433 Teams

MEDICINE

23 | Malaria and Travel

433medicine.team@gmail.com

جامعة الملك سعود
King Saud University

COLOR INDEX

Slides - Step-Up medicine - Kaplan Notes - Extre explanation - Doctor Notes

Epidemiology:

- Endemic disease
- Usually does not occur at altitudes – 1500 m
- World wide ease of travel
- Most important parasitic disease of humans
- Transmitted in over 100 countries
- Affecting more than 3 billion people world wide
- Causing 1-2 billion deaths per year
- Prevalent in Tropical Climates, Parts of Africa and Middle East.
- Transmitted Via Mosquito Bite.

Etiology:

-Plasmodium Falciparum.
-Plasmodium Vivax.
-Plasmodium Ovale.
-Plasmodium Malariae.

P.falciparm most important plasmodia → associated with the majority of the complications.

Pathogenesis:

- Plasmodium Falciparum >>Invades RBC of All Ages.
- Plasmodium Vivax >> Invades Only young RBC's.
- Plasmodium Ovale>>Invades Young RBC's.
- Plasmodium Malariae>>Invades Old RBC's
- Microvascular pathology: secondary Ischemia& Adherence of Non-deformable parasitezed RBC to endothelium.
- Renal failure: hemalysis, Ischemia secondary to microvascular pathology.
- Deep Coma: hypoglycemia, microvascular adherent parasitized RBC
- Pulmonary edema; Secondary to: Capillary leak Syndrome (without C.C.F.)
- Immune Complex Nephrotic Syndrome Secondary to P. Malariae

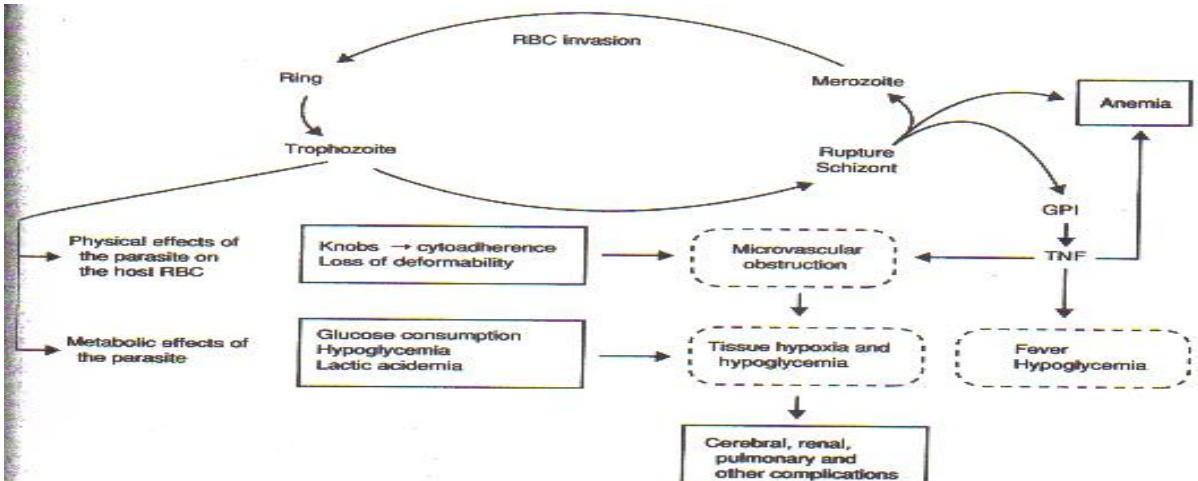
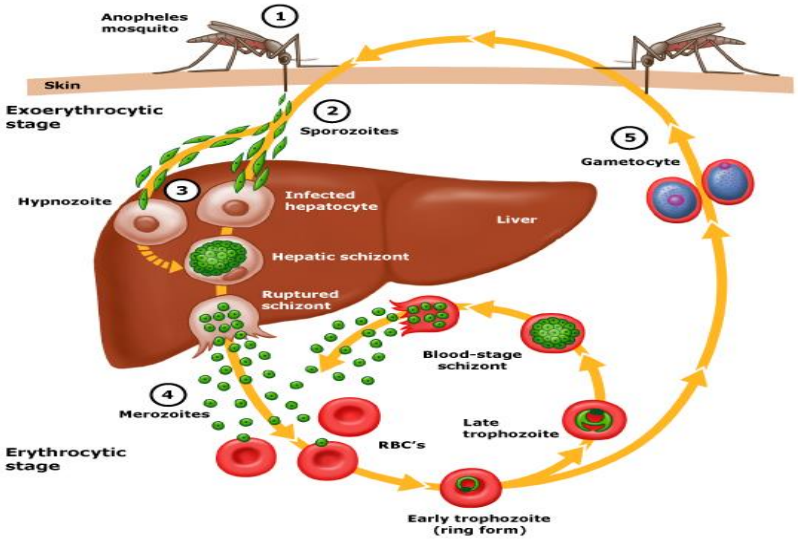
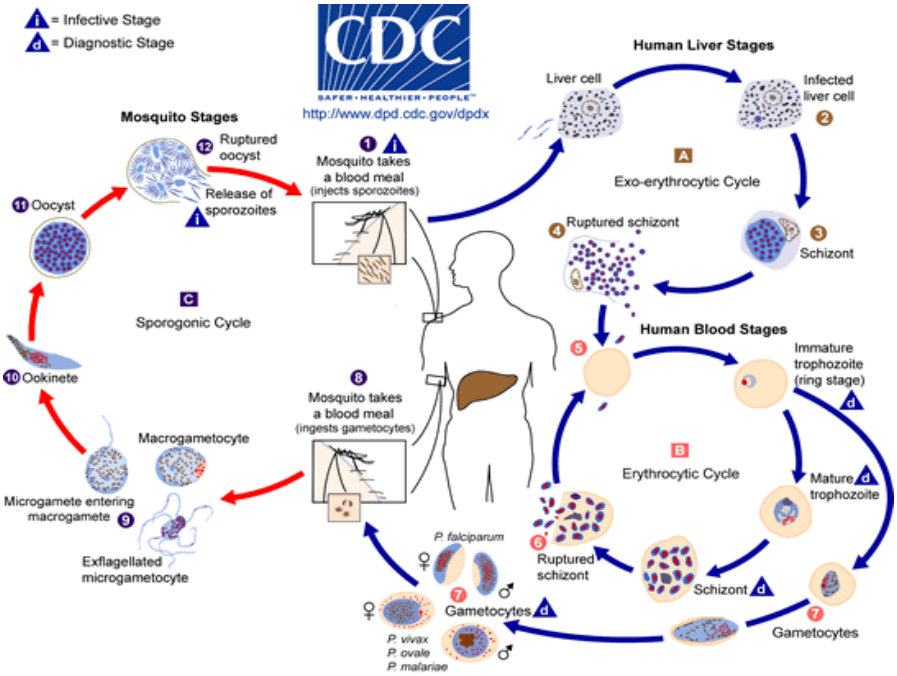


