Update in Anaesthesia

The child with malaria

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Summary

Malaria is a multi-system disease that can coexist with other infections and conditions, including those that may require surgery. Intensive care may be necessary.

Malaria can vary from an insidious febrile illness to an acute life-threatening disease. Rapid deterioration is much more likely in children. If malaria is suspected, it should be investigated rapidly and treated appropriately. WHO and national diagnostic and treatment guidelines should be followed. Children should be observed closely for the development of complications. Anaesthesia and surgery should be avoided in the child with malaria if at all possible, but, if it is necessary, the multi-system nature of the disease should be considered.

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MALARIA: CAUSE, TRANSMISSION & EPIDEMIOLOGY

Malaria is a life-threatening disease caused by four protozoan parasite species of the genus *Plasmodium* infecting humans: *P. falciparum, P. vivax, P. ovale,* and *P. malariae.* Co-infection with more than one species is possible. A 5th species *P. knowlesi*, which primarily affects primates, has also recently been found to infect humans. *P. falciparum* is the most deadly species, and *P. falciparum* and *P. vivax* the most common. *P. vivax* and *P. ovale* both lead to a dormant liver form (hypnozoites) that may cause relapses months or years later.

The parasites are transmitted through the bite of a vector, the infected female *Anopheles* mosquito. There are around 20 *Anopheles* species across the world. The intensity of malaria transmission depends on factors relating to the parasite, vector, host and environment. Mosquitoes exhibit different breeding and biting preferences, with the important vectors tending to bite at night. High humidity and warmer temperatures (between 20°C and 30°C) favour transmission of malaria due to increase in mosquito numbers. Consequently, the disease is often seasonal, relating to rainfall patterns. Some areas, with constant temperatures and humidity, have steady parasite rates. Climate changes may lead to alterations in the pattern of disease.

40% of the global population reside in malaria endemic areas. Most cases of malaria are found in sub-Saharan Africa, Asia and Latin America; a few cases occur in the Middle East and in some areas of Europe. Increased international air travel has also introduced malaria into malaria free zones, resulting in disease misdiagnosis. *The World Malaria Report 2011* estimated 216 (uncertainty range of 149-274) million cases of malaria with 655,000 deaths (uncertainty range 537-907,000). 80% of the deaths occur in African children, most of them being in the under five age range. Since 2000, deaths from malaria have been reduced by >25 % globally, and by 33% in Africa.

Partial immunity to the disease can develop over years of exposure; consequently the majority of deaths occur in children. The risk is greater across all ages when natural immunity is reduced:

- Limited previous exposure
- Pregnancy
- Severe concomitant illness
- Surgery.

Malaria in pregnancy affects both the mother and the foetus, which can lead to loss of the pregnancy or low birth weight.

Infants can be protected by maternal antibodies and by foetal haemoglobin, up to around 6 months of age. A behavioural tendency to cover infants may also be protective. Some inherited abnormalities of red cells can be protective against malaria, for instance, the sickle cell trait and Melanesian ovalocytosis, a genetic polymorphism associated with mild haemolytic anaemia, common in South East Asia.

Malaria is both preventable and curable. Where prevention and control measures have been applied aggressively, the malaria burden has been effectively reduced.

PREVENTION

Methods used to avoid disease transmission include prevention of mosquito bites using the following:

- Insecticide treated nets (ITNs)
- Use of mosquito repellents
- Indoor residual spraying with insecticides
- Maximum coverage clothing
- Reduction of mosquito breeding grounds by drainage of stagnant water and clearing of bushes.

Chemoprophylaxis is required for

- High-risk populations, such as travellers to malaria endemic regions
- Intermittent preventive treatment in pregnancy
- Infants in high transmission areas (infants receive 3 doses of sulfadoxine –pyrimethamine alongside routine vaccines).

Seasonal malaria chemoprevention was recommended in 2012 by the World Health Organisation (WHO) in areas of the Sahel sub-region of Africa.

Vaccinations against malaria are currently being evaluated in clinical trials, but there is, as yet, no licensed vaccine. One such study, for a vaccine against *P. falciparum*, is expected to finalise results towards the end of 2014, which will subsequently lead to a review by the WHO.

