

# Malaria

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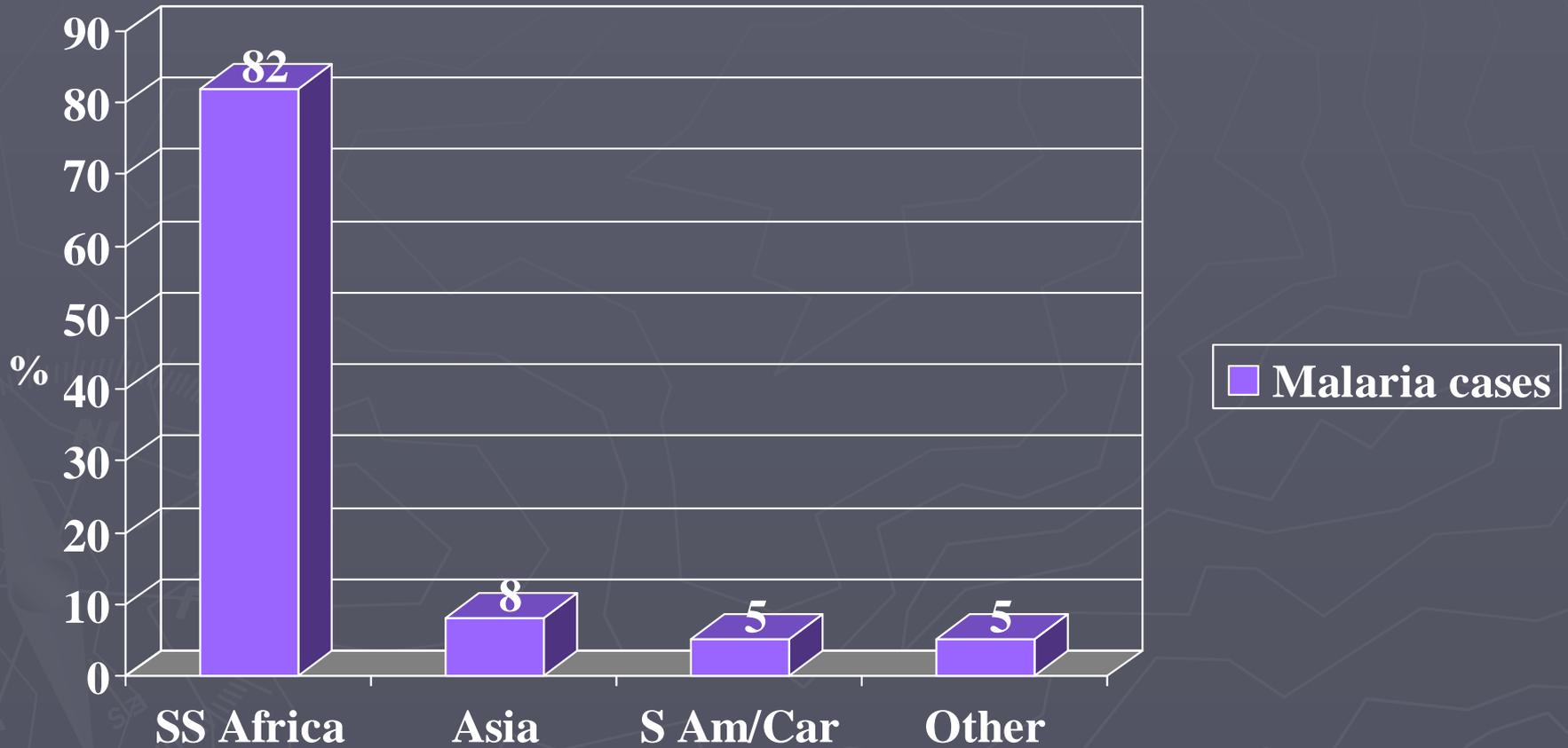
# Introduction

- ▶ Annually affects 300 million people with 3 million deaths
- ▶ One of 5 major causes of death in children < 5yo in developing countries (malaria, malnutrition, diarrhea, pneumonia, HIV/AIDS)
- ▶ Non-immune risk without precautions - 1.2% / month or 57% in 4 years
  - Solomon Islands - 8% / month
  - West Africa - 2.4% / month
  - South America - 0.05%
  - Central America - 0.01%
  - Adventure travelers - 48.8% (have circumsporozoite CS antibodies for P Falcip)
  - Tour travelers to sub-Saharan Africa - 5.6% (CS antibodies)

