INMED Humanitarian Health Conference

Tropical Diseases of Significance

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Tropical Diseases of Significance

Malaria

Daunting Challenges With Hopeful Horizons

Background and Experience

- Internal Medicine practice / Hospitalist for 26 years in Colorado Springs
  - Opted for early retirement to pursue more international medical volunteerism as a medical educator, advisor, and consultant

BACKGROUND AND EXPERIENCE *(2 OF 5)*

- 12 years (2010–2022) as Medical Director/Senior Advisor for 10-21 clinics in Haiti after the catastrophic Earthquake
  - Mentored and trained our employed Haitian Medical Teams
  - Supervised the deployment of hundreds of expat Medical Volunteers
  - *Heart to Heart International*, Lenexa, Kansas

BACKGROUND AND EXPERIENCE *(3 OF 5)*

- Lecturer addressing 4 Tropical Diseases for Global First Responders preparing to deploy to Disaster Zones worldwide (2016–2022)
  - Including Malaria presentations
  - *Heart to Heart International*, Lenexa, Kansas

Background and Experience *(4 of 5)*

- Consulting and Teaching in 13 sub-Saharan African countries
  - *Project C.U.R.E.*, Centennial, Colorado, & Kansas City
  - *Nazarene Compassionate Ministries International*, Lenexa, Kansas
  - *Water for Generations,* Denver, Colorado

BACKGROUND AND EXPERIENCE *(5 OF 5)*

- Facilitating the preparations of Medical Volunteers for deployments to clinics on **4** continents with these entities:
  - *Project C.U.R.E.,* Centennial, Colorado, & Kansas City
  - *Rocky Vista University College of Osteopathic Medicine*, Parker, Colo.
  - *Resurrection, A United Methodist Church*, Leawood, Kansas

Session Objectives

- Understand the Epidemiology and some Pathophysiology
- Know the criteria for Diagnosing this widespread tropical disease
- Understand the Triage Criteria for assessing disease severity
- Implement Treatment Options effectively
- Know the Preventive Measures available for yourself and the local population
- [Given the limited time we have tonight, your Handout is much more complete]

DISCLOSURE

There are no relevant financial relationships with ineligible companies to disclose.

OVERVIEW *(1 OF 2)*

- Malaria is the most important parasitic disease of humans
  - It is endemic throughout most of the tropics
- Since 2020, there has been an increase in cases and deaths due to the interruption of services attributable to the COVID-19 Pandemic

OVERVIEW *(2 OF 2)*

- The emergence of partial drug resistance to the primary treatment medication in the African region by the deadliest species, *Plasmodium falciparum,* is of great concern
- Mutations of *Plasmodia* rendering RDTs ineffective must be kept in mind
- Furthermore, increasing reports of *Anopheles* mosquito resistance to pyrethroid insecticides poses additional challenges

Epidemiology/Worldwide Disease Burden *(1 of 2)*

- According to the WHO's World Malaria Report 2025:
  - Almost half of the population of the world – throughout most tropical regions including 80 countries and territories – live in areas at risk of Malaria
  - Marked increase in Malaria cases and deaths reports in 2024
    - ~282,000,000 cases of Malaria occurred worldwide
    - ~610,000+ total deaths (including ~440,000 African Children <5y)

