AAFP GLOBAL HEALTH SUMMIT

Primary Health Care and Family Medicine: Health Equity for All

Clinical Presentation and Treatment of Malaria in Ugandan Refugee Settlements

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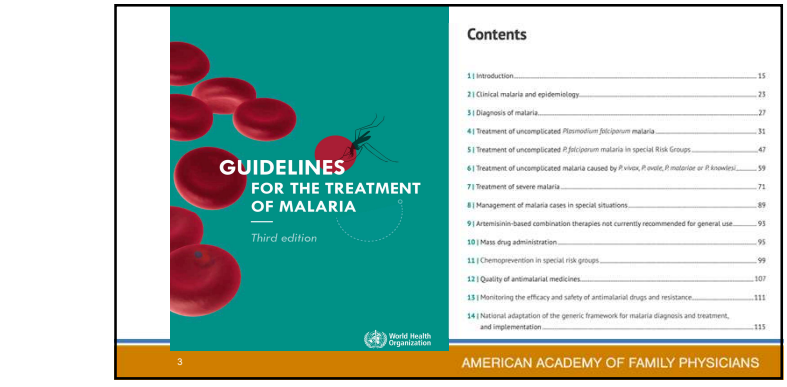
Nothing to Disclose

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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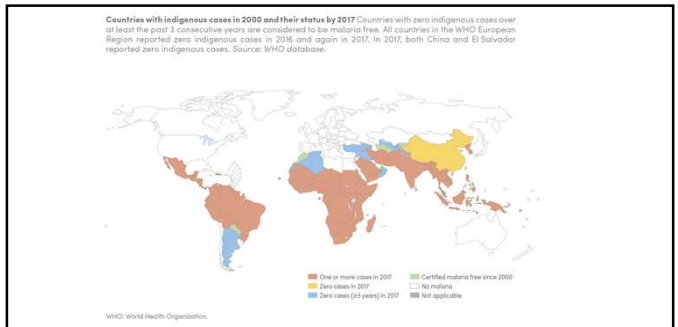
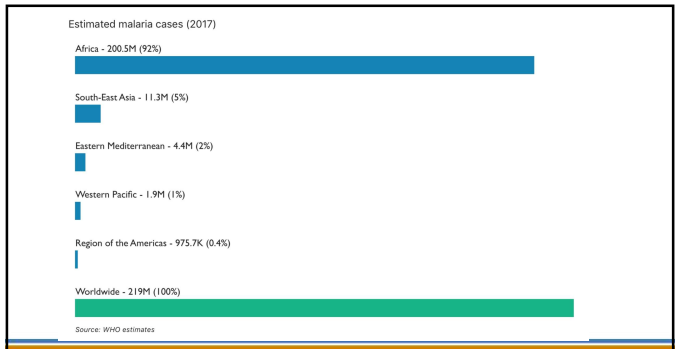
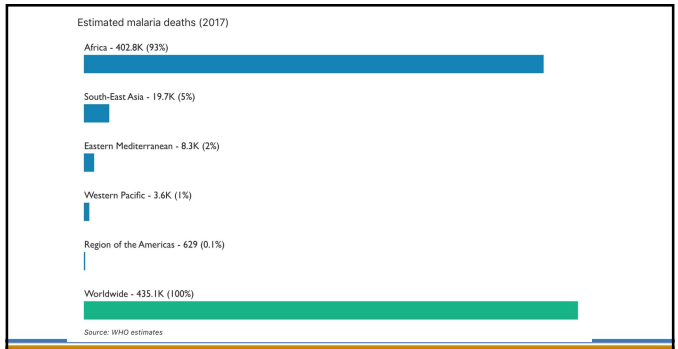






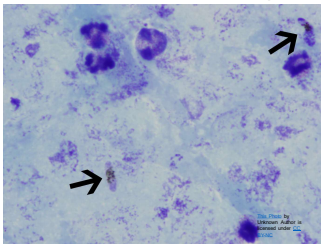
- Fifteen countries in sub-Saharan Africa and India carried almost 80% of the global malaria burden. Five countries accounted for nearly half of all malaria cases worldwide: Nigeria (25%), Democratic Republic of the Congo (11%), Mozambique (5%), India (4%) and Uganda (4%).