# Introduction

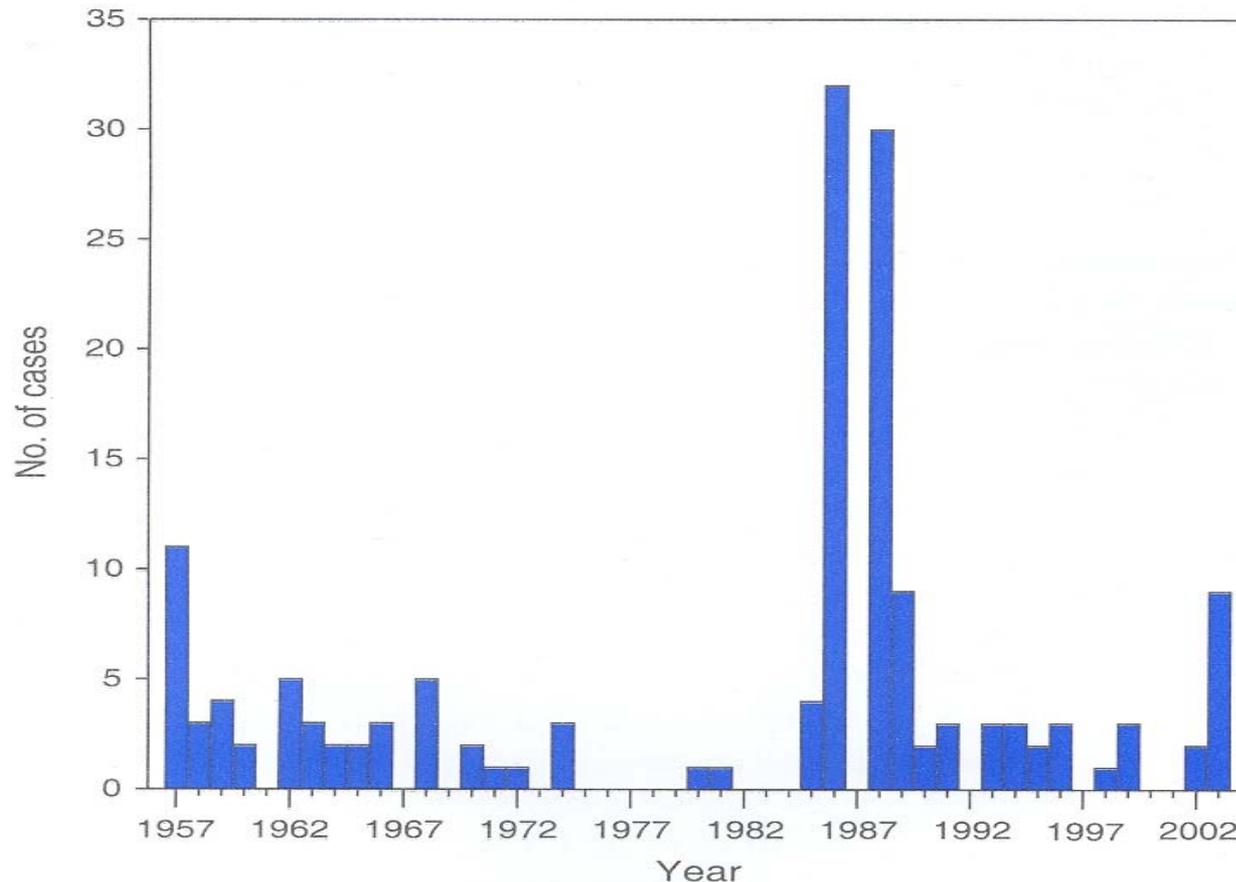
- ▶ The number 1 life threatening infectious disease for travelers
- ▶ 30,000 European and N American travelers infected annually
- ▶ The Gambia 1960-1990 - 1/25 children die of malaria < 5yo
- ▶ Mortality for *P. Falciparum*
  - 4% (range 0-8.7% in the non-immune)
  - 20% in severe cases