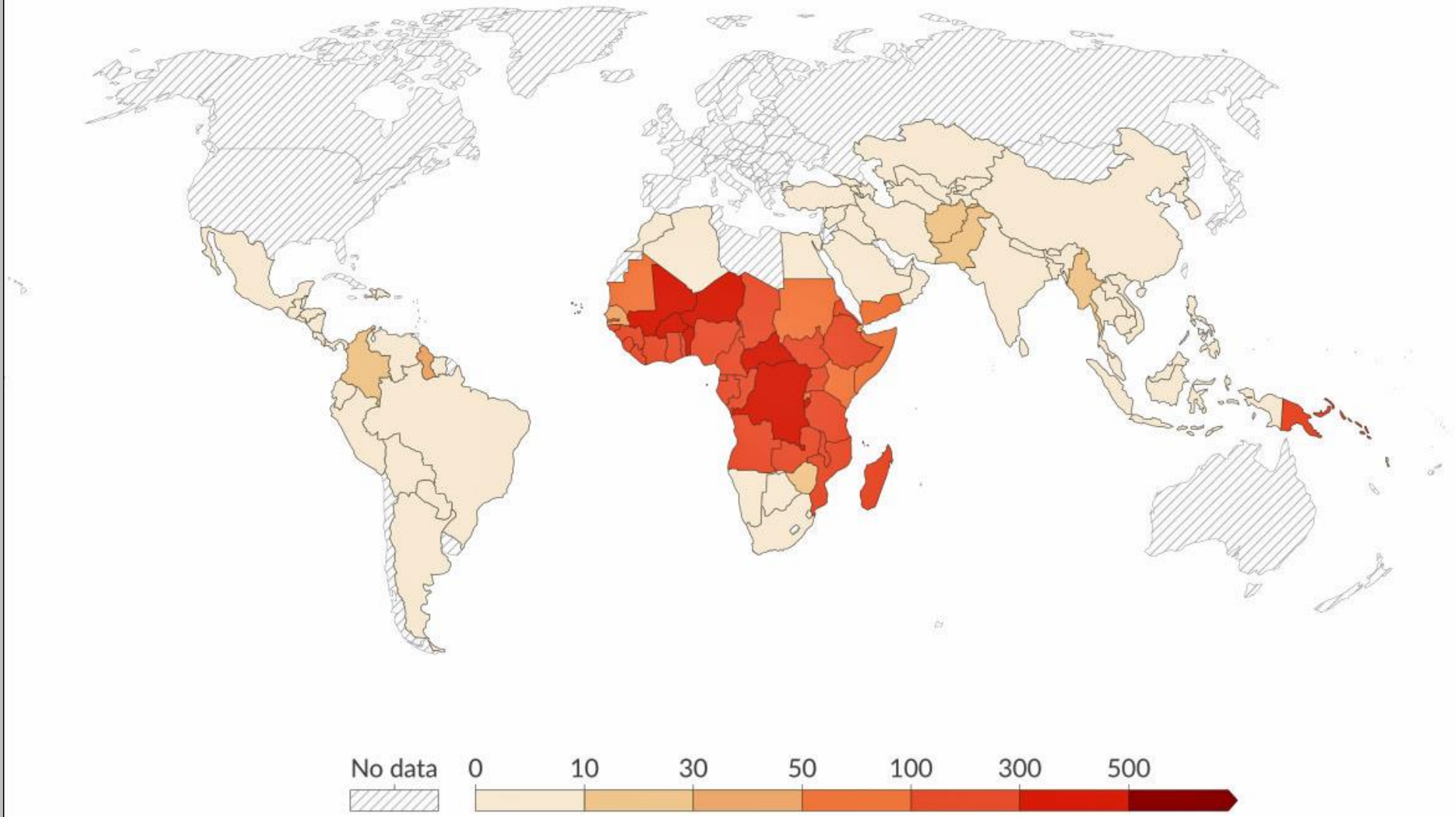
EPIDEMIOLOGY/WORLDWIDE DISEASE BURDEN *(2 OF 2)*

- The WHO Africa Region accounts for 95% of the global burden
  - Where Malaria is also the single leading infectious cause of disability and death for <5y
  - And pregnant women risk profound anemia and low birthweight newborns
- In 2023, the first locally acquired mosquito-transmitted Malaria (*P. vivax*) in 20 years occurred across 4 U.S. states…local transmission is possible!
- **SEE:** Page 14 in your Handout

New cases of malaria per 1,000 people at risk, 2024

Our World in Data

Malaria[1] is a life-threatening disease caused by parasites that are transmitted by certain types of mosquitoes.



Data source: World Health Organization (Global Health Observatory), via World Bank (2026)

OurWorldinData.org/malaria | CC BY

6 Species of Protozoan Parasite *Plasmodium*

- ***P. falciparum***
  - *P. falciparum* is most prevalent worldwide and causes the most serious disease
    - Often simply referred to as "Falciparum Malaria"
  - Predominates throughout Africa, Hispaniola, and Papua New Guinea
  - Multiplies rapidly in the blood potentially causing Severe Anemia
  - May clog small blood vessels in the brain resulting in potentially fatal "Cerebral Malaria" [see below]

PROTOZOAN *PLASMODIUM* (2 OF 6)

- ***P. VIVAX & P. OVALE***
  - ***P. vivax*** ranks second in global disease burden
    - More common in Africa, Asia, South Pacific, and Central & South America
    - ~80% of global ***P. vivax*** is found in just 4 countries:
      - India, Pakistan, Ethiopia, and Sudan

PROTOZOAN *PLASMODIUM* (3 OF 6)

- ***P. VIVAX & P. OVALE*** *(CONT'D)*
  - ***P. ovale*** is found especially in tropical West Africa
  - Adults: only occasionally do these 2 species cause severe disease
  - Children: ***P. vivax*** **&** ***P. ovale*** can cause serious illness
  - ***P. vivax*** **&** ***P. ovale*** can cause late relapses: >80% and ~10% respectively
    - Occurring weeks, months, or even 2–3 years after the initial illness
      - Due to persistent liver stage "hypnozoites" [more to come]

PROTOZOAN *PLASMODIUM* (4 OF 6)

- ***P. MALARIAE***
  - Relatively uncommon outside of Sub-Saharan Africa and Southeast Asia
  - Generally milder clinical disease in most Adults
  - Characterized by years of low-grade asymptomatic parasitemia
    - Unique ability to cause attacks even decades after exposure
  - May (exclusively) cause Nephrotic Syndrome of the kidneys in Children
    - Unless treated aggressively, most die in <2 years

