Microscopic Diagnosis of Malaria

• **False positives:**
  – Microscopist with limited experience
  – Not familiar with thick smear technique
  – Artifacts on slide

• **False negatives:**
  – Low parasitemias
  – Misdiagnosis - Pf (+) but called Pv or mixed Pf / Pv
P. falciparum

- Ring form trophozoites are major stage
- Banana-shaped gametocyte definitive, but rare
- Most infected RBC's are normal size
- Never see schizonts or mature trophozoites unless very high parasitemia
- Multiply infected RBCs, including >2/cell, common and pathognomonic
- Parasitemia may be high in very severe cases (all age RBCs infected)
- Accolé/appliqué forms are characteristic
Non Microscopic Diagnosis

Rapid Diagnostic Tests (RDT) are now standard

- **Binax NOW** most common and only assay US FDA approved
  - All assays are not created equal, many available OCONUS do not meet stricter US standards for sensitivity and specificity

- **Detects** *P. falciparum* & *P. vivax* (or general *Plasmodium* spp)
  - Immunochromatographic membrane
  - Monoclonal Pf HRPII antibodies
  - Monoclonal pan-malaria aldolase
Rapid Diagnostic Tests
aka RDTs or Hand Held Assays

Pros:
• Doesn't require lab or pathologist skilled with making or reading blood smears
• Allows for faster diagnosis when microscopy not available

Cons:
• Results must be confirmed by microscopy
• Not widely available in hospital or clinic labs
• Limited information on species is given
• Does not determine percent parasitemia
• Unreliable in patient with recent history of malaria. May remain positive up to 1 month after treatment.
• Some strains of *P. falciparum* have lost the HRP2 antigen which is one of two antigens targeted by the Binax RDT, leading to false negatives

WHO Malaria RDT Performance 2012:
http://apps.who.int/iris/bitstream/10665/77748/1/9789241504720_eng.pdf
Fastidious Diagnostic Approach

Don’t fall into the “negative smear” trap

- Thick and thin Giemsa-stained blood films
  - Diagnosis - thick blood films are sensitive
  - Species identification - thin films increase ability to determine species

- Calling a smear “negative”
  - Must examine at least 200 oil immersion thick fields
  - Threshold of 10 parasites per µl (approx 0.0002%)

- Repeat every 8-12 hrs for 24-48 hrs
  - *P. falciparum* infected red cells may remain sequestered in microcirculation of deep organs for first 18 - 24 hrs of erythrocytic stage cycle
Fastidious Diagnostic Approach

Parasite Count

Important for clinical classification (severity)

• Quantitative
  • Count = # parasites per 200 WBC
  • # parasites per µl = count per WBC count per µl
    – Standard 8000 WBC/µl
  • % Parasitemia = # parasites per µl/RBC per µl x 100%
    – Standard 5.4 million RBC per µl for males
    – Standard 4.8 million RBC per µl for females

• Semi-quantitative
  • + 1-10 parasites per 100 thick film oil immersion fields
  • ++ 11-100 parasites per 100 fields
  • +++ 1-10 parasites per 1 thick film field
  • ++++ >10 parasites per 1 thick film field
Parasitological Classification
Role in Determining Therapy and Setting

• Species
  – *P. falciparum* clearly the highest priority, most cases in Africa
  – *P. vivax, P. ovale* - relapse prevention

• Geographic origin of the infection
  – Knowledge about drug sensitivity

• Blood smear results (regardless of clinical picture)
  – Density >5% = hyperparasitemia
  – Malaria pigment in >5% neutrophils = severe
  – Pf mature stages >0.2% = grave prognosis
    • Presumed mixed infection blunder
Case Categorization
New, treatment failure, relapse ???