Anti-malarial drug treatment and drug resistance

Chloroquine: forms complexes with haem molecules in haemoglobin, interfering with haem polymerisation. This is effective at preventing formation of intraerythrocytic trophozoites. Resistance has occurred relating to genetic mutations in the transporter molecule, the '*P. falciparum* chloroquine resistance transporter' (PfCRT).

Doxycycline: binds to ribosomes to inhibit parasite protein synthesis.

Sulfadoxine-Pyrimethamine combination: interferes with the folate pathway and therefore parasitic nucleic acid synthesis through inhibition of dihydrofolate reductase (DHFR). Sulfadoxine inhibits parasite dihydropteroate synthase (DHPS). Pyrimethamine inhibits parasite (DHFR). Resistance due to point mutations in the DHPS has been found.

Atovaquone-Proguanil combination: affects the function of the parasite mitochondria via inhibition of the electron transport chain. Resistance to Atovaquone and combination therapy has been described due to substitution mutations. DHFR point mutation has been found in Proguanil resistance.

Artemisinin derivatives: the mechanism of action is not clear, but may relate to peroxide bond and production of oxide radicals, which destroy the parasite, or to inhibition of cellular redox cycling. Monotherapy is discouraged for fear of resistance. Consequently, they are usually used with other classes of anti-malarials, referred to as 'Artemisinin based Combination Therapy' (ACT).

Mefloquine, quinine, quinidine: bind with haem molecules, leading to the creation of parasite-toxic complexes. Mutations in the P-glycoprotein homolog-1 gene pfmdr-1 and PfCRT have been identified.

Resistance to antimalarials remains a concern. Combination therapy is preferred in order to prevent the development of resistant parasites. Routine monitoring of antimalarial resistance is essential. Resistance of mosquitoes to insecticides has also emerged in come countries, although in most areas they remain an effective prevention tool.

Widespread resistance to chloroquine and the sulfadoxine-pyrimethamine (SP) combination was identified in the 1970-1980s. Resistance to artemisinin derivatives was reported around the Cambodia/Thailand border in 2009. There has also been documented resistance to quinine in Africa and concerns over reduced efficacy of quinine in Southeast Asia.

HISTORY, CLINICAL FEATURES AND PARASITOLOGICAL DIAGNOSIS

History and clinical presentation

Children with malaria may present acutely unwell, or with a more indolent and asymptomatic picture. Malaria can be classified as simple/uncomplicated or severe/complicated.

Uncomplicated malaria is defined by the WHO as 'symptomatic infection with malaria parasitaemia without signs of severity and/or evidence of vital organ dysfunction'. Typical presentation of uncomplicated malaria includes a febrile illness with headache, night sweats, weakness, myalgia, arthralgia, diarrhoea, abdominal cramps and vomiting. Gastrointestinal symptoms are more common in children.

The acute febrile illness is sometimes associated with classic cyclical 'paroxysms', each lasting several hours. Paroxysms consist of chills and rigors, followed by fever spikes, then profuse sweating and, finally, extreme exhaustion. They occur in regular cycles every 48 or 72 hours, depending on the *P. lasmodium* species, and correspond with schizont rupture. However, these patterns may vary, and fever may be absent. Lack of such features, particularly with *P. falciparum*, should not delay diagnosis or treatment.

Complicated malaria occurs with falciparum malaria and is due to significant multisystem involvement. Presentation may include extreme weakness, confusion or drowsiness. WHO diagnostic features and manifestations of complicated malaria include:

- Cerebral malaria
- Generalised convulsions
- Hyperparasitaemia
- Hyperpyrexia
- Prostration
- Severe anaemia
- Hypoglycaemia
- Acute renal failure
- Acute pulmonary oedema
- Fluid and electrolyte abnormalities
- Metabolic acidosis with respiratory distress
- Shock
- Haemoglobinuria
- Abnormal bleeding
- Jaundice.

Falciparum malaria can be much more acute and severe compared to malaria caused by the other species and carries the greatest mortality. *P. vivax* may also be fatal.

