

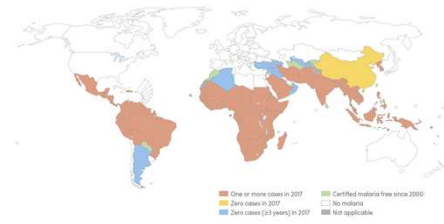


Clinical Presentation and Treatment of Malaria in Ugandan Refugee Settlements

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University of Colorado SOM

Nothing to Disclose

Countries with indigenous cases in 2009 and their status by 2017. Countries with zero indigenous cases over at least the past 3 consecutive years are considered to be malaria free. All countries in the WHO European Region reported zero indigenous cases in 2016 and again in 2017. In 2017, both China and El Salvador reported zero indigenous cases. Source: WHO database.



WHO: World Health Organization.

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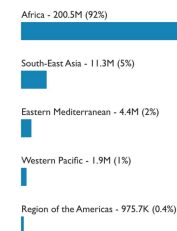
Objectives

- Review the current state of malaria around the globe
- Describe the presentations of mild and severe *P. falciparum* malaria
- Introduce artemisinin-based combination medication therapy (ACT)
- Practice diagnosis and treatment of malaria in an Ugandan refugee health clinic

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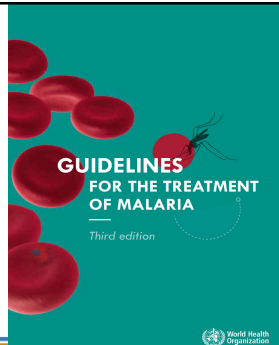
Estimated malaria cases (2017)



Source: WHO estimates

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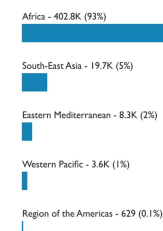
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Estimated malaria deaths (2017)



Source: WHO estimates

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- Fifteen countries in sub-Saharan Africa and India carried almost 80% of the global malaria burden. Five countries accounted for nearly half of all malaria cases worldwide: Nigeria (25%), Democratic Republic of the Congo (11%), Mozambique (5%), India (4%) and Uganda (4%).

Third leading cause of death in children aged 1-59 months



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Clinical Malaria

- Begins non-specific and could be any viral illness
- Headache, fatigue, abdominal pain and joint aches
- Then fever, chills, sweats, anorexia, vomiting, worsening malaise
 - The cold stage- patient feels cold and shivers
 - The hot stage- patients feels hot
 - the sweating stage- sweating and relief of symptoms
- Small children often have lethargy, poor feeding and cough
- Initially there is no organ dysfunction
- Severe malaria = organ dysfunction/metabolic acidosis

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Thick Blood Smear
looks for the presence of the parasite

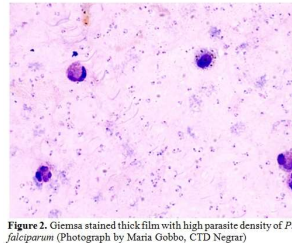
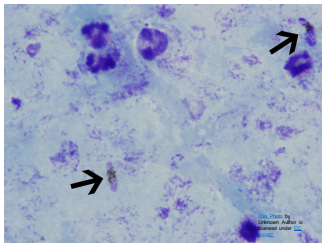


Figure 2. Giemsa stained thick film with high parasite density of *P. falciparum* (Photograph by Maria Gobbo, CTD Negart)

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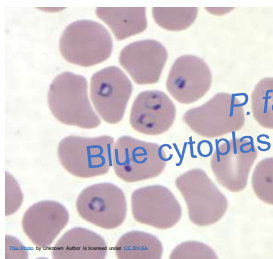
Severe/Cerebral *falciparum* Malaria

- Impaired consciousness/Glasgow coma score <11
- Multiple convulsions: more than two seizures within 24 hours
- Acidosis: bicarb <15, venous lactate >5
- Hypoglycemia: glucose < 2.2 mmol/L (<40 mg/dl)
- Severe malarial anemia: Hgb <5 or Hct <15% in children <12 years
- Renal impairment: Cr > 3
- Jaundice: bilirubin > 3 mg/dl with a parasite count >100,000/uL
- Pulmonary edema: O2 sat <92% with a RR > 30
- Significant bleeding: hematemesis or melena (*Blackwater Fever*)
- Shock: cap refill > 3, SBP < 70 mmHg in children and <80 mmHg in adults
- Hyperparasitemia: *P. falciparum* > 5%