PROTOZOAN *PLASMODIUM* (5 OF 6)

- ***P. KNOWLESI***
  - Originally a Malaria species of primate animals – natural hosts are Macaques
    - Human disease first described in 2004
    - A monkey reservoir may be required
    - Occurs throughout Southeast Asia
    - Most patients have uncomplicated disease, nevertheless,
      - Adults with suspected *P. knowlesi* require hospitalization for management

PROTOZOAN *PLASMODIUM* (6 OF 6)

- ***P. SIMIUM***
  - A Malaria species resembling *P. vivax*
  - Occurs in primates, but also has been found in humans in Brazil

Mosquitoes: The Bane of Human Existence

- An opinion article in the *NYTimes* by Timothy Winegard in 2019 made this unsettling statement:
  - Mosquitoes have, in general, remained the "Apex Predator/Killer" of humans throughout our history!
  - Estimating that 52 BILLION humans have been killed by mosquito-borne diseases!

The Vector – *Anopheles* Mosquitoes *(1 of 2)*

- Globally: ~3,500 species of mosquitoes
  - Including ~430 *Anopheles* species
    - Only 60–70 of which transmit Malaria (i.e. are "vectors")
  - Human Malaria is transmitted only by females of the genus *Anopheles*

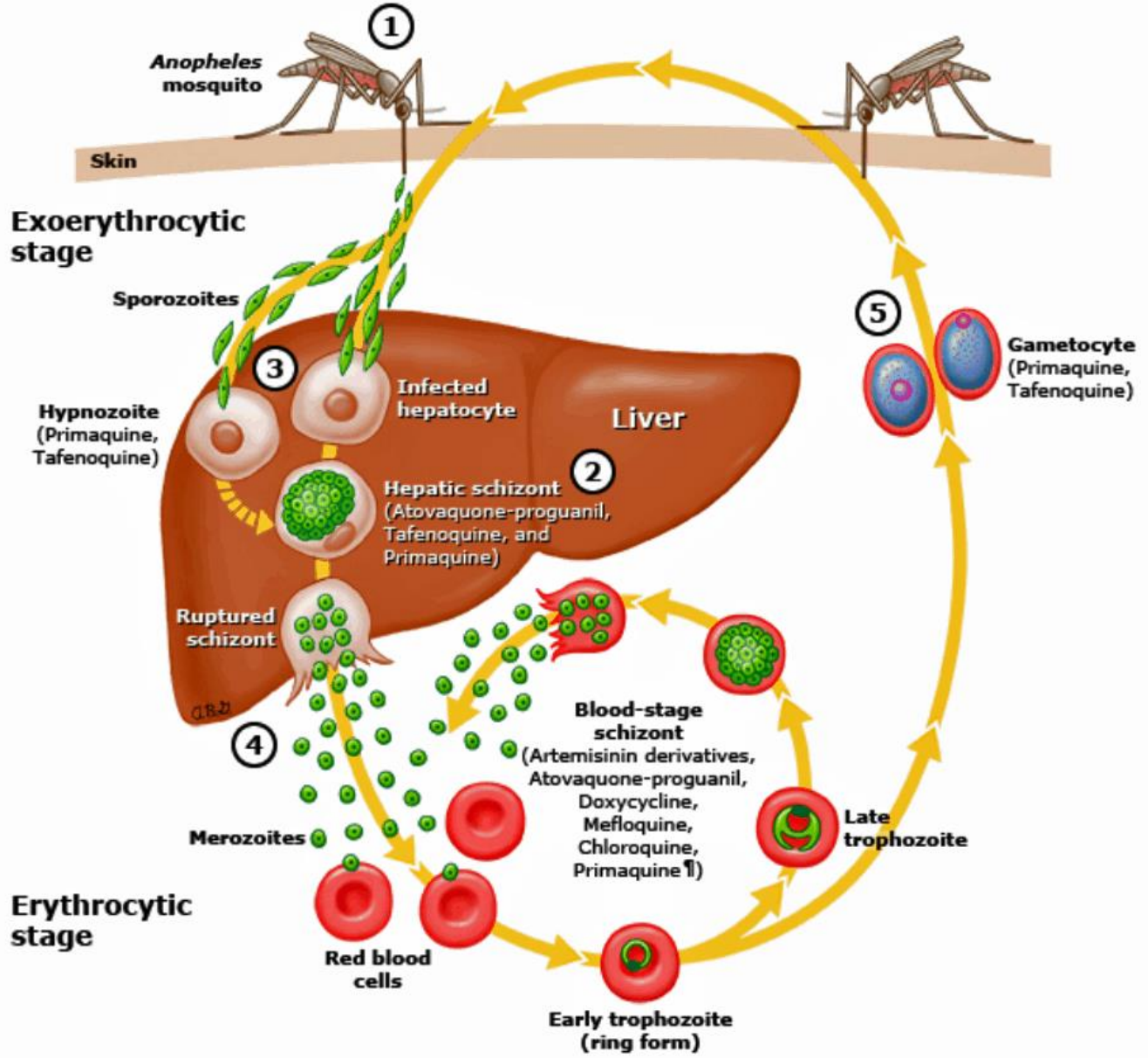
The Vector – *Anopheles* Mosquitoes *(2 of 2)*