• New infection vs treatment failure

• Relapse
  – Reappearance of asexual parasitemia after elimination
  – Delayed maturation of hypnozoites in the liver
    • *P. vivax* - months - 5 yrs (usually less than 1 year)
    • *P. ovale* - months - 5 yrs (usually less than 1 year)

• Recrudescence
  – Reappearance of detectable asexual parasitemia due to persistence of asexual erythrocytic stage at undetectable level
    • *P. falciparum* - days - 2 yrs
    • *P. malariae* - days - 50 yrs
Clinical Classification

Patients demonstrating any of the following are defined as severe/complicated malaria

- Obtundation, unarousable, coma
- Confusion, psychosis, delirium
- Decerebrate or Decorticate posturing
- Opisthotonos
- Focal neurologic deficits
- Recurring generalized seizures (≥ 3/24 hrs)
- Persistent focal seizures
- Prolonged hyper/hypothermia
- Hi output vomiting or diarrhea
- Pregnancy (especially primigravida)

- Parasitemia ≥5% (percent RBCs infected)
- Severe anemia (Hgb < 7 g/dL or rapid \(\downarrow\))
- Hypoglycemia (Glu < 60 mg/dL)
- Renal failure (Cr > 3 mg/dL)
- Hepatic dysfunction (ALT or Alk P > 3x nl)
- Acidosis (serum bicarb < 15mmol/dL or venous lactate > 45 mg/dL)
- Pulmonary edema
- Algid malaria (shock)
- Spontaneous bleeding (DIC or \(\downarrow\) plt)
- Massive intravascular hemolysis (hemoglobinuria and TB > 2.5 mg/dL)
- Splenic rupture
Severe Malaria

Poor Prognostic Signs

Clinical
- Impaired consciousness
- Repeated convulsions (>3 in 24 h)
- Respiratory distress
  - (rapid, deep, labored breathing or ARDS)
- Substantial bleeding
- Shock

Biochemical
- Renal impairment (Cr > 3 mg/dl)
- Acidosis (plasma bicarbonate, < 15 mmol/L)
- Jaundice (serum total bilirubin, >2.5 mg/dl)
- Hyperlactatemia (venous lactate, >5 mmol/L)
- Hypoglycemia (blood glucose, <40 mg/dl)
- Elevated Aminotransferase levels (>3 times ULN)

Hematological features
- Parasitemia >500,000 parasites/mm³, or >10,000 mature trophozoites and schizont/mm³
- >5% neutrophils contain malaria pigment
Cerebral malaria

Dangerous development in falciparum malaria

• More common in children 3-5 yo but can occur at any age
  – Knobs resulting in cytoadherence and microvascular sequestration
  – Microvascular obstruction of capillaries and venules
  – Seizures or coma

• 15-30% morality
  – 10-20% permanent neurological damage
Cerebral Malaria

• Unarousable coma in patient with asexual stage parasitemia and no other cause

• Potential confounders (CNS effects)
  – Fever
  – Hypoglycemia

• 90% deaths preceded by coma

• 20% mortality in tertiary setting
Cerebral Malaria

• Immobile
• Flailing
• Posturing (decerebrate/decorticate/opisthotonos)
• Recurrent generalized or persistent focal seizures
• Ocular findings
  – Ophthalmoplegia
  – Nystagmus
  – CN VI palsy
  – Corneal, pupillary, oculocephalic, oculovestibular reflexes abnormal (children)
• Upper motor neuron findings > LMN
Poor Prognostic Signs

• Deep coma
• Repeated seizures (> 3 in 24 hours)
• Respiratory distress
• Heavy bleeding
• Shock
• Mature asexual stage Pf parasites
Seizures

• **Must determine etiology**
  - Hypoglycemia (monitor BGs, D5NS + D50)
  - Febrile seizures (antipyretics, PR Tylenol)
  - Cerebral malaria (recurrent and prolonged)

• **Fluid management critical for children (↑ ICP)**
  - Elevate head of bed
  - Osmotic diuretics (mannitol), hyperventilation, corticosteroids without proven efficacy

• **Anticonvulsants**
  - Generally not necessary if etiology hypoglycemia or fever and controlled
  - IV or PR benzodiazepines
  - Prophylactic phenobarb not recommended
Other Complications

• Pulmonary edema
  – Portends grave outcome
  – Associated with hyperparasitemia
  – Normal PCWP with microcapillary leak
  – Treat as ARDS