The severity of *falciparum* malaria relates to the ability of the parasite to sequester in the microvasculature. Severe illness may be due to delayed or inadequate treatment and can occur very rapidly in children and in visitors from non-endemic areas. Rapid recognition and treatment is crucial and influences outcome. There should be a high index of suspicion of malaria in both endemic and non-endemic areas. It is important to elicit a travel history to at risk areas, as well as a history of exposure to infected blood through transfusion.

Table 1. *Differences between severe malaria in adults and in children. These features will vary depending on the region and levels of immunity in the population*

Signs or symptoms	Adults	Children
Duration of illness before severe features	Long (5-7 days)	Short (1-2 days)
Anaemia	Common	Very common
Convulsions	Common	Very Common
Pre-treatment hypoglycemia	Less common	Common
Metabolic acidosis	Less common	Common
History of cough	Uncommon	Common
Cerebral malaria	Common	Very common
Jaundice	Very common	Uncommon
Renal failure	Common	Uncommon
Pulmonary oedema, Acute Respiratory Distress Syndrome (ARDS)	More common	Rare
CSF pressures	Usually normal	Usually raised
Resolution of coma	Longer (2-4 days)	Shorter (1-2 days)
Bleeding/clotting disturbances	Up to 10%	Rare
Abnormality of brainstem reflexes (e.g. oculovestibular, oculocervical)	Rare	More common

Signs and symptoms can be non-specific and so other diagnoses must also be considered. Differential diagnoses include:

- Meningitis
- Influenza
- Typhoid and paratyphoid enteric fever
- Dengue fever
- Hepatitis
- Acute schistosomiasis
- Leptospirosis
- African tick fever
- East African trypanosomiasis
- Yellow fever
- Viral encephalitis.

For primary attacks, the incubation period may last 8-25 days, but can be longer. This relates to the patient's immune status, the *Plasmodium* strain, the sporozoite load, and chemoprophylaxis use. Relapses can cause delayed presentation months to years later and are due to dormant hypnozoites.

The features found in children may differ to those found in adults (see Table 1).

Parasitology

Diagnosis is based on clinical suspicion and on parasite detection in blood (parasitological diagnosis). Current WHO advice recommends rapid parasite diagnostic testing before treatment in suspected cases. Where such testing is not possible, or delayed, treatment can still be considered. Parasitological testing includes either light microscopy or rapid diagnostic tests (RDT).

Microscopy identifies the species, parasite density and parasite stage. Giemsa stained thick and thin films are the accepted standard for diagnosis, but require experienced personnel.

Malarial parasitaemia may be reported as:

- the percentage of parasite infected red blood cells, or
- the number of parasites per microlitre of blood.

The higher the parasite density, the greater the risk of developing severe malaria. The stage of the parasite in peripheral blood also influences prognosis.

RDTs detect parasite specific antigen. They may not identify low level infections and accuracy will depend on the manufacturer. They are useful if microscopy skills are not available or well developed.

Antimalarial treatment should be reserved for test positive cases. Occasionally the film can be negative when intense tissue sequestration has occurred. False negative cases are also more likely in recent artemisinin-derivative use. Rarely, treatment may therefore be considered in test negative cases where severity of suspected disease is significant. Differential diagnoses must be remembered.

Blood smears should be repeated 24-48 hours after initiation of treatment to monitor efficacy of the drugs used. A change in medication may be required if parasites have not been cleared.

Where clinically indicated, other laboratory tests include full blood count, clotting studies, renal function test, liver function test, blood glucose measurement, chest X-ray and lumbar puncture. Children with complicated malaria may be profoundly anaemic and hypoglycaemic. Hyponatraemia is common.

TREATMENT

Delayed diagnosis and treatment leads to increased morbidity and mortality. This may be due to

- Low index of suspicion

- Unclear history
- Failure to request blood films
- False negative results.

Treatment includes targeted antimalarial therapy as well as supportive therapy.