- Female *Anopheles* mosquitoes bite from "dusk to dawn",
  i.e., throughout the night
  - ✧ Blood meal is necessary for the female to produce eggs
- Mosquito vector does not suffer from these parasites
- Long lifespan and strong human-biting habits of the African *Anopheles* mosquito vector => 95% of the world's Malaria cases

Life Cycle of the Plasmodium Parasite

- **SEE:** Pages 15–16 in your Handout

Life cycle of *Plasmodium*[*]



Populations at Greater Risk

- Certain population are at considerably higher risk of contracting Malaria and developing SEVERE disease:
  - Children ages 6m–59m
  - Pregnant Women esp. in 2nd & 3rd trimesters
    - With Severe disease: Maternal mortality / adverse fetal outcomes ~50%
  - Patients with HIV/AIDS or other immunocompromised condition
  - Non-immune migrants
  - Mobile populations & Travelers

IMMUNITY *(1 OF 2)*

- Complete immunity does not occur
  - Either "semi-immune" or "non-immune"
- Semi-immunity develops over years of exposure in high-transmission areas, i.e., in Adults
  - Reducing the risk of Severe disease
- Thus, most Malaria deaths in Africa occur in Children <5y

IMMUNITY *(2 OF 2)*

- In areas of less transmission and low immunity: ALL ages at risk
- Local residents who leave high-transmission areas for >6 months lose their semi-immunity => NON-immune!
  - NON-immune persons are highly vulnerable – including SEVERE attacks
- Sickle Cell and Thalassemia significantly lower the Malaria risk

Incubation Period

- The incubation period in most types of Malaria varies from 7–35 days
- Shorter period ~12–14 days is more typical of *P. falciparum*

Classic Malaria Paroxysm *(1 of 2)*

- 3 Stages of the "Classic Malaria Paroxysm"
  - Primarily seen in Adults… but not until several days into the illness
  - The symptoms lasting several hours include:
    - "Cold": shaking chills (with rigors… unlike Typhoid Fever)
    - "Hot": temperature of ≥40°C (104°F), systemic symptoms, "dry" i.e., with minimal or no diaphoresis
    - "Sweating": diaphoresis and fatigue as the fever abates

Classic Malaria Paroxysm *(2 of 2)*

- The ABSENCE of this Paroxysm does NOT rule out a Malaria diagnosis
- With improved early diagnosis and treatment, this traditional description of fever cycles is seen less frequently

"Uncomplicated" Falciparum Malaria *(1 of 3)*

- Symptomatic infection
  - Fever >38.0°C (>100.4°F) or history of fever in the past 48 hrs
  - With or without other symptoms such as nausea & vomiting, diarrhea, headache, back pain, chills, myalgias…
  - Even abdominal pain and bronchitis!
- In whom other obvious causes of fever have been excluded

"Uncomplicated" Falciparum Malaria *(2 of 3)*

- ADULTS
  - Limited, nonspecific findings on Physical Exam:
    - Fever, tachycardia, tachypnea, ill appearance
  - Positive parasitemia <4% (if lab available)
  - Absence of Severe Malaria symptoms [see below]

"Uncomplicated" Falciparum Malaria *(3 of 3)*

- CHILDREN
  - Prominent features include:
    - Fever, generally quite high >40°C (>104°F)
    - General malaise, fatigue, listlessness
    - Gastrointestinal: nausea, vomiting, loose feces
    - Headache

Warning Signs: More Serious Malaria *(1 of 2)*

- In CHILDREN – these are the important Warning Signs:
  - Dehydration (if vomiting and diarrhea are severe)
  - Pallor (from hemolytic anemia)
    - Exacerbated by underlying nutritional deficiencies & intestinal geohelminths
  - Hepatosplenomegaly (may take days to appear)

(Cont'd on the next screen)

Warning Signs: More Serious Malaria *(2 of 2)*

- In CHILDREN *(Cont'd)*
  - Jaundice
  - Respiratory distress (Kussmaul's respirations)
    - May indicate Lactic Acidosis due to Severe Malaria
  - Decreased Level of Consciousness or Seizures
    - May be due to Hypoglycemia [&/or] Cerebral Malaria

Indications for Hospitalization

- The particular patients who may deteriorate rapidly and should be hospitalized include:
  - Young Children
  - Immunocompromised patients
  - Non-immune patients
  - Hyperparasitemia (4–10%) but no signs of Severe infection YET