• Aspiration pneumonia

• Hypotension/shock (IVF, RBCs, vasopressors)
  – Postural hypotension common
  – If pronounced, suspect
    • Gram-negative sepsis (aspiration and urinary tract)
    • Pulmonary edema
    • Metabolic acidosis (hydrate, correct electrolyte abnormalities)
    • GI hemorrhage
    • Splenic rupture
Other Complications

• Severe anemia
  – HCT < 15-20 and >10,000 parasites/µl
  – Hemolysis and BM suppression
  – Indications for transfusion
    • HCT <20% (variable depending on patient)
    • Rapidly falling HCT
  – PRBCs only (plasma → fluid overload)

• Obstructive jaundice (direct hyperbilirubinemia)
  – Poor prognostic sign

• DIC
  – Treat infection
  – Heparin not recommended
Oliguric Renal Failure

• Determine etiology
  – Hypovolemia (fluid and BP management)
    • Dx based on Is & Os, BUN/Cre ratio >20, PCWP
    • Consider fluid challenge 200ml over 5-20 minutes
      – If hemodynamics improve with little change in PCWP, continue fluid bolus
      – If marked increase in HR and increase in PCWP >5 and little improvement in hemodynamics, risk pulmonary edema with little impact on renal perfusion (consider cardiac inotropes dopamine 2-5 µg/kg/min)
  – ↓ renal capillary blood flow due to hyperparasitemia
  – Hemaglobinuria due to intravascular hemolysis

• If ATN develops with ARF (Cr > 5)
  – Hemodialysis (may last up to 6 weeks)
  – Frequently associated with DIC and ARDS
Hypoglycemia

• Measure on admission
  – Coma associated with serum glucose < 40mg/dL
  – Dextrose can reverse coma prior to initiation of antimalarials

• Exacerbated with quinine/quinidine

• Increased risk with pregnancy & hyperparasitemia

• Monitor glucose q 2-4 hrs

• Treatment
  – 1 AMP D50 + 10% dextrose over 4 hrs, then D5 if BG > 60
  – Glucagon (SQ, IM, IV)
    • > 20kg - 1mg
    • < 20kg - 30µg/kg
Treatment Goals

• Rapidly reduce asexual parasite burden with blood schizonticide
• Minimize complications and adverse events
• Achieve clinical and radical cure
  – Avoid agents with known resistance in region
  – Prevent recrudescence (Pf and Pm) - second agent
  – Prevent relapse (Pv and Po) - primaquine

Uncomplicated falciparum malaria
Oral treatment options are best

– Artemether-lumefantrine (*Coartem*)
  • 80mg Artemether /480mg Lumefantrine
  • 4 tabs, repeat 8 hours later, then 4 tabs po BID for 2 days = 6 doses

– Artesunate-amodiaquine (*Coarsucam or ASAQ*)
  • 100mg artesunate/270mg amodiaquine
  • 3 tabs qd for 3 days = 3 doses

– Atovaquone-proguanil (*Malarone*)
  • 1000 mg Atovaquone/400 mg proguanil
  • 4 tabs qd x 3 days = 3 doses

– Quinine sulfate and doxycycline
  • Quinine 650 mg q 8 hr x 3-7 days + Doxycycline 100 mg bid x 7 days

– Mefloquine
  • 1250 mg single dose (5 tablets)
  • or 750 mg initial and 500 mg 12 h later to minimize side-effects
Artemether/Lumefantrine

*Coartem* tablets (20/120mg)

- Rapid reduction in parasite density
- Food improves absorption
- Dose 4 tabs po q 8h x 2 then bid, total 6 doses
  - Pediatric dosing 1 tab for 5-15kg, +1 each 10kg
  - Pregnancy category C

- Side effects
  - HA, anorexia, dizziness, asthenia, myalgias, arthralgias (>30%)

- Contraindications
  - Known QT prolongation
  - Concomitant use with drugs that prolong QT
  - Hypokalemia or hypomagnesemia
  - Concomitant CYP3A4 inhibitors (grapefruit)
Artesunate-amodiaquine
Coarsucam or ASAQ tablets (100/270 mg)