FIG. 4. Pathogenesis of severe, complicated, and cerebral *P. falciparum* malaria. *Plasmodium falciparum* malaria is a microvascular disease with a strong metabolic component. It is a microvascular disease because cytoadherence of *P. falciparum*-infected RBCs to endothelial cells in capillaries and postcapillary venules,[8–10] plus the nondeformable nature of those cells[37,40] produces functional microvascular obstruction. Cytokines such as TNF-α contribute to the process by enhancing expression of receptor molecules on the endothelial cell surface[20,21] and thus further increasing cytoadherence and obstruction to flow. It is a metabolic disease because consumption of glucose and production of lactate by the parasite plus the hypoglycemic effects of TNF-α (and possibly IL-1 and TNF-β)[25] and treatment with quinine (or quinidine)[22,23] all contribute to glucose deprivation, lactate excess, and acidemia at the tissue level. Anemia results acutely from RBC lysis as schizont stage parasites mature, and chronically from the effects of TNF-α.[26] Recent studies have shown that rupture of schizont stage parasites exposes glycosylphosphatidylinositol (GPI) anchors on the parasite and RBC surface that elicit TNF-α and thus explain why the asexual erythrocytic cycle stimulates the release of TNF-α[22,23] in the absence of the gram-negative endotoxin previously associated with the release of TNF-α from macrophages.[24]

incubation Period and Life Cycle:

- Sporozoites reach the liver within 1-2 hours following female Anopheles mosquito bite.
- Patient asymptomatic for 12-35 days until RBCs stage of parasite life cycle.