MANIFESTATIONS OF SEVERE MALARIA

- Definition of "Severe Malaria" at ANY Age:
  - Symptoms like uncomplicated Malaria
  - PLUS parasitemia **>10%** (if lab available)
  - PLUS prostration
  - Associated major signs of organ dysfunction / failure with at least 1 of these:
    - **SEE:** Page 17 in your Handout

Definition of severe falciparum malaria

Manifestations	Definitions
Impaired consciousness	Glasgow coma score <11 in adults or Blantyre coma score <3 in children; inability to swallow
Prostration	Generalized weakness so that a person is unable to sit, stand, or walk without assistance
Multiple convulsions	More than two episodes within 24 hours
Acidosis	A base deficit of >8 mEq/L, a plasma bicarbonate level of <15 mmol/L, or venous plasma lactate ≥5 mmol/L. Clinical indicators of acidosis include rapid, deep, labored breathing.
Hypoglycemia	Blood or plasma glucose <40 mg/dL (<2.2 mmol/L) for children ≥5 years and adults; blood or plasma glucose <54 mg/dL (<3 mmol/L) for children <5 years
Severe anemia	Hemoglobin concentration ≤5 g/dL or hematocrit ≤15 percent in children <12 years of age (<7 g/dL and <20 percent, respectively, in adults) with parasite count >0.25 percent parasitemia
Renal impairment	Plasma or serum creatinine >3 mg/dL (265 mcmol/L) or blood urea >20 mmol/L
Jaundice	Plasma or serum bilirubin >50 mcmol/L (3 mg/dL) with *Plasmodium falciparum* parasite count >2.5 percent parasitemia or *Plasmodium knowlesi* parasite count >0.5 percent parasitemia
Pulmonary edema	Radiographically confirmed or oxygen saturation <92 percent on room air with respiratory rate >30/minutes, often with chest indrawing and crepitation on auscultation
Significant bleeding	Including recurrent or prolonged bleeding (from the nose, gums, or venipuncture sites), hematemesis, or melena
Shock	Compensated shock is defined as capillary refill ≥3 seconds or temperature gradient on leg (mid to proximal limb), but no hypotension. Decompensated shock is defined as systolic blood pressure <70 mmHg in children or <80 mmHg in adults, with evidence of impaired perfusion (cool peripheries or prolonged capillary refill).
Hyperparasitemia	*P. falciparum* parasitemia >10 percent

Severe malaria is defined as one or more of the above occurring in the absence of an identified alternative cause and in the presence of *P. falciparum or P. knowlesi* parasitemia.

Data from:

1. *World Health Organization. Guidelines for the treatment of malaria, 3rd ed. WHO: Geneva 2015. Available at: http://www.who.int/malaria/publications/atoz/9789241549127/en/*
2. *Severe malaria. Trop Med Int Health 2014; Suppl 1:7.*

Cerebral Malaria *(1 of 2)*

- Defined as:
  - Encephalopathy presenting with impaired consciousness, delirium, and/or seizures
- Generally caused by *P. falciparum*
- Onset may be gradual or sudden
- Focal neurologic signs are unusual
- These patients require hospitalization

Cerebral Malaria *(2 of 2)*

- Overall, Children are at much greater risk of developing Cerebral Malaria
- Prognosis:
  - If untreated, Cerebral Malaria is almost 100% fatal
  - With treatment, mortality is 15–20%

Sequelae of Cerebral Malaria

- Adults: Causes permanent neurological sequelae <3%
- Children: Are also at MUCH higher risk of adverse effects
  - E.g., ~50% of 20,000 Kenyan Children with Falciparum Malaria reportedly had neurologic involvement!
  - Persistent cognitive impairment
    - Primarily attention and language problems
    - ~25% of Children persisting even 2 years post episode
  - Significant residual neurologic deficits also reported:
    - Hemiplegia, Cerebral Palsy, Cortical Blindness, Deafness, Epilepsy

Diagnostic Laboratory Tests *(1 of 5)*

- Microscopy
  - Thick smear
    - Considered the "gold standard" for diagnosis
    - But labor-intensive requiring ~40 minutes of Lab Tech time
    - Also requires ongoing training, quality equipment, and electricity!
  - Thin smear – Better for identifying species

Diagnostic Laboratory Tests *(2 of 5)*

- Rapid Diagnostic Tests ("RDTs")
  - Useful alternative if microscopy is not available
    - Results in 10–15 minutes
    - Sensitivity/specificity: *P. falciparum* (>90%), *P. vivax* (>80%)
  - Limitations:
    - Inability to quantify level of parasitemia
    - FALSE positives occur after recent successful treatment

DIAGNOSTIC LABORATORY TESTS *(3 OF 5)*

Rapid Diagnostic Tests ("RDTs") *(Cont'd)*

- **NEW ISSUE:** pfhrp2/3 gene deletions…clinically significant / expanding
  - These *P. falciparum* parasites are undetectable by HRP2-based RDTs