Drug therapy

WHO recommends use of ACTs for uncomplicated *P. falciparum*. Initial treatment of *P. falciparum* malaria should be started according to national and/or local guidelines. National malaria treatment policies should be in place, and should be assessed by in vivo monitoring for therapeutic efficacy to ensure the correct antimalarial regimen is in use. Treatment depends on local resistance patterns and species of plasmodium. Uncomplicated malaria can be treated with oral medication and on an outpatient basis.

ACTs are commonly used in Africa and South East Asia for uncomplicated malaria due to multi–drug resistant *P. falciparum*. Combination with another drug is necessary to reduce the risk of recrudescence and resistance. Combinations will depend on patterns of resistance to the partner drug.

In severe malaria, treatment should commence with one of the following parenteral drugs: artesunate IV or IM/ quinine IV or IM / artemether IM. If definitive treatment is delayed, pre-referral treatment may include rectal artesunate. Parenteral antimalarials should be given for 24 hours. Once this is complete, and oral therapy can be tolerated, antimalarial cover should be continued with either 1) an ACT, or 2) artesunate with clindamycin or 3)quinine with clindamycin. Refer to the latest online WHO guidelines on treatment of malaria.

Adult studies comparing quinine to artemesinin derivatives (artesunate, artemether and artemortil) show superiority of the artemesinins. This relates to the artemesinins' wider range of action in the lifecycle of the parasite and faster clearance of the parasite, alongside a reduced incidence of hypoglycaemia. Neurological outcomes are not felt to differ between artesunante and quinine use.

Supportive therapy

Monitoring and supportive therapy are key to the management of the child with malaria. This includes regular measurement of vital signs, level of consciousness, urine output, blood sugars and oxygen saturation, alongside intensive nursing care.

Fluid resuscitation is often needed. There is a risk of pulmonary overload, although it is rare in children. The requirement for respiratory support ranges from oxygen supplementation to full ventilatory support. Renal failure may require haemodialysis. The nature of multi organ involvement will determine the support required.

Pharmacological adjuncts may include anitpyretics, antibiotics, anticonvulsants and antiemetics.

ANAESTHETIC CONSIDERATIONS – THE CHILD WITH MALARIA PRESENTING FOR SURGERY

If a child with malaria presents for surgery, you must assess the urgency of the surgery. Surgery in the presence of acute malaria is associated with increased morbidity and mortality, both intra- and post-operatively. Where possible, delay surgery to allow for time to respond to anti-malarial treatment. The following precautions should be taken if surgery cannot be delayed:

- Preoperative assessment should include routine history and examination, specific to the child, and with an emphasis on the multi-system effects associated with malaria. The anaesthetic plan will depend on which systems are affected. Determine features and severity of the malaria should be determined, assisted by a full examination. A complete set of observations is required, including temperature and blood sugar measurement.
- Preoperative assessment should include the level of consciousness, with documentation of the GCS/Blantyre Coma Scale and identification of any features of cerebral malaria (see below). There is an increased risk of deterioration post operatively if the child has signs of CNS involvement preoperatively. Place a nasogastric tube if there is a reduced level of consciousness.
- Avoid premedication with sedative drugs in complicated malaria, to prevent confusion between the drug's sedative effects and clinical deterioration, as well as to avoid the risk of airway compromise.
- Aim for low normal $PaCO_2$ and good oxygenation. Reduced respiratory effort may lead to raised $PaCO_2$ and falling PaO_2, risking cerebral vasodilatation and a raised ICP. The airway should be secured and controlled ventilation used to prevent a rise in intracranial pressure (ICP). Avoid drugs that lead to an increase in ICP such as halothane and ketamine and prevent hypertension at intubation and extubation. Vigilance is required to identify convulsions under anaesthesia: use signs such as hypertension, tachycardia and pupil changes.
- Consider atracurim or cis-atracurim due to its reliance on Hoffman degradation, although renal failure is less common in children compared to adults. Avoid halothane if hepatic dysfunction is present. If hyperkalaemia is present, avoid suxamethonium. Avoid vecuronium and pancuronium due to delayed clearance. Quinine will enhance the effect of neuromuscular blockade.
- Transfusion requirements and the use of invasive monitoring will depend on factors such as proposed surgery and expected blood loss. Beware of the possibility of a low platelet count and the presence of coagulopathy when considering regional techniques such as a caudal block or spinal anaesthesia.
- Intraoperative vigilance with blood glucose monitoring and treatment is vital.
- Post-operative assessment of consciousness is important - patients should not be returned to the ward if they are not awake and alert. If there is deterioration in the GCS/BCS, hypoglycaemia, seizures or the child is post-ictal, consider worsening cerebral malaria in addition to anaesthetic causes. The child should be monitored carefully postoperatively, ideally in a high dependency area. Anti-malarial treatment must be continued postoperatively.