- Rapid reduction in parasitemia
- Easiest regiment of the ACTs for pediatrics
- Infants and children: 1 tab qd for 3 days, can be dissolved in water
- Adolescents and adults: 2 tabs qd for 3 days
- Side effects:
  - Hepatotoxicity
  - Agranulocytosis
  - Avoid with efavirenz in HIV as increased liver toxicity
Atovaquone/Proguanil

Malarone

- 1 tablet = 250mg atovaquone/100mg proguanil or 62.5mg/25mg
- Ingestion with food or milk improves absorption.
- Repeat dose if vomiting occurs within 1 hour
- Dose (adults)
  - 4 tablets po qd x 3 days
- Dose (children)
  - 5-8kg: 125/50mg po qd x 3 days
  - 9-10kg: 187.5/75mg po qd x 3 days
  - 11-20kg: 250/100 mg po qd x 3 days
  - 21-30kg: 500/200 mg po qd x 3 days
  - 31-40kg: 750/300 mg po qd x 3 days
  - >40kg: adult dose
- Extremely well tolerated (mild GI upset and CNS effects)
Quinine Sulfate
Oral Dosing for uncomplicated malaria

• 648 mg (10mg/kg) po TID x 7-10 days
  – Rarely used alone because of high recrudescence
  – Cinchonism poorly tolerated over time
    • Tinnitus, high-tone deafness, n/v, dysphoria

• Quinine x 3-4 days in combination with:
  – Tetracycline 250mg (5mg/kg) TID X 7D
    • Contraindicated in pregnancy and in children under 8
  – Doxycycline 100mg (2mg/kg) BID X 7D
    • Contraindicated in pregnancy and in children under 8
  – Clindamycin 10mg/kg BID X 7D
Mefloquine

*Lariam*

- Easy dosing, lots of experience with it’s use
  - Adults: 1000-1250 mg po x 1
  - Peds: 20-25mg/kg po x 1
  - Dosing with food increases absorption
  - Repeat full dose if vomits within 30 min, 50% if 30-60 min

- Minor side-effects
  - GI disturbance
  - Insomnia
  - Dizziness
  - Vivid dreams
  - Headache

- Contraindications
  - Known hypersensitivity
  - Cardiac conduction abnormalities
  - Neuropsychiatric disorders
    - Seizure disorders
    - Affective disorders and psychoses

- Pregnancy (safe 2nd and 3rd trimester, probably 1st)
Severe Malaria
IV Therapy

• Artesunate:
  – 2.4 mg/kg loading dose over 5 minutes repeat 12 hours later and once daily for 3 days
  – PO when clinically stable: 4 mg/kg qd x3 days (with mefloquine or clindamycin)

• Artemether:
  – 3.2 mg/kg IM then 1.6 mg/kg daily x 3 days
  – PO when stable at 2.0 mg/kg/daily (with 2\textsuperscript{nd} drug)

• Quinine hydrochloride:
  – Loading dose 20 mg/kg then 12 mg/kg q 8h for 7 days
  – PO when stable 650 mg q 8h to complete 7 days (with 2\textsuperscript{nd} drug)

Rosenthal. *Artesunate for the Treatment of Severe Falciparum Malaria* NEJM 358;17
www.nejm.org 2008
Pre Referral Treatment

In Patients with Severe Malaria

• If complete treatment for severe malaria is not possible, patients should be given pre-referral treatment and referred immediately to an appropriate facility for further treatment.