    => **false-negative RDTs!**
    - With potentially lethal clinical consequences
  - Reported in >40 countries
    - Requiring official RDT changes in South American and Horn of Africa

Diagnostic Laboratory Tests *(4 of 5)*

- Other Laboratory Findings:
  - Anemia (due to hemolysis) is seen in prolonged, severe, or recurrent disease
  - Mild leukopenia (3,000–6,000 WBC/µl)
    - IF Leukocytosis is present – consider an alternative diagnosis
  - Hypoglycemia most often found in:
    - Young Children & Pregnant Women => poorer prognosis
    - Severe disease
    - Patients treated with Quinine

Diagnostic Laboratory Tests *(5 of 5)*

- "Hyperparasitemia" recently re-defined as:
  - >2% of RBCs parasitized in low Malaria endemic areas
  - >5% of RBCs parasitized in high Malaria endemic areas

Differential Diagnosis

- Malaria may mimic – or coexist with – other common diseases:
  - Typhoid / Enteric Fever
  - Dengue and other Viral Infections
  - Pneumonia
  - Sepsis due to Bacteremia
  - Meningitis, etc….
- Differentiating Cerebral Malaria vs Meningitis in Children
  - Requires a lumber puncture

Medicines for Treating Malaria

- Chloroquine or Hydroxychloroquine
- Artemisinin from the Qinghaosu plant (China, 4th century)
- Quinine from the Cinchona tree (South America, 17th century)
- Primaquine
- Mefloquine (Lariam®)
- Atovaquone/Proguanil (Malarone®)
- Sulfadoxine/Pyrimethamine (Fansidar®), also abbreviated "S/P"
- Amodiaquine (not available in the U.S.)

Counterfeit Anti-Malarial Drugs

- There is an alarming prevalence of counterfeit antimalarial drugs
  - 30–50% in multiple countries across Southeast Asia
- Africa also has increasing evidence of counterfeiting & poor-quality drugs
  - Esp. those purchased outside the formal healthcare system
- This criminal behavior requires more attention

TREATMENT OF UNCOMPLICATED MALARIA *(1 OF 11)*

- **CHLOROQUINE**: First-line therapy in limited Chloroquine-sensitive areas
  - I.e., without known drug resistance including:
    - Caribbean: Haiti, Dominican Republic
    - Mexico
    - Central America: West (and north) of the Panama Canal Zone
    - Middle East: Historically some areas of the Arabian Peninsula

TREATMENT OF UNCOMPLICATED MALARIA *(2 OF 11)*

- **CHLOROQUINE** *(Cont'd)*
  - Orally as Tablets [or] Suspension in divided doses over 3 days
  - Safe for use throughout pregnancy
- **HYDROXYCHLOROQUINE**
  - Tablets are slightly different strength
  - Dosage schedule and regional limitations are the same

TREATMENT OF UNCOMPLICATED MALARIA *(3 OF 11)*

- **ARTEMISININ DERIVATIVES**:
  - First-line therapy in Chloroquine-resistant regions (i.e., most of the world)
  - Oral, parenteral, and rectal formulations – very well tolerated
  - Effective against MOST Chloroquine-resistant *P. falciparum* [more to come]
  - Should **not** be used as monotherapy (risk of developing resistance)
  - Not used for prophylaxis (due to short half-lives)

TREATMENT OF UNCOMPLICATED MALARIA *(4 OF 11)*

- **ARTEMISININ DERIVATIVES *(Cont'd)***
  - Preferred fixed-dose combination for oral therapy:
    - Artemisinin Combined Therapy ("ACT")
      - WHO recommends these ACTs (depending on local resistance data):
        - Artemether + Lumefantrine (taken after a full meal or milk; special issues >65kg – **SEE:** your Handout for details)
        - Artesunate + Mefloquine
        - Artesunate + Amodiaquine
  - First-trimester Pregnancy: ACTs are the second choice

TREATMENT OF UNCOMPLICATED MALARIA *(5 OF 11)*

- Reducing Transmissibility with low-dose **PRIMAQUINE**
  - Gametocytes may persist in the blood after successful treatment with ACT or Chloroquine
    - Serve as a source of ongoing transmission (via new mosquito bites)
    - WHO recommends Primaquine 0.25 mg/kg single dose on Day#1
      - Exceptions: Avoid for Pregnant Women and Infants <6m
  - Recent studies: G6PD testing NOT required for a low-dose treatment protocol

TREATMENT OF UNCOMPLICATED MALARIA *(6 OF 11)*

- **TAFENOQUINE** (Krintafel™, Arakoda™)
  - Was FDA-approved in 2018 for 2 indications:
    - Curative treatment for *P. vivax* Malaria
    - Malaria prophylaxis in non-pregnant individuals ≥16y
  - Requires only a single dose
    - HOWEVER, requires G6PD testing before use