MULTI-ORGAN INVOLVEMENT, ICU MANAGEMENT

Malaria is a multi-system disease that can coexist with other infections

Table 2. *The Blantyre Coma Scale*

Blantyre Coma Scale	
	Score
Best MOTOR response	
Localises to painful stimulus	2
Withdraws limb from painful stimulus	1
No response or inappropriate response	0
Best VERBAL response	
Cries appropriately with painful stimulus, or, if verbal, speaks	2
Moan or abnormal cry with painful stimulus	1
No vocal response to painful stimulus	0
EYE Movements	
Watches or follows (e.g. mother's face)	1
Fails to watch or follow	0

and conditions, including those that may require surgery. Intensive care may be necessary.

Remember, a child may deteriorate rapidly, particularly if hyperparasitaemia is present. Severe anaemia (Hb <5g.dl^{-1}), respiratory distress due to metabolic acidosis and cerebral malaria are seen more frequently in children.

Laboratory and diagnostic tests should include: full blood count, liver function tests, urea, creatinine and electrolytes, clotting profile, blood type and crossmatch where appropriate (depending on FBC and coagulation findings). Pulse oximetry is helpful. Arterial blood gas, ECG and chest Xray may also be indicated.

Criteria for intensive care admission include:

- Presence of immediate life threatening complications such as coagulopathy or end organ failure
- Presence of signs or symptoms of cerebral malaria
- Non-immune patients with *P. Falciparum* parasitemia >2% or semi-immune patients with *P. Falciparum* parasiteamia >5%
- Presence of any other severe complications of malaria.

Cerebral malaria

Cerebral malaria has been defined by the WHO as:

- 'Severe *P. falciparum* malaria with cerebral manifestations, usually including coma (Glasgow Coma Scale <11, Blantyre Coma Scale <3)' (see below)
- 'Malaria with coma persisting for more than 30 minutes after a seizure'.

Other causes for reduced cerebral function should be sought and excluded.

Cerebral malaria is more common in children and non-immune adults. Mortality can be as high as 40% in children, who are also at a greater risk of developing neurological sequelae (10%). Such sequelae include hemiparesis, cerebellar ataxia, cortical blindness, hypotonia, mental retardation and cerebral palsy.

Pathogenesis is thought to include sequestration of parasitised erythrocytes in cerebral microvasculature with associated inflammatory responses. Inducible nitric oxide production is also thought to play a role through inhibition of neurotransmission. There is reduced oxygen and glucose delivery with raised temperature, hypoglycaemia and metabolic acidosis exacerbating the effects.

In children, febrile convulsions may occur, with a post-ictal state lasting several hours. Hyperpyrexia and hypoglycaemia should be excluded as causes of both coma and convulsions.

The optic fundi should be examined. Meningitis should be considered in the differential diagnosis. In cerebral malaria, Kernig's sign is negative (if positive, the child is unable to straighten the leg whilst lying down with the hip flexed – a sign of meningism e.g. due to meningitis). Neck stiffness, photophobia and focal neurology are rare in cerebral malaria. However, cerebral malaria may present with coma, convulsions or posturing. Retinal haemorrhages may be present in 15%. CSF pressure at lumbar puncture may be elevated in children, but is often normal in adults. Cerebrospinal fluid (CSF) is clear with < 10 white blood cells per microlitre but protein is often slightly raised. Computed tomography scans are usually normal.

In older children and adults the Glasgow Coma Scale (GCS) is used to measure the level of consciousness. In younger children either a modified GCS or the Blantyre Coma Scale (BCS) can be used (see Table 2).