• The following are options for pre-referral treatment:
  – rectal artesunate
  – quinine IM
  – artesunate IM
  – artemether IM

• In children <5 years of age, the use of rectal artesunate (10 mg/kg) reduces risk of death and permanent disability.
Parenteral Quinine

• Quinine dihydrochloride dose
  – IV: loading dose of 20 mg/kg salt over 4 hours, followed by 10 mg/kg over 2-8 hours every 8 hours until improved and able to convert to oral
    • Optimal plasma level: (10-15 mg/l)
    • Cardiac monitoring required with h/o CV disease
  – IM: 20mg/kg bolus then 10mg/kg split dosing q 8hrs or 10 mg/kg q 4 hours X 3 doses then q 8 hours until able to convert to oral
  – PR (children): 20mg/kg in 2ml H$_2$O, then 15mg/kg q 8 hrs as effective as IM or IV, similar Pk, simpler, fewer adverse events
Management of complicated cases

• **Control glucose**
  – Fatal hypoglycemia can occur especially in children

• **Carefully manage fluids** and watch for development of ARDS 24-48 hours AFTER parasitemia clears and patient appears to be improving

• **Monitor/manage**- acidosis, seizures, pulmonary edema and renal failure
Severe Malaria

ICU Care

• Nursing in lateral decubitus position
• Frequent suctioning for comatose patient
• Hydration
  – Avoid overhydration → pulmonary edema
  – Avoid underhydration → hypotension and renal insufficiency
  – Is and Os (hourly, urinary catheter)
  – CVP monitoring (maintain at 5cm H2O)
• Fingerstick blood glucose q 4hrs
  – Especially on quinidine/quinine
• Electrolyte balance (Na, K, Cl, Mg, CO2, BUN, Cr q 8 -12h)
• Maintain Temp <38.5°C (antipyretics, cooling blankets, etc.)
• Monitor for respiratory distress and potential causes
  – Pneumonia/pulmonary edema (CXR daily or clinical change)
  – Metabolic acidosis (ABG)
Exchange Blood Transfusion (ET)

- First introduced 1979
- Recent case series/case control studies
  - 30-60% parasitemia reduced to <1% within 24 hrs after ET with full recovery
  - 18% parasitemia reduced to <1% with full recovery
  - Similar death rates with ET (2/9) compared to no ET (3/12) but for parasitemia >30%, death rate much lower for ET (0/4) vs no ET (3/3)
  - 35-80% parasitemia reduced to <1% within 24 hrs after ET with recovery
- Meta-analysis
  - No difference in survival but only evaluated 8 studies and ET groups had much higher parasitemia than no ET groups

Riddle et al., CID, 2002
Exchange Transfusions
The jury is still out

• Consider exchange transfusion if:
  – Significant hyperparasitemia (typically > 15%)
  – No response to antimalarials in 24-48 hours with persistent elevated parasitemia

• Survival has been reported with parasitemia > 50% without exchange transfusion

• Availability and safety of PRBCs in Africa may limit this as an option
Assessment of Parasitological Response

• Parasitemia may increase during the 6-12 hours after initiation of therapy

• Parasitemia should be reduced by 75% within 48 hours. If not:
  – Inappropriate therapy
  – Inadequate drug absorption
  – High level drug resistance
Optimal treatment of malaria requires:

- Rapid case identification
- Rapid clinical and parasitological classification
- Initiation of therapy to rapidly reduce, and then eliminate parasitemia based on the clinical or parasitological classification
- Recognition and treatment of recrudescence and relapse
- Initiation of supportive and ancillary therapy based on clinical or parasitological classification
- Recognition of inadequate clinical or parasitological response to therapy and development of complications, and initiation of appropriate therapy
Treatment in Pregnancy

Scant data for most newer drugs

• First Trimester:
  – uncomplicated falciparum malaria should be treated with quinine plus clindamycin for seven days (and quinine monotherapy if clindamycin is not available).
  – Artesunate plus clindamycin for seven days is indicated if this treatment fails.
  – Mefloquine, atovaquone/proguanil, sulfa/pyrimethamine and ACTs can be used if other drugs are not available and have NOT demonstrated fetal harm.

• Second and Third Trimesters:
  – ACT or artesunate plus clindamycin to be given for 7 days or
  – quinine plus clindamycin to be given for 7 days
Malaria in Pregnancy

Special precautions

WHO recommendations for malaria in pregnant women:

- use of long-lasting insecticidal nets (LLINs)
- in areas of stable malaria transmission of sub-Saharan Africa, intermittent preventive treatment (IPT) with sulfadoxine-pyrimethamine
- prompt diagnosis and effective treatment of malaria infections.