TREATMENT OF UNCOMPLICATED MALARIA *(7 OF 11)*

- **MEFLOQUINE** (Lariam®)
  - Effective against Chloroquine- and S/P-resistant *P. falciparum* and *P. vivax*
  - Side effects: neuropsychiatric problems, vomiting, diarrhea
  - Contraindications: 1st trimester pregnancy, neuropsych, or cardiac issues
- **ATOVAQUONE/PROGUANIL** (Malarone®)
  - Effective in Chloroquine-resistant *P. falciparum* and *P. vivax*
  - Excellent safety but expensive and requires fatty meal
  - Not approved in pregnancy

TREATMENT OF UNCOMPLICATED MALARIA *(8 OF 11)*

- **SULFADOXINE/PYRIMETHAMINE** (Fansidar®) "S/P"
  - Used for suspected Chloroquine resistance
  - *P. falciparum* resistance is increasing
  - Avoid in 1st trimester and last 2 weeks of pregnancy (due to sulfa content)

- IF POSSIBLE:
  - Should not use the same or related drugs to treat a patient's episode of acute Malaria that had recently already been used for prophylaxis

Treatment of Uncomplicated Malaria *(9 of 11)*

- **QUININE SULFATE** (esp. IV; but only PO formulation available in U.S.)
  - Primarily reserved for resistant or Severe Malaria, becoming second-tier agent
  - Highly effective but not well tolerated
  - Typically used in combination with an antimalarial antibiotic
    - E.g., Doxycycline, Tetracycline, or Clindamycin
  - Side effects may include:
    - Cinchonism (tinnitus, hearing loss, nausea, vomiting)
    - Hypoglycemia (thus, must administer in D10W = 10% Dextrose in Water)
    - Cardiac arrhythmias

Treatment of Uncomplicated Malaria *(10 of 11)*

- In the U.S., 3 Malaria treatment choices are currently available:
  - Artesunate IV
    - 2020: FDA-approved
    - 2024: CDC guidelines: use for Severe Malaria of ALL Plasmodium species
  - Artemether–Lumefantrine – preferred follow-on PO treatment (but if >65kg…)
  - Atovaquone–Proguanil
- Monitoring and Follow-Up
  - With appropriate treatment, fever and parasitemia should resolve within 2–4 days…but if not…

Treatment of Uncomplicated Malaria *(11 of 11)*

- Please Note:
  - Dosages of these medications are not included in this presentation
  - Readily available at UpToDate® or in the most recent WHO publication which was updated in August 2025
    - **SEE:** Reference #4 in your Handout for this latest information

TREATMENT OF SEVERE FALCIPARUM MALARIA *(1 OF 2)*

- Severe Malaria is a medical emergency requiring urgent ICU treatment
- Parenteral, i.e., IV or IM antimalarials are preferred:
  - WHO treatment of choice: Artemisinin derivatives parenterally (vs Quinine)
  - Especially Artesunate:
    - This is the preferred treatment for ALL Adults and Children with Severe Falciparum Malaria
    - Administer for ≥24 hrs
    - Thereafter, give a complete course of oral ACT treatment

TREATMENT OF SEVERE FALCIPARUM MALARIA (*2 OF 2*)

- Exchange transfusions are explicitly no longer recommended in the CDC's 2024 guidelines

- FYI: PRE-Referral intramuscular administration of Artemisinin derivatives can be potentially life-saving in Severe Malaria in Adults
  - Rectal suppositories ONLY if <6y

RESISTANCE OF *P. FALCIPARUM* (1 OF 2)

- "Antimalarial Resistance"
  - Defined as ≥3 days of persistent parasitemia despite proper treatment and compliance
- Artemisinin *Partial* Resistance (ART-R) WHO-confirmed in East Africa
- Mefloquine Resistance overlaps with Quinine Resistance: SE Asia & Africa
- Atovaquone-Proguanil Resistance – occasional reports

RESISTANCE OF *P. FALCIPARUM* (2 OF 2)

- Encouraging News:
  - Researchers reported an entirely new compound class = 1st in 25 years
    - Labeled the Imidazolopiperazine (IZP) class
    - Late 2025: Ganaplacide-Lumefantrine (GanLum – Novartis) Phase 3 – good!
      - Effective against drug-resistant Falciparum Malaria
      - Approval / licensing expected in 2026

Treatment of NON-Falciparum Malaria *(1 of 2)*

- Chloroquine in the preferred first-line in MOST areas
- However, *P. vivax* Chloroquine resistance is reported
  - Esp. in Oceania and Indonesia
    - Instead, use ACT + Piperaquine, Lumefantrine, or Mefloquine

TREATMENT OF NON-FALCIPARUM MALARIA *(2 OF 2)*

- *P. vivax* and *P. ovale* : Need to ADD full-dose Primaquine
  - Used to eradicate parasites (hypnozoites) from the liver
    - But only after testing for G6PD Deficiency (risk of severe hemolysis)
    - Never use Primaquine in Pregnancy (cannot test the fetus for G6PD)
- RECENTLY: Rapid POC (<5 min.) G6PD spot test from a fingerstick blood sample
- Severe NON-Falciparum Malaria should be treated as if *P. falciparum* regardless of the causative species