Convulsions should be treated with intravenous or rectal diazepam, or intramuscular or rectal paraldehyde.

Patients require meticulous nursing care. The level of consciousness must be regularly monitored alongside temperature, blood pressure, heart rate, and respiratory rate. A urinary catheter is required, with strict input/output recordings. There is currently no role for drugs to reduce cerebral oedema.Respiratory and ventilatory support may be required.

Respiratory distress

There may be several processes present leading to respiratory distress including:

- Pulmonary oedema
- Respiratory compensation for metabolic disturbance, particularly acidosis
- Superadded chest infections
- Severe anaemia.

Non-cardiogenic pulmonary oedema involves sequestration of erythrocytes in the lungs and associated inflammatory responses in the pulmonary vasculature, alongside increased capillary permeability. Mild ARDS may develop and can progress to be severe. Patients can appear to otherwise be improving clinically at the time it develops. Excessive fluid administration, renal failure and hypoalbuminaemia can contribute. Pulmonary oedema can occur in both *falciparum* and *vivax* malaria.

Abnormal breathing patterns can be due to effects on the respiratory centre. Patients may have a superadded chest infection due to immune suppression.

Metabolic acidosis is more common in children than in adults. Confirm with arterial blood gas results where possible. Consider and treat bacterial infection and the impact of a reduced level of consciousness.

Although there is a risk of pulmonary oedema and ARDS in children, this is much less common than in adults. Care is needed with fluid therapy. In anaemic children, dyspnoea is more commonly related to acidosis and hypovolaemia, which therefore needs urgent correction. Ventilatory support may become necessary. Increased FiO_2 and positive end expiratory pressure may be required. In the event of fluid overload, intravenous furosemide can be used.

Circulatory collapse

Cardiovascular collapse in malaria may be due to:

- Secondary bacterial infection
- Metabolic acidosis
- Dehydration
- Bleeding, including a ruptured spleen
- Pulmonary oedema.

Often the bacterial infection is Gram-negative sepsis. Seek possible infection sites, including respiratory tract, urinary tract, meningitis and intravenous lines. Correct hypovolaemia and commence broad-spectrum antibiotics, ideally after blood cultures are sent. Myocardial function is often well preserved, however there is potential for impaired myocardial function and a preoperative echocardiogram may be advised.

Preoperative assessment of hydration is important, with identification and treatment of hypovolaemia, as well as sepsis and shock. Consider fluid therapy, possible blood transfusion and potential inotropes. Children with severe anaemia may present with tachycardia and dyspnoea.

Haematological disturbances

All patients with malaria are prone to anaemia. Children and non-immune patients with high parasite loads are at the greatest risk. The anaemia can be severe, with a haemoglobin <5g.dL^{-1}. Causes are multifactorial and relate to:

- Haemolysis
- Removal of both parasitized and non-parasitized erythrocytes in the spleen
- Impaired bone marrow function
- Reduced erythropoietin production and response to erythopoeitin
- Nutrition
- Infective causes (e.g. hookworm).

Thrombocytopenia is very common in falciparum malaria, often occurring in the absence of other clotting dysfunction. It relates to an increase in splenic clearance of platelets. Disseminated intravascular coagulation (DIC) can occur and may present as bleeding gums, epistaxis, petechiae, haematemesis, and malaena. DIC and significant bleeding occurs in < 10%, with the greatest risk among non-immune patients.

Determine the degree of anaemia alongside the clinical picture and consider transfusion if the haematocrit is <25%, or when hypovolaemic shock is present. Transfuse whole blood (20ml.kg^{-1}) or packed cells (10ml.kg^{-1}) as per hospital guidelines. Transfusion should be carried out cautiously due to the risk of pulmonary oedema. Children with a hyperdynamic circulation may need intravenous furosemide for transfusions. Platelet and fresh frozen plasma transfusions may be required in the presence of coagulopathy.