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Thin Blood Smear
looks for the identity of the parasite



P. falciparum
Blue cytoplasm with red chromatin

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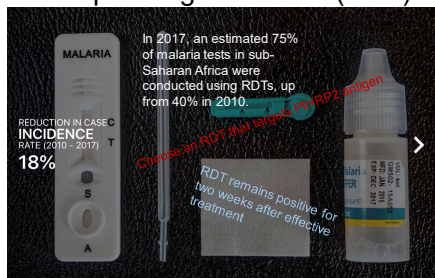
WHO Core Principles for the treatment of Malaria

- Early diagnosis and prompt, effective treatment
 - Early diagnosis
 - Effective treatment initiated within 24-48 hours
- Rational use of antimalarial agents
 - Confirm the presence of malaria before treating (RDT, blood smears)
 - Look for other causes of febrile illness
 - Adherence to full treatment course
- Combination therapy
 - All episodes of malaria should be treated with at least two effective antimalarial medicine with different mechanisms of action (ACT, artemisinin combination therapy)
- Appropriate weight-based dosing

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Rapid Diagnostic Test (RDT)



In 2017, an estimated 75% of malaria tests in sub-Saharan Africa were conducted using RDTs, up from 40% in 2010.

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7.4.1 | ARTESUNATE

Treating severe malaria

Treat adults and children with severe malaria (including infants, pregnant women in all trimesters and lactating women) with intravenous or intramuscular artesunate for at least 24 h. Once a patient has received at least 24 h of parenteral therapy and can tolerate oral therapy, complete treatment with 3 days of an ACT.

Strong recommendation, high-quality evidence

GRADE (see Annex 4, A4.12)

In a systematic review of artesunate for severe malaria, eight randomized controlled trials with a total of 1664 adults and 5765 children, directly compared parenteral artesunate with parenteral quinine. The trials were conducted in various African and Asian countries between 1989 and 2010.

In comparison with quinine, parenteral artesunate:

- Reduced mortality from severe malaria by about 40% in adults (RR, 0.61; 95% CI, 0.50–0.75, five trials, 1664 participants, *high-quality evidence*);
- Reduced mortality from severe malaria by about 25% in children (RR, 0.76; 95% CI, 0.65–0.90, four trials, 5765 participants, *high-quality evidence*).

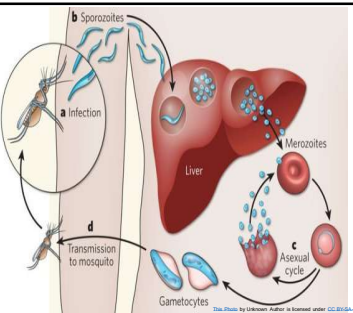
Artesunate is used to treat severe Malaria

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Artemether

- Artemisinin, a natural product, is the active ingredient in Artemether.
- Artemether is a derivative of Artemisinin.
- Artemether is used in the treatment of malaria.
- Kills faster than other drugs against parasites.



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Treating cases of suspected severe malaria pending transfer to a higher-level facility (pre-referral treatment)

Pre-referral treatment options

Where complete treatment of severe malaria is not possible but injections are available, give adults and children a single intramuscular dose of artesunate, and refer to an appropriate facility for further care. Where intramuscular artesunate is not available use intramuscular artemether or, if that is not available, use intramuscular quinine.

Strong recommendation, moderate-quality evidence

Where intramuscular injection of artesunate is not available, treat children < 6 years with a single rectal dose (10mg/kg bw) of artesunate, and refer immediately to an appropriate facility for further care. Do not use rectal artesunate in older children and adults.

Strong recommendation, moderate-quality evidence

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Recommendations

Diagnosis of malaria

All cases of suspected malaria should have a parasitological or Rapid diagnostic test (RDT) to confirm the diagnosis. Both microscopy and RDTs should be supported by a quality assured Good practice statement.