# US Civilians



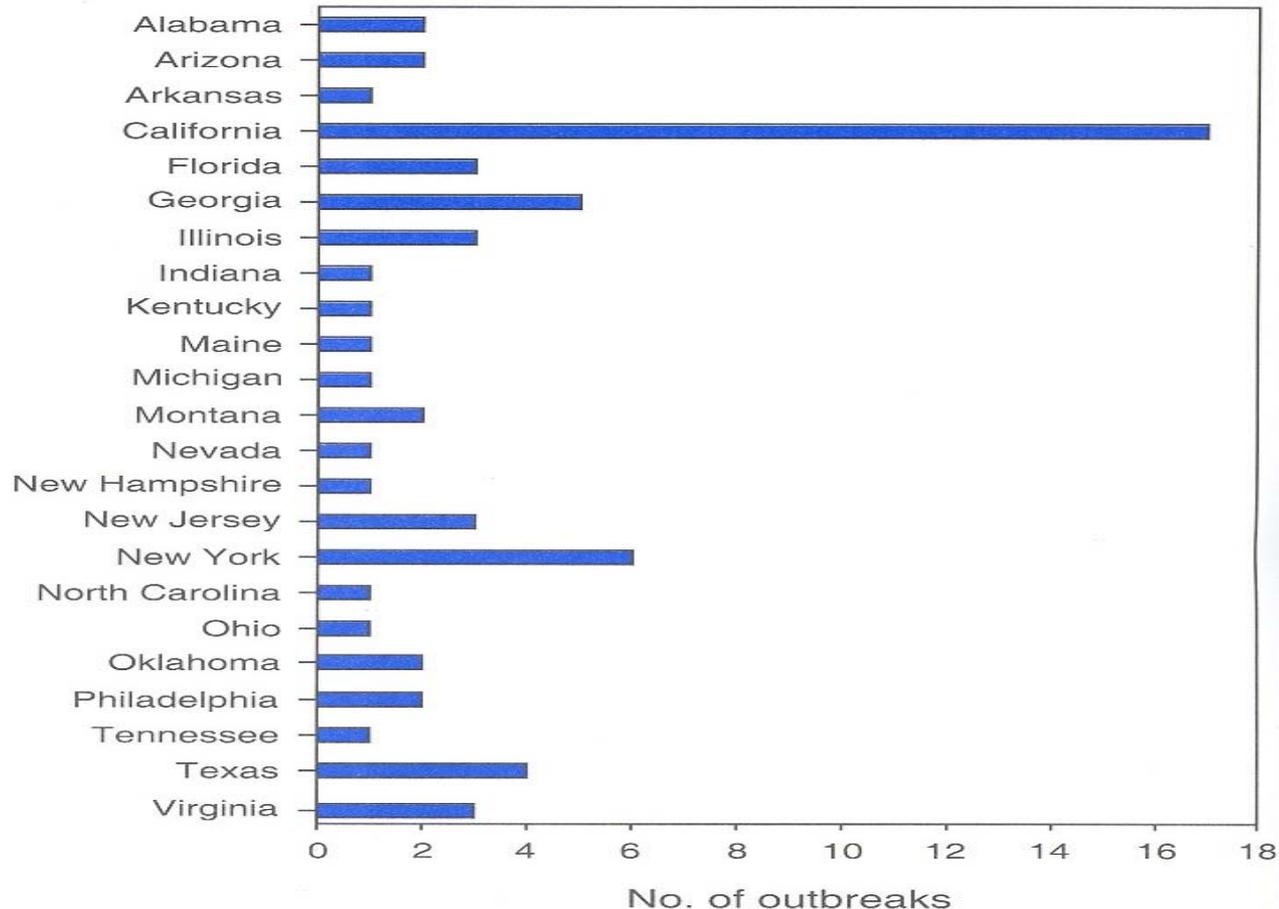
# Locally Acquired Malaria in the US

**FIGURE 1. Number of locally acquired malaria cases, by year — United States, 1957–2003**



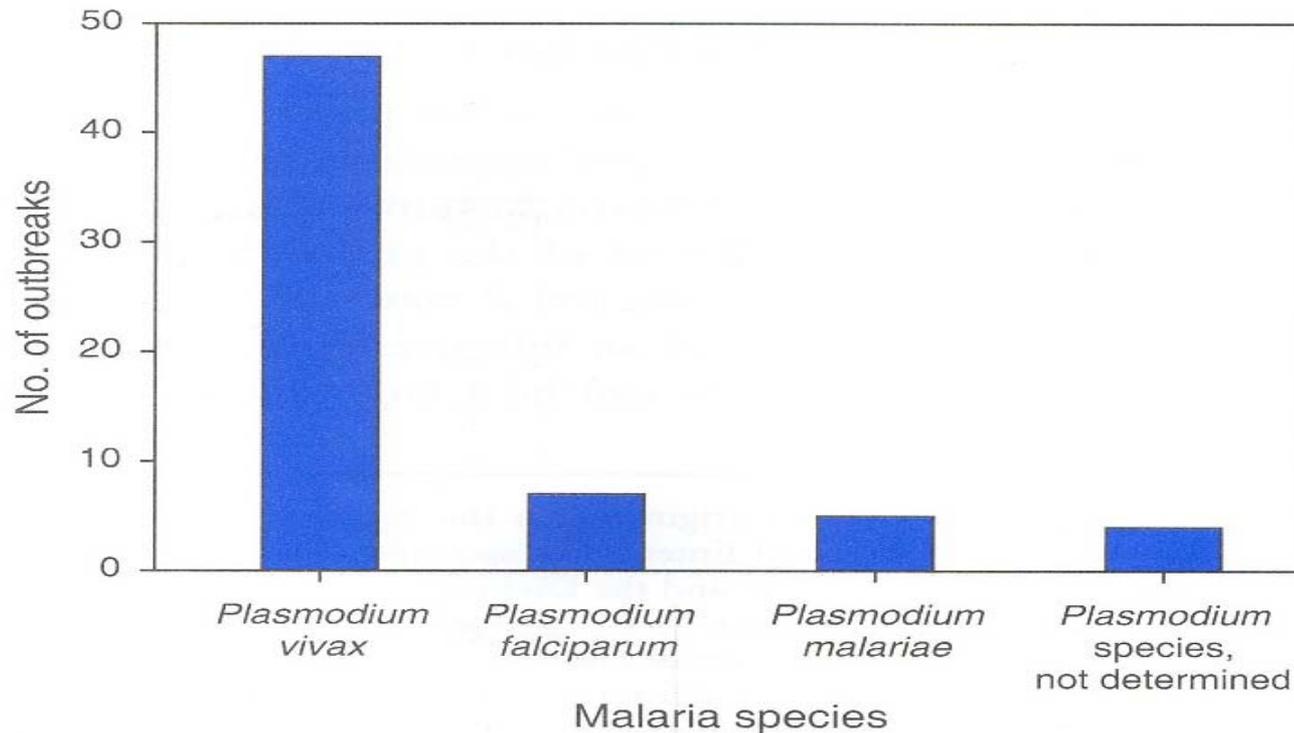
# Locally Acquired Malaria in the US