In high-transmission settings:

- levels of acquired immunity tend to be high, infection usually asymptomatic
- parasites may be present in the placenta and contribute to maternal anaemia even in the absence of documented peripheral parasitemia.
- Both maternal anemia and placental parasitemia can lead to low birth weight.
- most pronounced for women in their first pregnancy

http://www.who.int/malaria/areas/high_risk_groups/pregnancy/en/
Malaria in Pregnancy
Low-transmission settings

• relatively little acquired immunity to malaria
• malaria in pregnancy is associated with:
  – Anemia
  – an increased risk of severe malaria
  – may lead to spontaneous abortion, stillbirth, prematurity and low birth weight.
• In such settings, malaria affects all pregnant women, regardless of the number of times they have been pregnant
Intermittent Preventive Treatment in pregnancy (IPTp) with Sulfadoxine-Pyrimethamine (SP)

• Recommended only in sub Saharan Africa

• In areas of stable (moderate-to-high) malaria transmission, IPTp with SP is recommended for all pregnant women at each scheduled antenatal care visit. In particular:
  – The first IPTp-SP dose as early as possible during the 2\textsuperscript{nd} trimester
  – Each dose should be given at least 1 month apart and up to time of delivery
  – The last dose of IPTp can be safely administered late (after 36 weeks) in the 3\textsuperscript{rd} trimester of gestation
  – IPTp should be administered as directly observed therapy (DOT)
  – SP can be given on an empty stomach
  – Folic acid at a daily dose ≥5 mg should not be given concomitantly with SP as this counteracts its efficacy as an antimalarial
  – SP is contraindicated in women receiving TMP/SMX prophylaxis for HIV

• HIV infected women are more likely to have problems with malaria during pregnancy and should be focused on

Malaria Prevention in Infants
Intermittent Preventive Therapy (IPTi)

- Passive maternal immunity against malaria wanes by 3 months

WHO recommendations for the prevention and control of malaria in infants:
- use of long-lasting insecticidal nets (LLINs);
- intermittent preventive therapy for infants (IPTi) in areas of moderate to high transmission in sub-Saharan Africa;
- prompt diagnosis and effective treatment of malaria infections.
- SP-IPTi reduces clinical malaria, anemia and severe malaria in infants in the first year of life
- Dose SP-IPTi at routine vaccination for 2\textsuperscript{nd} and 3\textsuperscript{rd} doses of DTP/Penta3 and measles vaccination at 8-10 weeks, 12-14 weeks, and ~9 months of age

WHO. 2011. *Intermittent preventive treatment for infants using sulfadoxine-pyrimethamine (SP-IPTi) for malaria control in Africa: implementation field guide*
Malaria Pitfalls in Africa

Items to Consider

• **Malaria masquerades as other diagnoses**
  – Dengue, chikungunya, African tick typhus overlap in many areas
  – Populations with high prevalence may not be having their current sx caused by their malaria infection
  – Patients from endemic areas who have had multiple bouts often know when they have malaria again

• **Trust but verify. Lab results may be spurious:**
  – Malaria smears are notoriously overcalled as positive due to poorly trained technicians, poor quality stains and inadequate microscopes
  – Rapid Diagnostic Tests increasingly available but many have inferior sensitivity and specificity. Some are complicated and may be prone to error.

• **Counterfeit antimalarials are a scourge and very common**
  – If a patient does not respond (or partially responds) to therapy consider poor quality drugs BEFORE you think resistance
Malaria Prevention

• Take advice from local physicians with a grain of salt

• Personal Protection Measures (PPMs) to prevent mosquito bites
  – Bed nets (factory impregnated with insecticide)
  – Repellents (25% DEET or Picaridin)
  – Permethrin impregnated clothing

• Chemoprophylaxis
Anti-malarial chemoprophylaxis

US FDA approved

- Chloroquine - weekly
  - *Aralen®*

- Mefloquine - weekly
  - *Lariam®*

- Doxycycline - daily

- Atovaquone/Proguanil - daily
  - *Malarone®*

- Primaquine - daily
  - Not FDA approved but CDC reco
# Antimalarial Prophylaxis

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<th>Mefloq</th>
<th>Doxy</th>
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<td><strong>Start</strong></td>
<td>1-2 wk</td>
<td>1-2wk</td>
<td>1-2d</td>
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<td><strong>End</strong></td>
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<td>3-7d</td>
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Mefloquine

*Lariam*

- Once weekly dosing is the main advantage
  - Half life 3 weeks!