Treating uncomplicated *P. falciparum* malaria

Treat children and adults with uncomplicated *P. falciparum* (pregnant women in their first trimester) with one of the following artemisinin-based combination therapies (ACT):

- artemether + lumefantrine
- artesunate + amodiaquine
- artesunate + mefloquine
- dihydroartemisinin + piperaquine
- artesunate + sulfadoxine-pyrimethamine (SP)

Strong recommendation, high-quality evidence

Treating uncomplicated *P. falciparum* malaria in special risk groups

First trimester of pregnancy

Treat pregnant women with uncomplicated *P. falciparum* malaria during the first trimester with 7 days of quinine + clindamycin.

Strong recommendation

Infants less than 5 kg body weight

Treat infants weighing < 5 kg with uncomplicated *P. falciparum* malaria with ACT at the same mg/kg bw target dose as for children weighing 5 kg.

Strong recommendation

Patients co-infected with HIV

In people who have HIV/AIDS and uncomplicated *P. falciparum* malaria, avoid artesunate + SP if they are being treated with co-trimoxazole, and avoid artesunate + amodiaquine if they are being treated with efavirenz or zidovudine.

Good practice statement

Non-immune travellers

Treat travellers with uncomplicated *P. falciparum* malaria returning to non-endemic settings with ACT.

Strong recommendation, high-quality evidence

Hyperparasitaemia

People with *P. falciparum* hyperparasitaemia are at increased risk for treatment failure, severe malaria and death and should be closely monitored, in addition to receiving ACT.

Good practice statement

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Chemoprevention for special risk groups

Intermittent preventive treatment in pregnancy

In malaria-endemic areas in Africa, provide intermittent preventive treatment with SP to all women in their first or second pregnancy (SP-IPTp) as part of antenatal care. Dosing should start in the second trimester and doses should be given at least 1 month apart, with the objective of ensuring that at least three doses are received.

Strong recommendation, high-quality evidence

Intermittent preventive treatment in infants

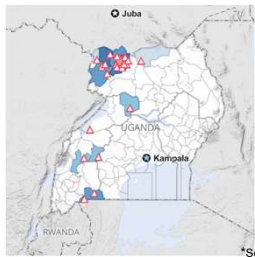
In areas of moderate-to-high malaria transmission of Africa, where SP is still effective, provide intermittent preventive treatment with SP to infants (< 12 months of age) (SP-IPTi) at the time of the second and third rounds of vaccination against diphtheria, tetanus and pertussis (DTP) and vaccination against measles.

Strong recommendation

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Ugandan Refugee Situation



- **1,331,565 refugees** (31 Aug 2019)*
- Live in settlements, not camps
- Land donated by land owners
- Allotted a small plot of land
 - build a house
 - farm, start of business= self-sufficiency
- Allowed free movement
- Supported by UNHCR
- Lessons we could learn!

*Source - UNHCR, Government of Uganda, Office of the Prime Minister

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Is this malaria?

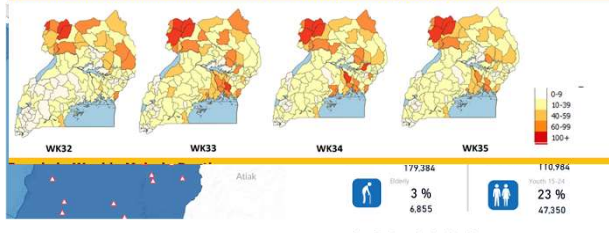
- What additional history would you like to know?
 - Is anyone else sick in the house?
 - Recent GI illness/what is their water source?
 - Vaccination status?
 - HIV/TB status?
- What else might this be?
 - Pneumonia/upper resp tract infection/influenza
 - measles (before rash), any viral illness
 - Any virus/viral gastroenteritis/UTI
- What tests would you like to obtain?
 - RDT - thick smear
 - Glucose - Hgb
 - Urine for ketones/blood/bilirubin

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Adjumani District

Trends in Weekly Confirmed Incidence of Malaria (Cases/1,000 population)