**FIGURE 2. Number of locally acquired malaria outbreaks, by state — United States, 1957–2003**



# Locally Acquired Malaria in the US

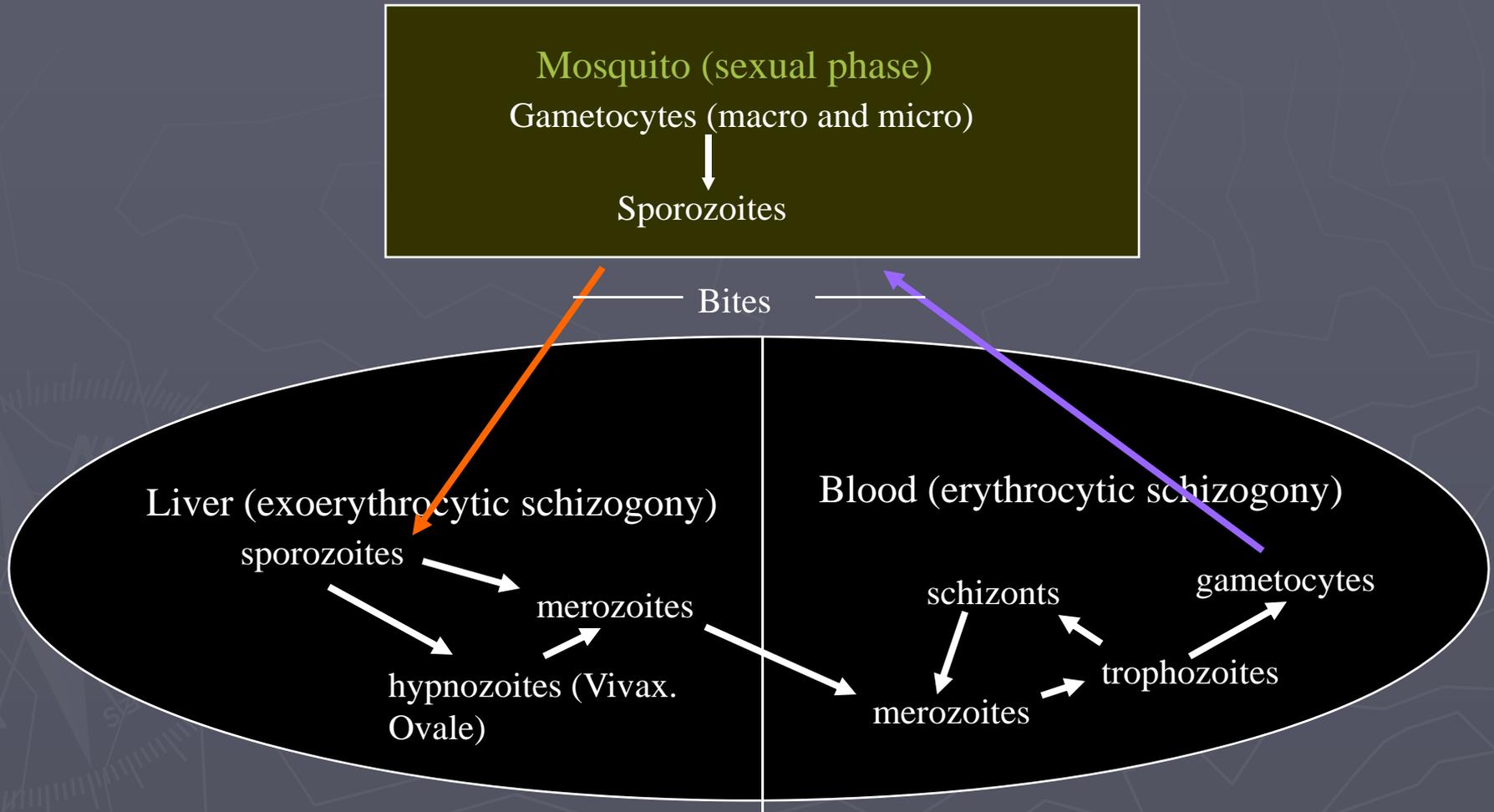
**FIGURE 3. Number of locally acquired outbreaks, by malaria species — United States, 1957–2003**