- CNS side effects are common but also over emphasized in lay press
  - 90% of patients have no or minimal side effects
  - Children have fewer side effects than adults

- Only drug FDA approved for use in pregnancy and breast feeding
  - Best data in 2nd and 3rd trimester but 1st appears safe as well

- Should not be used in those with seizure disorder or psychiatric illness (stable depression probably probably okay)

- Problems in those with baseline cardiac conduction defects especially QT prolongation or in combination with other QT drugs (macrolides and quinolones)

- If patients have unacceptable side effects then change to an alternative
**Doxycycline**

- May photosensitize some
- GI intolerance, especially reflux is common
  - take with food and not at bedtime
- Adherence is the major issue
  - a single missed dose can lead to malaria
  - 4 weeks post travel
- No resistance reported
- Broad spectrum activity:
  - rickettsia, lepto, bacteria mycoplasma, chlamydia
- Generics are inexpensive
- Not in pregnancy and peds <8 yo

**Atovaquone/Proguanil**

*Malarone*

- Well tolerated combination
- Very efficacious even with occasional missed doses
- Causal activity (i.e. kills hepatic schizonts)
  - 5-7 days post-travel
- No geographic considerations for resistance (yet)
- Optimal choice for short term (2-3 weeks) travel
- Prohibitively expensive
- Not approved in pregnancy but probably okay in 2nd and 3rd trimesters
Relapsing *P. vivax* malaria

**Hypnozoites are different**

- Use of chloroquine, mefloquine, doxycycline, or atovaquone-proguanil will not prevent relapsing *P. vivax* malaria.

- Only weight appropriate dose of primaquine will prevent *P. vivax* relapse.
  - Primary prophylaxis
  - Radical cure
  - Preventive Anti-Relapse Treatment (PART)

- Generally not used in Africa due to the prevalence of falciparum vs vivax and ovale.
Primaquine for Pv and Po
“Preventing Relapse”

• Tropical strains relapse more commonly/rapidly
  – Asia/Pacific - 72-100% within 2wks-5months
  – Korea - 32% in 4-6 months
  – India - 9-19% in 12 months
  – Overall worldwide 5%

• Dosing based on Korean War observations
  – Total dose of 200mg key to cure
  – 30mg base qd X 14d
  – 45mg base qwk X 8wks

• Check G6PD levels before administration
  – Normal (B+ or African A+) - standard dose
  – Mild deficiency (African A-) - dose 45mg (0.8mg/kg) q wk X 8wk
  – Severe deficiency (Mediterranean/Asian)- not rec
G6 PD Deficiency

• **Protects RBCs from oxidants**
  – 2 predominant types of deficiency in US population (total of over 200 variants found)
  – Severe deficiency is fully expressed in males and rare in females

• **G-6-PDA**
  – ~12% of African-American Males (~1% females)
  – 50% decline of baseline activity in 13 days (normally takes 60 days)
  – Young RBCs have normal enzyme activity

• **G-6-PDMED**
  – **Rare** - found in Greeks, Sardinians, Sephardic Jews, Arabs and other males of Mediterranean descent
  – 50% decline of baseline activity in 1-2 days
  – All RBCs have deficient enzyme activity
Malaria Summary

• Add malaria to the differential dx for almost any condition you are evaluating

• Since it is so common in MTU it is often overdiagnosed, so conversely, keep other dx in mind when you are told a patient has malaria

• Be careful to assess for evidence of severe malaria and be prepared to treat those complications

• Focus on pregnant women and children <5 yo

• Learn what your lab can actually do and how reliable the results are

• Be aware of the prevalence of counterfeit drugs
Thanks for your attention!

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