Hypoglycaemia

Hypoglycaemia is common in severe malaria. Pregnant women and children are at a greater risk, especially neonates and infants. It should be suspected in all those with a reduced conscious level, and may present with coma or convulsions. Regular blood sugar monitoring is essential and hypoglycaemia must be appropriately treated and observed. Hypoglycaemia can be due to:

- Increased demand (anaerobic glycolysis, febrile illness and demand from parasites)
- Failed hepatic glycogenolysis and gluconeogenesis
- Quinine-stimulated pancreatic beta-cell insulin secretion.

Hypoglycemia contributes to central nervous system dysfunction and associated neurological deficits in survivors of cerebral malaria.

Fluid and electrolyte disturbance, metabolic acidosis

There is often evidence of hypovolaemia and dehydration. Metabolic acidosis can occur with severe illness, hypoglycaemia, hyperparasiteamia, or renal failure. Lactic acidosis is mainly due to reduced oxygen delivery to tissues caused by hypovolaemia, sequestration, and anaemia. Contributing factors include parasite anaerobic glycolysis, impaired hepatic and renal function with reduced lactate clearance and cytokine release. In children with severe malaria, lactate level >5mmol.L^{-1} is a major predictor of death. Hyponatraemia is a common finding. Children with acute renal tubular dysfunction may have raised potassium levels.

Hyperpyrexia

High fevers are more common in children and may contribute to convulsions (febrile convulsions) and coma, with increased mortality. Persistently high temperatures (≥42°C.) may cause permanent neurological sequelae.

Monitor temperature carefully. Children are also prone to hypothermia and so hyperthermia must be aggressively treated, whilst avoiding hypothermia. Treatment of a raised temperature includes the use of antipyretics and cooling methods such as tepid sponges and fans, aiming to keep the temperature <39°C.

Gastrointestinal (GI) system

GI symptoms of malaria are frequently found in children, presenting with nausea and vomiting, abdominal pain and diarrhoea. There may be gastric/duodenal ulceration, malabsorption and an increase in gastrointestinal infections such as *salmonella*. Jaundice may be present due to haemolysis, hepatocellular dysfunction, cholestasis, or a combination of each. Serum bilirubin and liver enzymes may be elevated, although less than with viral hepatitis. Splenomegaly is also common and most likely related to the clearance of erythrocytes.

Spontaneous splenic rupture can occur with P.vivax infection.

Renal dysfunction

Acute renal failure usually occurs in adults. It can be due to prerenal or renal causes and is often secondary to acute tubular necrosis (ATN). Microvascular obstruction and cellular damage due to filtration of free haemoglobin, myoglobin and cellular material can lead to ATN. Usually there is a protracted period of oliguria, followed by anuria; occasionally a polyuria may be found. IV fluids and antimalarial treatment will aid pre-renal factors.

Monitor blood urea, creatinine and electrolytes and hydration status. A urinary catheter is required, with close monitoring of input and output balance. In severe cases, dialysis may be required.

Blackwater fever, although uncommon, can occur in severe malaria and is due to massive haemoglobinuria. It is more likely found in adults with renal failure. The urine is tea/coca-cola coloured. Those with glucose-6-phosphate dehydrogenase (G6PD) deficiency are at a greater risk of developing the condition, especially if receiving oxidant drugs such as primaquine and sulphonamides.

Hyperparasitaemia

High parasite densities (>5%) and peripheral schizontaemia tend to be associated with severe disease, particularly in children and those who are non-immune. In endemic areas, and in the partially immune, higher mean densities (20-30%) may be found without clinical symptoms.

Exchange transfusions can be considered in high parasitaemia, but must be weighed against the risk of the transfusion itself.

Miscellaneous

Malaria can be transmitted via a needle stick injury. Observe universal precautions.

SUMMARY

Malaria can vary from an insidious febrile illness to an acute life-threatening disease. Rapid deterioration is much more likely in children. If malaria is suspected, it should be investigated rapidly and treated appropriately. WHO and national diagnostic and treatment guidelines should be followed. Children should be observed closely for the development of complications. ICU admission may be required. Anaesthesia and surgery should be avoided in the child with malaria if at all possible, but, if it is necessary, the multi-system nature of the disease should be considered.

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