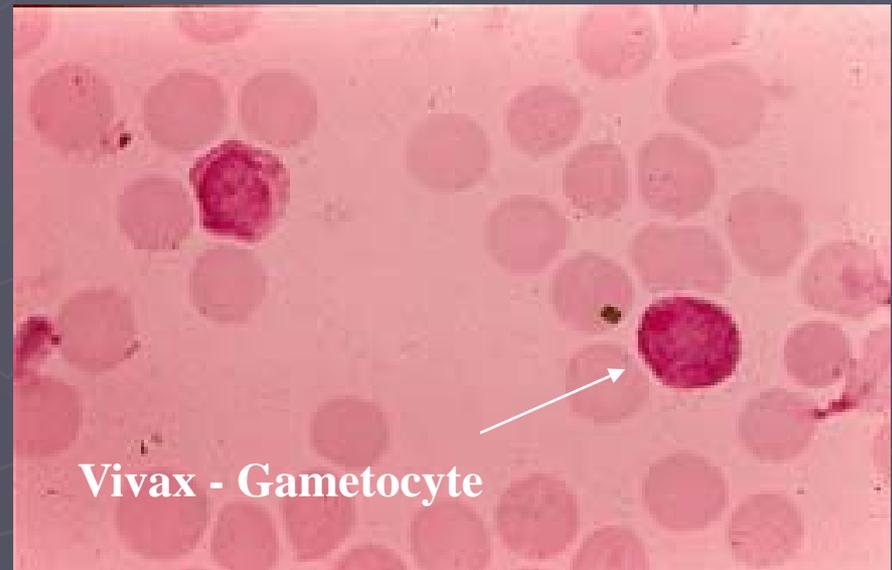
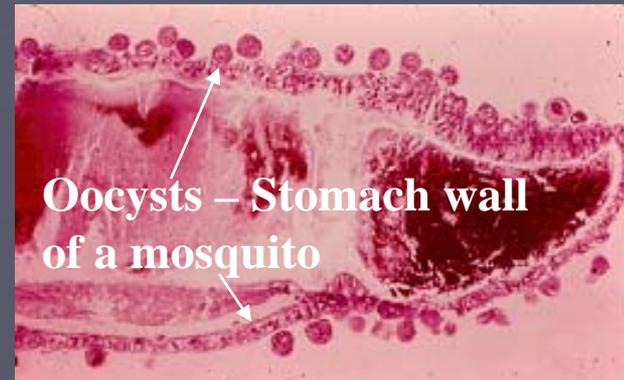
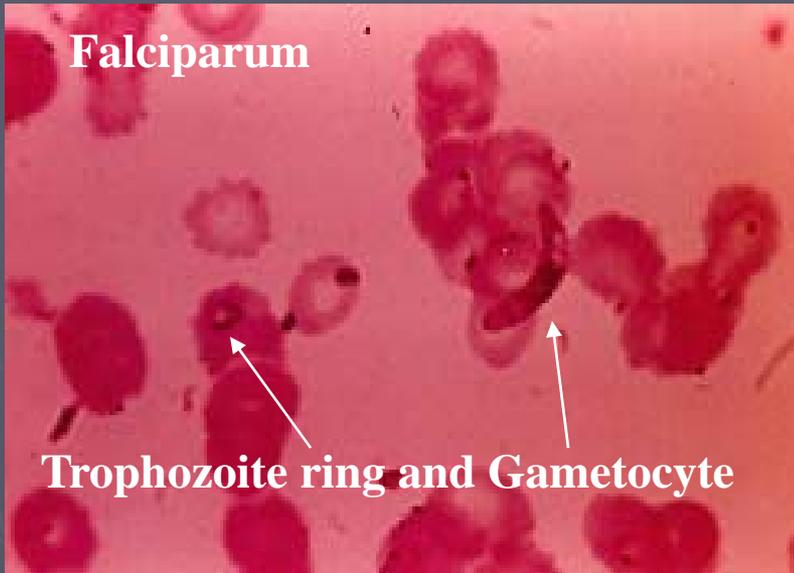
# Organisms

- ▶ *Plasmodium vivax*
- ▶ *Plasmodium ovale*
- ▶ *Plasmodium malariae*
- ▶ *Plasmodium falciparum*

# Life Cycle



# Malaria



# Malaria - General

- ▶ All malaria drugs except Primaquine and Atavaquone treat the blood phase only
- ▶ Hypnozoites
  - Vivax and Ovale
  - Relapses - 2-4 years
  - Cured with Primaquine

# Vector

## ▶ Anopheles mosquitoes

- Cannot fly > 4 km
- Generally remains within 2 km of breeding sites
- Bites inside houses



# Incubation Periods

- ▶ Time from infection to symptoms
- ▶ *P. Falciparum* - 12 days (8-17 days)
- ▶ *P. Vivax* and *P. Ovale* - 9 days - 2years
- ▶ *P. Malariae* - 28-30 days