PREVENTION – PUBLIC HEALTH *(1 OF 4)*

- WHO: Vector (mosquito) control is the primary method of reducing and preventing Malaria transmission
- WHO: Progress is threatened by emerging resistance to insecticides
  - Now reported in >100 countries
  - New insecticidal agents are in the pipeline…

Prevention – Public Health *(2 of 4)*

- 3 forms of vector control: 2 current / 1 future
  - (1) Indoor residual spraying (IRS) with effective insecticides
    - Reaches its full potential when >80% of houses are sprayed
    - Remains effective for 3–6 months

PREVENTION – PUBLIC HEALTH *(3 OF 4)*

- (2) Long-Lasting Insecticidal Nets (LLINs)
  - The preferred mosquito bednets for public health
  - Netting is impregnated with Pyrethroids, etc. by manufacturer
    - Vis-à-vis UNtreated bednets…of minimal benefit
  - Pyrethroids generally kill any mosquito that comes in contact
    - However, as Pyrethroid resistance is surging in sub-Saharan Africa
    - WHO recommends PBO-treated bednets or other newer insecticides
  - **SEE:** Proper Care of LLINs in your Handout

Prevention – Public Health *(4 of 4)*

- (3) Genetic Engineering for Control – Future
  - Entails using male *Anopheles* mosquitoes to introduce genetic factors:
    - Prevent the eggs from hatching, or
    - Prevent larvae from surviving, or
    - Produce adult insects incapable of transmitting human disease
- Despite years of intense investigation, the optimal approach remains uncertain

Prevention – Prophylactic Treatment

- Intermittent Preventive Treatment (IPT) in-country
  - Useful for reducing the risk of Malaria among high-risk individuals
    - Esp. Pregnant Women
- Monoclonal Antibodies – novel approach published in *NEJM* in 2022
  - May be useful against antimalarial resistance or for immunocompromised individuals

Prevention – Travelers & Volunteers *(1 of 3)*

- Chemoprophylaxis
  - Mefloquine weekly – usually for trips >4 weeks
  - Atovaquone-Proguanil daily – for trips <4 weeks
  - Doxycycline daily (only in those non-pregnant persons and >8y)
  - If a Chloroquine-sensitive region: Chloroquine weekly

PREVENTION – TRAVELERS & VOLUNTEERS *(2 OF 3)*

- Must combine chemoprophylaxis with the use of "personal protective measures" including:
  - Long sleeves, long pants, and socks
  - Sleeping in a mosquito-free setting or using an insecticide-treated bednet
  - Repellants: e.g., DEET 30–50% (Pregnancy & Breastfeeding – OK)
  - Permethrin, etc. pre-treated or sprayed onto clothing (never onto skin)

PREVENTION – TRAVELERS & VOLUNTEERS *(3 OF 3)*

- Travelers to malarious areas must understand:
  - Compliance with these prophylactic measures is essential
  - However, NO chemoprophylaxis/personal protective regimen guarantees 100% protection
  - Be advised: Fever during or after travel to a malarious area is a medical emergency requiring urgent medical attention

PREVENTION – VACCINES *(1 OF 3)*

- RTS,S/AS01 a.k.a. **"RTS,S"**
  - Falciparum Malaria vaccine from GSK, et al.
  - FINALLY approved by WHO (2021) after 30 YEARS of R&D
  - FIRST-EVER vaccine approved against ANY parasite in world history!!
  - 4-dosage schedule for African Children ages ≥5m
    - But only ~30% reduction in Severe/deadly Falciparum Malaria

PREVENTION – VACCINES *(2 OF 3)*

- Second vaccine: R21/Matrix-M a.k.a. **"R21"**
  - Reporting >75%(!) efficacy against Falciparum Malaria in Young Children
  - WHO recommended and prequalified this vaccine in 2023
  - Now deployed in 17 African countries with routine childhood immunizations

PREVENTION – VACCINES *(3 OF 3)*

- Other Malaria vaccine candidates are under investigation including:
  - mRNA-based vaccine strategies

Reasons to Expect Improving Trends

- Factors that contribute toward reducing Malaria:
  - More sensitive diagnostic tools
  - Effective use of antimalarial drugs
  - Improved personal and community protection
  - Better vector (mosquito) control
  - Deployment of new Malaria vaccine(s)

Progress to Elimination

- Because there are no non-human reservoirs for the human Plasmodia
  - Malaria is a candidate for global eradication
- Efforts towards elimination are continually expanding worldwide
  - Countries reporting ZERO indigenous cases and officially WHO-certified as Malaria-free are increasing
    - From 2010 to 2025: the initial report of 15 countries is now at 47!

Information Resources

Please see your Handout for details

Tropical Diseases of Significance

THANK YOU!