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

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

Thick Blood Smear
looks for the presence of the parasite



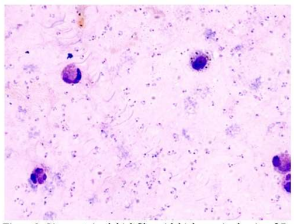
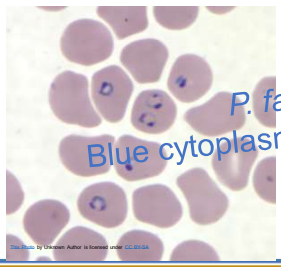


Figure 2. Giemsa stained thick film with high parasite density of *P. falciparum* (Photograph by Maria Gobbo, CTD Negrar)

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/*u*L
- 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%

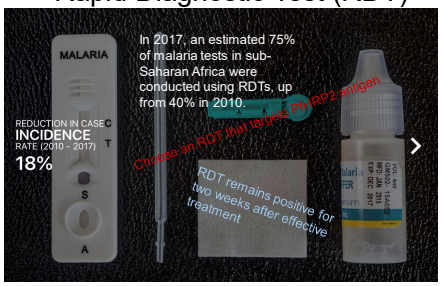
Thin Blood Smear
looks for the identity of the parasite



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

Rapid Diagnostic Test (RDT)



Artemether

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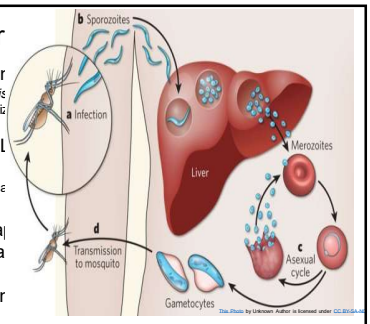
- Kills faster than other drugs ar… parasites



Recommendations

Diagnosis of malaria

All cases of suspected malaria should have a parasitological t… or Rapid diagnostic test (RDT)) to confirm the diagnosis.

Both microscopy and RDTs should be supported by a quality assura…
Good practice statement

Treating uncomplicated *P. falciparum* malaria

Treatment of uncomplicated P.falciparum malaria

Treat children and adults with uncomplicated *P. falciparum* pregnant women in their first trimester) with one of the followin… 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 5kg 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

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*

Artesunate is used to treat severe Malaria

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

Chemoprevention for special risk groups

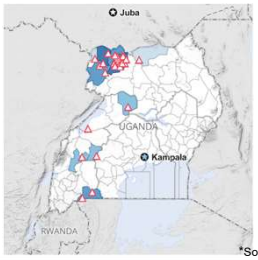
Intermittent preventive treatment in pregnancy

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

Ugandan Refugee Situation



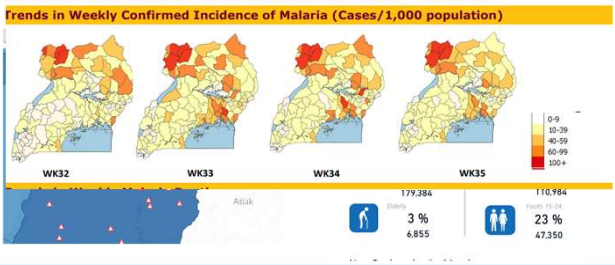
- **1,331,565 refugees** (31 Aug 2019)*
- Live in settlements, not camps
- Land donated by land owners
- Allotted a small plot of land
  - -build a house
  - -farm, start of business= self-sufficiency
- Allowed free movement
- Supported by UNHCR
- Lessons we could learn!

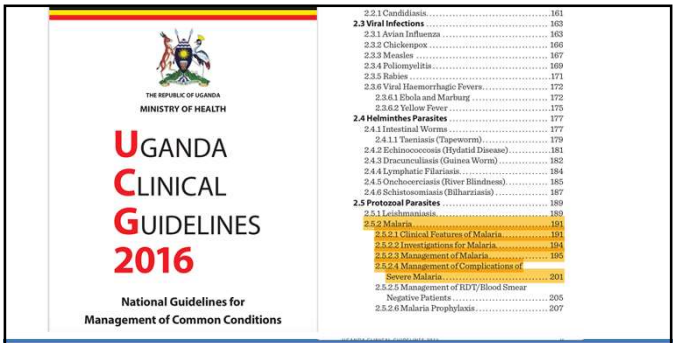
*Source - UNHCR, Government of Uganda, Office of the Prime Minister

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

Adjumani District



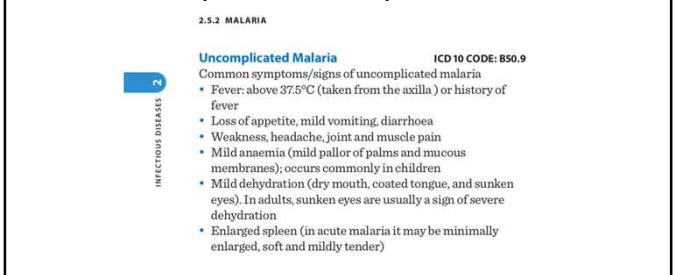


Let's Get to Work! Welcome to Uganda

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

Uncomplicated *P. falciparum* malaria



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/Lumefan

First line alternative
- Artesunate/Amodiaq

Second line medicine
- Dihydroartemisin/ Piperaquine
- If not available: quinine

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

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.

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

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.

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

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

2.5.2 MALARIA

2 INFECTIOUS DISEASES

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 pa medication, then give a f	

Dosage of IM artemether

Artemether		
DOSE	TIME	QUANTITY
First dose: on admission Loading dose	At 0 hours	3.2 mg/kg
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		

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)

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

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

Questions??

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