# Epidemiology

- ▶ P. Falciparum - worldwide
  - Resistance to chloroquine - worldwide
  - Chloroquine sensitive in some areas of Latin America / South America, Middle East, and Egypt.
  - Thailand - multi-drug resistance
    - ▶ 1992
      - Mefloquine - 60-70%
      - Quinine - 50-60%
      - Fansidar - <10%
      - Chloroquine - <10%

# Epidemiology

- ▶ Major cities in Asia and S. America are nearly malaria free.
- ▶ Cities in Africa, India and Pakistan are not malaria free.
- ▶ Less risk of malaria at altitudes  $> 1500$  meters (4500 feet)

# Chloroquine Sensitive

- ▶ Mexico
- ▶ Caribbean
- ▶ Central America (north of the Panama canal)
- ▶ Middle East (Egypt, Turkey, Syria, Iraq, UAE)

# Chloroquine Resistant Areas

- ▶ Central America - south of the Panama canal
- ▶ South America
- ▶ Middle East (Iran, Oman, Yemen)
- ▶ Africa (sub-Saharan)
- ▶ SE Asia
- ▶ Thailand (border along Cambodia and Burma)
- ▶ Oceania

# Return of Chloroquine Efficacy in Malawi

- ▶ 1993 Malawi replaced chloroquine with sulfadoxine / pyrimethamine for the Rx of malaria since chloroquine sensitivity was < 50%
- ▶ Measured the Plasmodium Falciparum chloroquine resistance transport (PfCRT) gene
- ▶ From 1992 to 2001 the gene gradually decreased and disappeared (99% chloroquine efficacy)
- ▶ Neighboring countries where chloroquine was still being used more than 90% of Falciparum was resistant
- ▶ Chloroquine efficacy can return after withdrawal from usage

NEJM 2006;355:1959-66

# Epidemiology

## ▶ P. Vivax

- Most common form
- SE Asia, Africa, Central / S America
- Chloroquine resistance - 12.5%
  - ▶ New Guinea, Indonesia, Irian Jaya
  - ▶ Primarily in those < 4 yo

# Epidemiology

- ▶ P. Ovale - West Africa
- ▶ P. Malariae
  - SE Asia, Tropical Africa
  - Recrudescences for up to 20 years

# Clinical Presentation

## ▶ Classic - "flu-like"

- Fever - initially irregular then spikes (tertiary or quartan)
- Headache
- Arthralgias
- Vomiting
- Mild diarrhea

# Fever

- ▶ Fever is associated with parasite load – temps  $> 38.5^{\circ}\text{C}$  associated with parasitemia  $> 180 / \mu\text{l}$
- ▶ Fever associated with various strains of *P Falciparum* – ie lower fever threshold with Cam/Eth/Viet (2,115) – 75 /  $\mu\text{l}$  vs EILim/Santee (1A,120) – 1800 /  $\mu\text{l}$

AJTMH 2002;66:467-473

# Clinical Presentation

## ► Cerebral malaria

- Coma - most frequent manifestation of severe malaria
- Seizures - 50%
- Endothelial damage and vasculitis

# Clinical Presentation

## ► Acute Renal Failure

- Blackwater fever due to hemolysis - most resolve but some progress to renal failure
- Oliguria
- Associated with Primaquine with G6PD deficiency
- Associated with Quinine use in severe disease (often sub-therapeutic)

# Clinical Presentation

- ▶ Acute pulmonary edema - Adult RDS
- ▶ Hypoglycemia
  - Pregnant women treated with quinine increases insulin release
  - Children

# Clinical Presentation

## ▶ Chronic malaria

- Anemia
- Splenomegaly especially in children in endemic areas - good estimate of malaria prevalence
  - ▶ due to an exaggerated immune - responds to antimalarials
  - ▶ tropical splenomegaly syndrome

# Clinical Presentation

- ▶ Nephrotic syndrome
  - Children
  - *P. Malariae* due to Ag-Ab complexes

# Clinical Presentation

## ▶ Pregnancy

- Increased mortality and low birth weight
- Congenital transfer
  - ▶ Primarily with Vivax - 16-34% (no liver phase)
  - ▶ Greater in the non-immune (7.4%) vs immune (0.3%)
  - ▶ Onset - 5.5 weeks
  - ▶ Rx - Quinine + Fansidar
- Major complications particularly in primips
  - ▶ hypoglycemia
  - ▶ anemia
  - ▶ pulmonary edema

# Clinical Presentation

- ▶ Vivax, Ovale and Malariae - generally milder disease vs Falciparum - serious organ dysfunction

# Severe Malaria - WHO

- ▶ Cerebral malaria - unarousable coma
- ▶ Severe anemia - hgb < 5, Hct < 15, parasite count > 10,000
  - >2% parasite count - increased fatality (falcip)
  - >5% dangerous in the non-immune
  - >10% dangerous for everyone
- ▶ Renal failure - urine output < 400 ml / d, < 12 ml/kg/d for children, S.Cr. >3 mg/dl.