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 UGANDA CLINICAL GUIDELINES 2016 National Guidelines for Management of Common Conditions		2.2.1 Candidiasis 161 2.3 Viral Infections 163 2.3.1 Avian Influenza 163 2.3.2 Chikungunya 166 2.3.3 Measles 167 2.3.4 Poliovirus 169 2.3.5 Rabies 171 2.3.6 Viral Haemorrhagic Fevers 172 2.3.6.1 Ebola and Marburg 172 2.3.6.2 Yellow Fever 175 2.4 Helminthes Parasites 177 2.4.1 Intestinal Worms 177 2.4.1.1 Tricostema (Tapeworm) 179 2.4.2 Echinococcosis (Hydatid Disease) 181 2.4.3 Dracunculiasis (Guinea Worm) 182 2.4.4 Lymphatic Filariasis 184 2.4.5 Onchocerciasis (River Blindness) 185 2.4.6 Schistosomiasis (Bilharzia) 187 2.5 Protozoal Parasites 189 2.5.1 Leishmaniasis 189 2.5.2 Malaria 191 2.5.2.1 Clinical Features of Malaria 191 2.5.2.2 Investigations for Malaria 194 2.5.2.3 Management of Malaria 195 2.5.2.4 Management of Complications of Severe Malaria 201 2.5.2.5 Management of RDT, Blood Smear Negative Patients 205 2.5.2.6 Malaria Prophylaxis 207
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Medical Teams International

September 2 at 9:10 AM

You might think this full room looks like chaos, but we love the number of refugees we get to see every day! Hundreds of lives are changed by the simple act of checking a baby's weight, taking a mother's temperature or providing nutritious foods. We love what we do!



Let's Get to Work! Welcome to Uganda

Your first patient of the morning is a two year old whose mother reports "felt hot" in the night. He is not eating well, has a slight cough and appears ill. Mother reports he had one episode of vomiting this morning.

He is afebrile, P 100, RR 18 O2 sat 97% 12 kg
 He is responsive and shy, dry mucus membranes
 HEENT-no jaundice, + mucosal pallor, TM's wnl
 Heart tachycardic, with clear lungs
 Abd is soft and mildly tender, no spleen tip
 Skin has no rash, cap refill <3 sec

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Uncomplicated *P. falciparum* malaria

2.5.2 MALARIA

Uncomplicated Malaria

ICD 10 CODE: B50.9

Common symptoms/signs of uncomplicated malaria

- Fever: above 37.5°C (taken from the axilla) or history of fever
- Loss of appetite, mild vomiting, diarrhoea
- Weakness, headache, joint and muscle pain
- Mild anaemia (mild pallor of palms and mucous membranes); occurs commonly in children
- Mild dehydration (dry mouth, coated tongue, and sunken eyes). In adults, sunken eyes are usually a sign of severe dehydration
- Enlarged spleen (in acute malaria it may be minimally enlarged, soft and mildly tender)

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2.5.2.3 Management of Malaria

NATIONAL MALARIA TREATMENT POLICY (2015)

Uncomplicated Malaria

All patients: including children <4 months of age and pregnant women in 2nd and 3rd trimesters

First line medicine
 ▶ Artemether/Lumefantrine

First line alternative
 ▶ Artesunate/Amodiaquine

Second line medicine
 ▶ Dihydroartemisinin/Piperaquine
 ▶ If not available: quinine

You have weight dosed Artemether/Lumefantrine and prescribed it to be given every 12 hours for 3 days;
 You give ORS packets to the mother to use at home and make sure she has access to clean water;
 The nurse gives further education and she heads back home.

Treatment of uncomplicated malaria
 The following tables contain dosages for medicines used in treatment of uncomplicated malaria.

Dosage of artemether/lumefantrine 20/120 mg

WEIGHT (KG)	AGE	DAY 1	DAY 2	DAY 3
5–14	4 months–3 years	1 tab twice daily	1 tab twice daily	1 tab twice daily
15–24	3–7 years	2 tab twice daily	2 tab twice daily	2 tab twice daily
25–34	7–12 years	3 tab twice daily	3 tab twice daily	3 tab twice daily
>35	> 12 years	4 tab twice daily	4 tab twice daily	4 tab twice daily

Note: Give doses every 12 hours

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Manage Your Patient

In your hospital tent, you have the following available:

-medications: ACT, Artesunate IV/IM, quinine, paracetamol, diazepam, gentamycin, ceftriaxone, Augmentin, piperacillin/tazobactam, IV fluids, IV glucose ampules, albuterol, diphenhydramine, dexamethasone, phenytoin, phenobarb, diclofenac, heparin

-rapid tests: vitals, RDT, UA, Hgb, glucose, HIV, RPR, CMV, cryptococcus, thick smear for malaria, stool tests for heme, hepatitis

-there are no supplies for a lumbar puncture
 -the amazing nurse has established an IV line for you

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You are feeling pretty good about this malaria treatment protocol when the triage nurse arrives with a child limp in her arms and asks you to come with her to the hospital tent.