Clinical Features:

- Fever, Chills, Mylagias, Headache, Nausea, Vomiting and Diarrhea.
- Fever Patterns:

1. P.Falciparum >> Usually Constant, Non-regular or hectic especially In non- immune
2. P.Vivax & P. Ovale >> Spikes Every 48 Hr
3. P. Malariae>> Spikes Every 72 Hr

Malaria Paroxysm:

- Paroxysms associated with synchrony of merozoite release
- Between paroxysms temperature is normal and patient feels well
- Falciparum may not exhibit classic paroxysms (continuous fever)
    1. Rigors, Headache associated with pale cold skin(1-2 Hr)
    2. Delirium, Tachypnoea, Hot Skin(Several hours)
    3. Fever (Marked sweating and fatigue)

Diagnosis:

- Detailed targeted history including travel History and clinical examination together with High Index of Suspicion (HIS)
- Serology: not useful in managing acutely ill patient
- DNA probe: similar thick film sensitivity
- Infection with more than one parasite spp: 5-7%

Blood Film :

- Usually done by Giemsa or wright's stain
- Correct identification of malarial Species is essential for treatment because of P.Falciparum Resistant to Chloroquine & other Drugs
- On Giemsa stain – Cytoplasm: light blue, nucleus: dark blue
- In P. Falciparum:
    1. Only ring stage a sexual parasite and gametocytes seen in periph. Blood.
    2. While RBC with Trophozoites or Schixonts stage – sequestered in peripheral, Microvasculature, and NOT circulating P-blood.
- All asexual erythrocytic stages of P. Vivax, Ovale & malariae circulate in peripheral blood, thus seen on Blood Smear
- Accutly Ill Patient : Differential Diagnosis is P. Falciparum Or P.Vivax
  Because:
    1. P. Ovale – Vivax – clinical, morphological
    2. P. malariae - chronic Infection.

Thin blood film

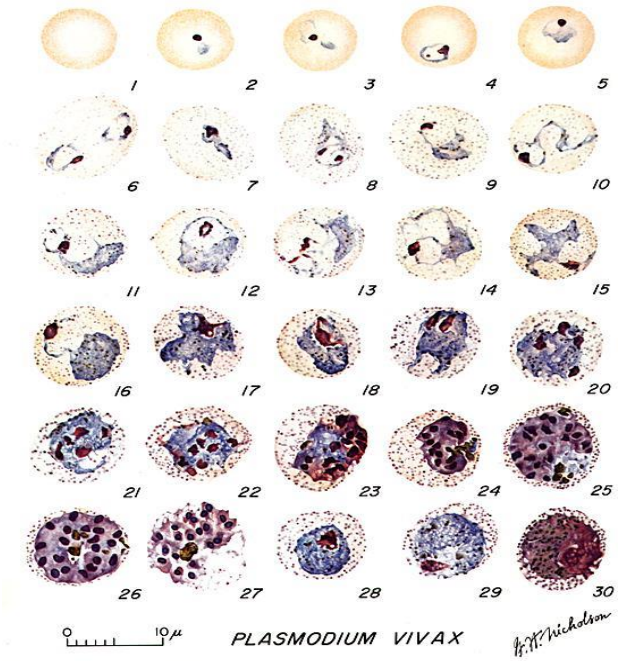
- RBC morphology preserved
- P. Vivax; infected RBC
- RBC enlargement with parasite maturation
- Scuffner's dots (eosinophilic dots in RBC cyto.)
- May see Maurer's clots in RBC eytoplasm

Thick blood film

- RBC lysed
- You may examine 10X. Blood more than in thin film
- More diagnostic in lower degree of parasitemias

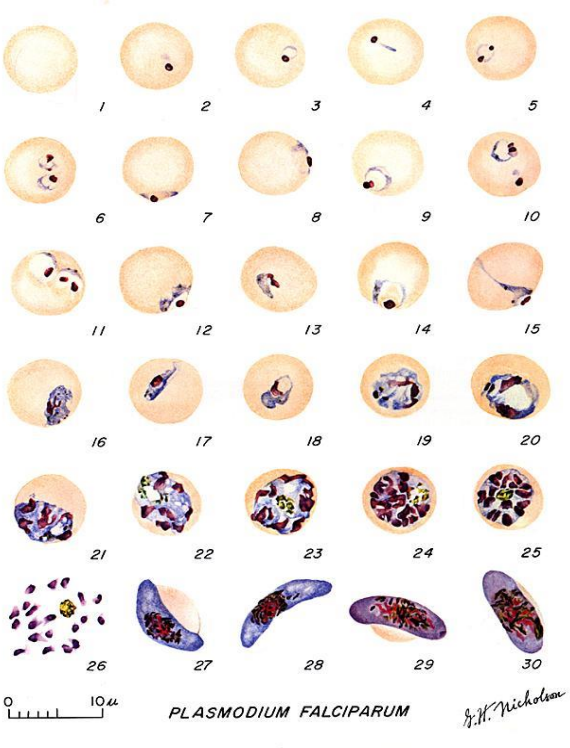
P. vivax: Blood Stage Parasites Thin Blood Smears