# Severe Malaria

- ▶ Pulmonary edema or adult RDS
- ▶ Hypoglycemia -  $< 40$  mg/dl
- ▶ Circulatory collapse (shock) Sys bp  $< 50$  (1-5 yo),  $< 70$  adults
- ▶ Spontaneous bleeding or lab evidence of DIC
- ▶ Repeat general seizures ( $>2/24$  hours)
- ▶ Acidosis - art. Ph 7.25, bicarb  $< 15$  mmol/l
- ▶ Macroscopic hemoglobinuria
- ▶ Everyone you are clinically worried about

# Thrombocytopenia – Severe Malaria

- ▶ Children 0 – 15 yo
- ▶ Senegal, West Africa
- ▶ Platelet counts  $< 100,000/\text{mm}^3$  – odds ratio for death – 6.31

AJTMH 2002;66:686-691

# P. Falciparum Complications

	Non-pregnant adults	Pregnant women	Children
Anemia	+	++	+++
Seizures	+	+	+++
Hypoglycemia	+	+++	+++
Jaundice	+++	+++	+
Renal failure	+++	+++	-
Pulmonary edema	++	+++	+

# Resistance



# Diagnosis

- ▶ Gold standard – thin and thick smears
- ▶ PCR – can be available in 6 hours
- ▶ PCR can differentiate species
- ▶ Is a good second-line method when conventional techniques are negative in patients thought to have malaria.
- ▶ PCR is better than the quantitative buffy coat system

AMTMH 2002;66:503-508

# Rapid Tests

- ▶ Compared 10 rapid tests
- ▶ ICT Malaria Pf test had the best 50% detection limit – 3.28
- ▶ OptiMal (OP) and ParaSight – F (OS) produced fewer false positives (18-19% respectively) vs the others (38-56%)
- ▶ Microscopy, PCR, OP and OS disagreed largely as to specimens that are remaining positive.

# Rapid Tests

- ▶ Sensitivity (65-97%) and specificity (87-100%) of rapid tests are still below that of microscopy
- ▶ ICT pf (Makromed) seems to have the best overall sensitivity (65-97%) and specificity(89-100%) but has varied with the study
- ▶ Dipstick tests can only be recommended to travelers for specific situation (long term, far away from medical assistance, expedition travel, etc.) after appropriate instruction and training, including a successful performance of the test procedure

# Uncomplicated Malaria

Type	Regimen	Notes
C sensitive	C	4 doses over 48 hours
C resistant, F sensitive	F	1 dose
Multidrug resistant	Malarone, F + Q, D + Q, Ata + Q, M (low dose for M sensitive or high dose for M low grade resistance), A + M (high grade M resistance) or H	M – 1 or 2 doses over 12 hours. H – 3 doses over 6-8 hours, Q – 3 X per day for 7 days. D – 1 / day for 7 days. A – 1 / day for 5 days. M – 1 dose
Vivax and Ovale – C sensitive	C + P	C – as above. P – 1 / day for 14 days. The first dose following the last dose of C.
Vivax – C resistant	M + P or H + P or Q + D + P	

C - Chloroquine, F - Fansidar, M - Mefloquine, Q - Quinine, D - Doxycycline, A - Artesunate, P - Primaquine, Malarone (Atavaquone + Proguanil), Ata - Atavaquone

# Tafenoquine for P Vivax

- ▶ 8-aminoquinolone related to primaquine
- ▶ 2 patients treated with Tafenoquine only, 400 mg initially followed by 200 mg bid for 2 days
- ▶ Neither soldier was G6PD deficient
- ▶ Rapid parasite clearance, good clinical response and lack of recrudescence over a two year period

RSTMH(2005) 99, 2-5

# Self Medication for Malaria

Medication	Adult Dose	Notes
Quinine with or without Doxycycline	Q – 600 mg tid X 7d, D – 100 mg od X 7 d	D not used in pregnancy
Co-artemether	4 tabs per dose (hrs – 0, 8, 24, 36, 48, 60)	With fatty food (milk, full-fat yogurt)
Atavaquone – proguanil	4 tabs od X 3d	With fatty food (milk, full-fat yogurt)
Mefloquine	750 mg base stat then 500 mg at 12 hours	250 mg tabs (228 mg base) in the US. Outside the US 275 mg tabs (250 mg base)
Fansidar	3 tabs once	Due to resistance not recommended
Chloroquine	600 mg base stat then 300 mg at 6, 30, 54, and 72h	Only sensitive areas. One tab = 150 mg base
Halofantrine		Cardiac toxicity precludes use

# Anti-malarial Efficacy

Anti-Malarial	Failure rate
Chloroquine	83.5%
Fansidar (sulfadoxine/pyrimethamine)	25.3%
Amodiaquine	20%
Artemisinin based combinations	1.2%

RSTMH (2005) 99, 485-492

# Standby Treatment Scenarios

Scenario	% Agree	% Disagree
Areas with inadequate medical services	98.6	1.4
Remote areas out of reach of medical Rx within 24 h	98.5	1.5
Contra-indication for chemoprophylaxis	97.1	2.9
Frequent short term visitors to risk areas	70.6	29.4
Long term stays in risk areas remote from medical services	68.6	31.4
Visits to low endemic areas	50.8	49.2
To semi-immune	43.3	56.7

# Standby Treatment

- ▶ Generally standby treatment is not indicated if exposure to malaria is for less than one week before returning to country with appropriate medical support

RSTMH (2004) 2, 119-126.