The mother has walked for over an hour to arrive at the clinic, stating her 3 year old child has felt hot for 2 days and had a seizure last night; A prostrate child is laid on the cot; her temperature is 40 C; As the nurse begins to insert the IV, the child seizes.

Your nearest referral hospital is 2 hours away but it takes 3 hours or more to arrange transportation.

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Management of a febrile child with seizures in the middle of malaria country

- ABC's – maintain the airway, check glucose
- Febrile seizure vs malarial seizure??
 - There is likely an overlap between them
 - Treat for severe malaria if there are two seizures within 24 hours
 - Generalized seizures are more common with *P. falciparum* than other malarial species
- If seizures continue, treat with benzodiazepines (parenteral or rectal) or load with phenobarb
- Prophylactic anticonvulsants are not recommended

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Is this Severe Malaria?

- Differential diagnosis of fever in a severely ill child is broad
- Cerebral malaria is not associated with signs of meningeal irritation
 - Meningoencephalitis should always be considered in a febrile child with coma/obtundation
 - Lumbar puncture should be performed to exclude bacterial meningitis
- Considerable clinical overlap exists between septicemia, pneumonia and severe malaria
- All three of the above may coexist

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2.5.2 MALARIA

Dosage of intravenous artesunate for severe malaria

Artesunate IV	
DOSE	
First dose: on admission	
Loading dose	
Second dose	
Third dose	
Then once a day until patient is able to tolerate oral medication, then give a full course of oral ACT	

Dosage of IM artemether

Artemether		
DOSE	TIME	QUANTITY
First dose: on admission	At 0 hours	3.2 mg/kg
Loading dose		
Second dose	At 24 hours	1.6 mg/kg
Third dose	At 48 hours	1.6 mg/kg
Then once a day until patient is able to tolerate oral medication, then give a full course of oral ACT		

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Immediate Clinical Management of Severe *P. falciparum* malaria

- Coma—maintain airway, place patient on their side
- Hyperpyrexia—cool with sponging, paracetamol, fan
- Hypoglycemia—correct/maintain w/glucose infusion for <3 (54)
 – Child: dextrose 10% 5 ml/kg by slow IV bolus over 5-7 min (to prepare, take 1 ml/kg of dextrose 50% and dilute with 4 ml/kg water for injection)
- Severe anemia—transfuse fresh whole blood if <6 Hgb
- Acute pulm edema- keep at 45 deg angle, oxygen, diuretic, PEEP/CPAP
- Acute kidney injury—trial furosemide, hemofiltration/hemodialysis
- Spontaneous bleeding-transfuse with fresh whole blood, Vit K
 – (cryoprecipitate, fresh frozen plasma and platelets if available)

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Questions??

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Treatments to Avoid in Severe Malaria

- IV fluid/IV albumin—significant increase in mortality in children receiving any bolus treatment compared to no bolus therapy (FEAST trial, NEJM June 30, 2011)
- Corticosteroids —increased risk of GI bleeding and seizures, and prolonged coma resolution
- All anticoagulants
- Aspirin; anti-TNF antibody; cyclosporine A; N-acetylcysteine
- Seizure medications

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Your patient is doing well after three days due to your rapid interventions:

1. ABC's, child on her side
2. Gave IV diazepam to stop seizures
3. Quickly gave IV ceftriaxone and ran an RDT for malaria, which was positive, so Artesunate was quickly given IV, followed with a thick smear
4. The initial glucose was < 3, so you gave the appropriate glucose bolus and maintained a normal level with IV infusion
5. The Hgb was 6.7 and monitored
6. You avoided NS boluses/used ORS for hydration



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