1: Normal red cell
2-6: Young trophozoites (ring stage parasites)
7-18: Trophozoites
19-27: Schizonts
28,29: Macrogametocytes (female)
30: Microgametocyte (male)



P. falciparum: Blood Stage Parasites Thin Blood Smears

1: Normal red cell
2-18:Trophozoites (2-10: ring-stage trophozoites)
19-26: Schizonts (26 is a ruptured schizont)
27, 28: Mature macrogametocytes (female)
29, 30: Mature microgametocytes (male)



P. ovale: Blood Stage Parasites Thin Blood Smears

1: Normal red cell

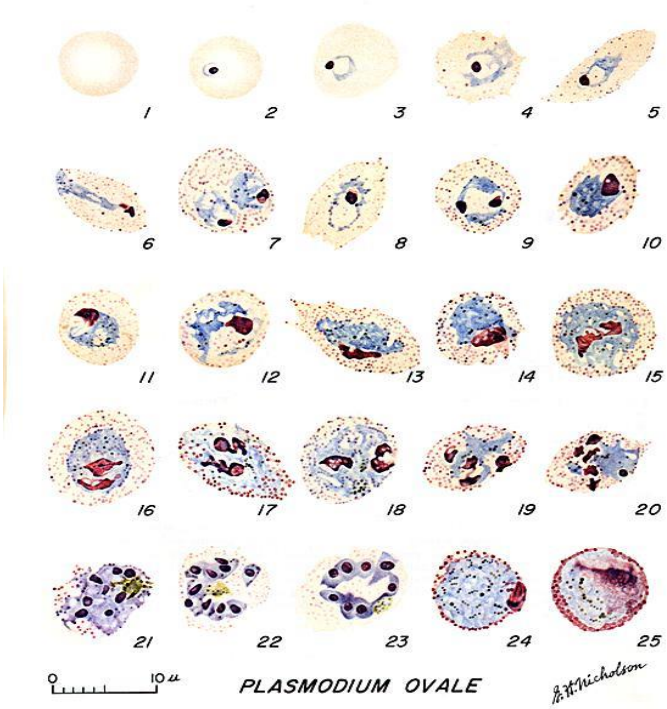
2-5: Young trophozoites

6-15: Trophozoites

16-23: Schizonts

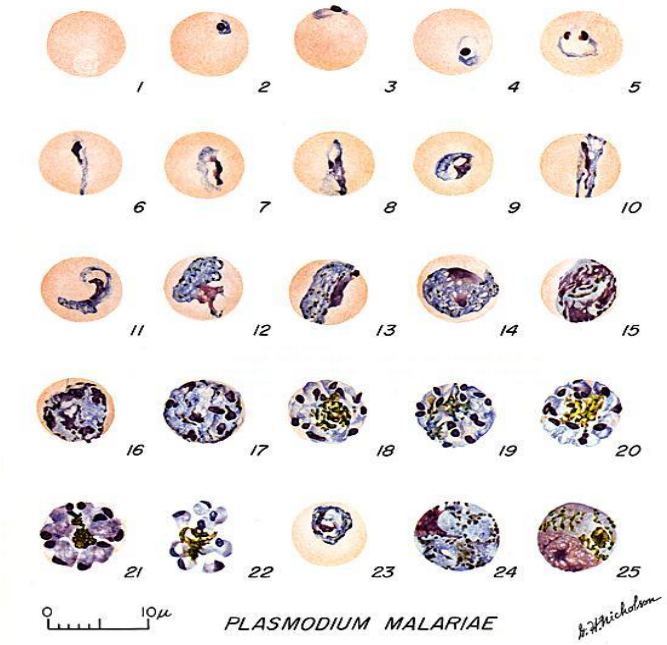
24: Macrogametocytes (female)

25: Microgametocyte (male)



P. malariae: Blood Stage Parasites Thin Blood Smears

1: Normal red cell
2-5: Young trophozoites (rings)
6-13: Trophozoites
14-22: Schizonts
23: Developing gametocyte
24: Macrogametocyte (female)
25: Microgametocyte (male)



Differential Diagnosis of Malaria in Acutely ill Patients Based on P.B. Smear

	P. Falciparum	P. Vivax/P. Ovale
Multiply Infected RBC	Common	Rare
Mature (Trophozoite and schizont) parasites	Absent	Common
RBC enlargement with later parasite stages	Absent	Common

- Mature (trophozoites & schizont) stage P. falciparum. Typically sequestered in the peripheral microvasculature.
- RBC enlargement in P. vivax typically occurs with later stage parasites that do not circulate in P. falciparum infection.

