisis:

- Anemia
- Impairment of microcirculation

Complicated (Severe) Malaria symptomes:

- Cerebral malaria Most series
- Generalized convulsions
- Hypoglycemia Very common
- Acute renal failure
- Acute pulmonary edema
- Hyperparasitaemia

Cerebral Malaria symptomes:

- Increased intracranial pressure in majority of children
- Hypoglycemia (presenting feature, less common in adults)
- Disconjugate gaze
- Decerberate rigidity
- Opisthotonus (tetanus like hyper-extension)

Cerebral Malaria mangment:

- We exclude any other possible illnesses first (**hypoglycemia and meningitis**)
- Treatment using anti-malarial drugs
- General managemnt: insert a urethral catheter, monitor consciousness, treat convulsions

Questions:

1- Most pathogenic parasite is:

A. Plasmodium falciparum
B. Plasmodium vivax
C. Plasmodium ovale
D. Plasmodium malariae

2- A patient comes to the hospital with a fever recurring every 72 hours (3 days). Which of the following is the most likely pathogen?:

A. Plasmodium ovale
B. Plasmodium malariae
C. Plasmodium falciparum
D. Plasmodium vivax

3- A patient presents with opisthotonus and a deconjugate gaze. Which of the following is the most effective drug:

A. Diazepam
B. Artesunate
C. Amoxicillin
D. Gentamicin

Answers: -

1- (A)
2- (B)
3- (B)

Adjunctive Treatment (for informative purposes)

Manifestation/complication	Immediate management
Coma (cerebral malaria)	Maintain airway, nurse on side, excluded other treatable causes of coma, (e.g. hypoglycaemia, bacterial meningitis); avoid harmful ancillary treatment such as corticosteroids, heparin and adrenaline, intubate if necessary
Hyperpyrexia	Tepid sponging, fanning, cooling blanket and antipyretic drugs
Convulsions	Maintain airways; treat promptly with diazepam or paraldehyde
Hypoglycaemia (Blood glucose <2.2 mmol/l, or < 40 mg/dl)	Measure blood glucose, correct hypoglycaemia and maintain with glucose containing infusion
Severe anaemia (Hb <5g%, or PCV <15%)	Transfuse with screened fresh whole blood or packed cells
Acute pulmonary oedema	Prop up at 45o, give oxygen, give diuretic, stop intravenous fluids, intubate and add positive pressure ventilation in life threatening hypoxaemia; haemofilter.
Acute renal failure	Exclude pre-renal causes, check fluid balance, urinary sodium; if in established renal failure; haemofilter or haemodialysis or peritoneal dialysis. Benefits of diuretics/dopamine in ARF are not proven.
Spontaneous bleeding and coagulopathy	Transfused screened fresh whole blood (cryoprecipitate, /fresh frozen plasma and platelets if available; vitamin K injection
Metabolic acidosis	Exclude or treat hypoglycaemia, hypovolaemia and septicaemia
Shock	Suspect gram negative septicaemia, make blood cultures; give parenteral antimicrobials, correct haemodynamic disturbances.
Hyperparasitaemia (e.g. >10% of circulating erythrocytes parasitized)	Monitor closely for the first 48 hours after starting treatment; start total or partial exchange transfusions

Blantyre Scale (for informative purposes)

BLANTYRE COMA SCALE

	Score
a) Best Motor Response	
• Localizes painful stimulus [a]	2
• Withdraws limb from pain [b]	1
• Non-specific or absent response	0
b) Verbal response	
• Appropriate cry	2
• Moan or inappropriate cry	1
• None	0
c) Eye movements	
• Directed (follows mother's face)	1
• Not directed	0

A state of unrousable coma is reached at a score of < 3
This scale can be used repeatedly to assess improvement or deterioration.
a Rub knuckles on patient's sternum.