Malaria Complications :

- Majority of complications (apart from anemia) associated with P. falciparum
- Mild unconjugated jaundice common, and parallels hemolysis. Hepatocellular dysfunction may contribute to jaundice.

❖ Anemia

presents in most severe infections and parallels parasitaemia

- Hemolysis of infected RBC
- Delayed retics. release from BM
- Immune – mediated hemolysis of non-infected RBC

❖ Non-immune:(primary infection)

- Haemoglobinuria
- Black water fever
- Exaggerated haemolytic response to quinine – sensitized RBC

❖ Tissue hypoxia related complications

- Hypoxia results from altered microcirculation + anemia.
- Maturation of erythyrocyte schizonts in P. falciparum takes place in tissue capillaries and venules.
- P. falciparum parasitized RBC sequestered in micro circulation because:

1. Altered deformability of parasitized RBC
2. Adhesion involving parasite – derived proteins within RBC and glycoproteins on vascular endothelium.

❖ Cerebral Malaria

- Most severe common complication

RISK FACTORS FOR POOR PROGNOSIS IN CEREBRAL MALARIA

✓ **increase bilirubin → hepatic cirrhosis**
✓ **increase Creatinine → Renal failure**
✓ **increase Lactate → Lactic acidosis**
✓ **any patient presnts with one of the above should be admitted**

❖ Renal Failure

- Most severe common complication
- ATN
- Dehydration
- Hypotension
- Hypervescosity

❖ Pulmonary Edema

- ARDS – may complicate acute phase of severr malaise. Fluid overload may contribute.

❖ Hypoglycemia

we should correct the glucose level before starting the treatment for malaria

- Glucose consumption
- Lactic acidosis
- Quinine/quinidine --- increase insulin secretion

❖ Bleeding

- Thrombocytopenia
- Consumption coagulopathy
- Shock: Endotoxemia

❖ Diarrhea

❖ Hyponatremia (? SIADH)

❖ LATE COMPLICATION

- Tropical splenomegaly in P. Falciparum endemic areas.
- N. syndrome with P. malariae.
- Burkett's lymphoma (PF - EBV)

Malaria and Pregnancy

- Mortality
- Anemia, hypoglycemia, pulmonary edema: > common
- Abortion
- Stillbirth
- Premature delivery high infant mortality
- LB wt.
- Placental insufficiency
- High parasitaemia - placenta favorable site for P.falciparum.

Congenital Malaria

- Transplacental infection
  - Can be all 4 species
  - Commonly *P.v.* and *P.f.* in endemic areas
  - *P.m.* infections in nonendemic areas due to long persistence of species
- Neonate can be diagnosed with parasitemia within 7 days of birth or longer if no other risk factors for malaria (mosquito exposure, blood transfusion
- Fever, irritability, feeding problems, anemia, hepatosplenomegaly, and jaundice
- Be mindful of this problem even if mother has not been in malarious area for years before delivery

Malaria and Hemoglobinopathies

- Heterozygous sickle cell train children less likely to contract P. falciparum
- C.S. disease: no such protection, rather mortality is higher > normal
- Thalassemics: partially protected (? Fetal Hb)
- G-6-phosphatase RBC : less prone to P. falciparum.

Risk Factors for Poor Prognosis

- High Creatinine
- High Bilirubin
- High Lactates

Treatment

1. Use chloroquine phosphate unless resistance is suspected. In many countries, chloroquine resistance is so prevalent that it should be assumed.
2. If chloroquine resistance is suspected, give quinine sulfate and tetracycline. Alternative agents are atovaquone–proguanil and mefloquine.
3. *P. falciparum* infection may require IV quinidine and doxycycline.
4. Relapses can occur in *P. vivax* and *P. ovale* infection as a result of dormant hypno- zoites in the liver. Add a 2-week regimen of primaquine phosphate for these types of malarial infection.
5. Prophylaxis is important for travelers to endemic regions. Mefloquine is the agent of choice in chloroquine-resistant areas. Chloroquine can be used in areas where chloroquine resistance has not been reported.

Uncomplicated P falciparum infection :

- Artemether-Lumefantrine or,
- Atovaquone-proguanil or,
- Quinine or,
- Mefloquine.

Uncomplicated Plasmodium malariae, Plasmodium knowlesi, or chloroquine-sensitive P falciparum infection:

- Chloroquine phosphate or,
- Hydroxychloroquine.

Uncomplicated P vivax or P ovale infection, expected to be chloroquine-susceptible:

- Chloroquine phosphate or,
- Hydroxychloroquine.

Acutely ill patient usually vivax of ovale, however if it is unknown treat as p.falciparm

Resistance Patterns

- Chloroquine-resistant P falciparum:Eastern Hemisphere: All of sub-Saharan Africa, Saudi Arabia, Yemen, Iran, Pakistan, Afghanistan, China, Nepal, and all of Southeast Asia Western Hemisphere: Panama, Haiti, Brazil, Peru, Bolivia, Colombia, Venezuela, Ecuador, French Guiana, Guyana, and Surinam

- Chloroquine-sensitive P falciparum:Eastern Hemisphere: Turkey, Iraq, Syria, Georgia, Azerbaijan, Tajikistan, Turkmenistan, and Kyrgyzstan Western Hemisphere: Argentina, Paraguay, Mexico, Guatemala, Costa Rica, Honduras, Nicaragua, El Salvador, and Dominican Republic

- Mefloquine-resistant P falciparum:Southeast Asia: Regions of Vietnam, Laos, Thailand, Burma, and Cambodia

- Chloroquine-resistant P vivax:Papua New Guinea and Indonesia

Complicated Malaria

- Quinidine gluconate 10 mg/kg loading dose over 1-2h, then 1.2 mg/kg/h for at least 24h
- Once parasitemia is < 1% and patient can take oral medication, switch to quinine 650 mg PO TID to complete 3-d course (7-d course if malaria was acquired in southern Asia)
- In addition, give doxycycline 100 mg IV or PO BID for 7d.
- For pregnant women, instead of doxycycline, give clindamycin 20 mg base/kg/day PO divided TID for 7d

Chemoprophylaxis

- Atovaquone-proguanil
- Chloroquine phosphate
- Doxycycline
- Mefloquine
- Primaquine

Other Methods in treating Sever Malaria

1-Antibodies against TNF - α they Decrease fever, No effect on mortality & morbidity, Why ?

- Effects of other cytokines as IL – 1, TNF- β
- On pathogenesis of complicated severe malaria

2) Steroids:
   - Harmful by controlled trials
   - Dexamethasone longer duration of coma + worseoutcomes than patient receiving quinine alone.
3) Reducing mosquito – human contact
4) Malaria vaccine

MCQs

A businessman traveling around the world asks about prevention of malaria. He will travel to India and the Middle East and plans to visit several small towns. What is the most appropriate advice for the traveler?

a. **Common sense measures to avoid malaria such as use of insect repellants, bed nets, and suitable clothing have not really worked in preventing malaria.**

b. The decision to use drugs effective against resistant P falciparum malaria will depend on the knowledge of local patterns of resistance and the patient's very specific travel plans.

c. Prophylaxis should be started the day of travel.
d. Chemoprophylaxis has been proven to be entirely reliable.
e. He should stay inside at the noon as this is the mosquito's peak feeding time.

The answer is b. (Fauci, pp 1291-1293.) Whether or not to use drugs such as atovaquone-proguanil, mefloquine, or primaquine for resistant P falciparum will depend on knowledge of specific local patterns of drug sensitivity of plasmodia. Specific information can be obtained from the CDC malaria hotline or the CDC emergency operation center. The common sense measures described are extremely important and part of the overall worldwide plan to contain the spread of malaria. Prophylaxis should begin 2 days to 2 weeks before departure in order to have adequate levels of drug on arrival and to identify potential side effects before leaving. Chemoprophylaxis is not entirely reliable, and malaria should always be in the differential diagnosis of a febrile illness in a traveler to endemic regions, even if the drug regimen has been faithfully followed. Mosquito peak feeding periods are dawn and dusk.

Done by

Abdulaziz alsudairi	Albatoul alsuhaibani
Yzeed alharbi	**Fisal alghamdi**
Faroq Abdulfattah	Areej Alwahaib