# Malarone (atavaquone / proguanil) efficacy

- ▶ Against *Plasmodium falciparum*
  - Malarone - 100%
  - Mefloquine - 86%
  - Amodiaquine - 81%
  - Chloroquine + Fansidar - 88%
- ▶ Malarone was as effective as Q + D, F or H

# Indonesia - Uncomplicated Malaria

## ▶ Hospital based study

## ▶ *P. Falciparum*

- C + D cured 90.6%
- D cured 64.7%
- C cured 20%

## ▶ *P. Vivax*

- C + D cured 70.6%
- D cured 33.3%
- C cured 29.4%

# Severe Malaria

Type	Regimen	Notes
C Sensitive	C (IV, IM, SQ, NG)	IV in a well staffed hospital. IM, SQ, NG in rural facility
C Resistant	Q (IV, IM) or Quin (IV) or Artemether (IM) or Artesunate (IV) or Artemisinin suppositories	Artemisinin suppositories used in rural clinics where injections aren't possible. Artemisinin – 6 doses over 60 hours.

- Switch from parenteral medications as soon as the patient is able to take oral drugs
- Artemether Rx is associated with a 10-50% recurrence therefore use with M or Q
- Use of M after Rx of severe malaria with A or Q may cause a post malaria neurologic syndrome
- Artemil (IM) load 3.2 mg / kg then daily 1.6 mg / kg for 5 days as good as IV quinine for cerebral malaria in children.

# Cerebral Malaria - Cameroon

- ▶ Children 1-10 yo
- ▶ IM Arteether - 3.2 mg/kg on day 0, then 1.6 mg/kg on days 1 to 4
- ▶ Quinine - IV 20 mg salt / kg initially then 10 mg / kg q8h to day 6. Switch to PO 10 mg / kg q 8h when possible.
- ▶ Results
  - Arteether mortality - 11.8% lower (NS)
  - Cure at 28 days - Arteether 73.2% vs Quinine 64.9%
  - Arteether is as good a Quinine and easier to administer in a rural setting.

ATTM 64(4, 5) 2001, 229-32

# Thailand - Multidrug resistant

Regimen	Notes
Artesunate (po)	96.7% cure. Increased recurrence with Artesunate used alone
Quinine (po) + Doxycycline (po)	100% cure
Artesunate (po) + Mefloquine (po)	98-100% cure
Halofantrine (po) high dose	99% cure in multidrug resistant cases not M resistant. Cure rate 70% in M resistance therefore may not be very useful in Thailand.
Artemether-lumefantrine (Coartem, Riamet, Novartis, Switzerland) – 20 mg A + 120 mg L	95.5% cure. Oral regimen. Tolerated well. 2% had QTc prolongation but no cardiac complications. AJTMH 64(4, 5) 2001:247-56
Malarone (atavaquone-proguanil)	98-100% cure. AJTMH 60:526-32. AJTMH 60:533-41.

WHO recommends using a combination of artemisinin with a second agent to avoid emergence of resistance.

# Predictors of Traveler Malaria

- ▶ Inadequate prophylaxis
- ▶ Sweating
- ▶ No abdominal pain
- ▶ Temperature  $\geq 38\text{C}$
- ▶ Poor general health
- ▶ Enlarged spleen – 85% probability
- ▶ Leukocytes  $\leq 10000 / \text{L}$
- ▶ Platelets  $< 150,000 / \text{L}$  – 82% probability
- ▶ Hgb  $< 12 \text{ g} / \text{dL}$
- ▶ Eos  $\leq 5\%$

# General Notes

## ► Halofantrine

- Increases QT and PR intervals and associated tachyarrhythmias
- Cardiac effects seen in > 60% of patients after 3 doses
- Associated with several cases of sudden death particularly after Mefloquine prophylaxis.

# Prevention

- ▶ Can be 98% effective
- ▶ Without precautions or prophylaxis - 1.2% rate / month (57.6% risk / 4 years)

# Precautions / Preventive measures

- ▶ Insect repellants - dawn to dusk
  - Adults - Ultrathon (35%) DEET works for 12 hours.
  - Children - Skedaddle - 10% DEET, uses molecular entrapment technology
  - Coconut oil and DEET soap bar – cheap
  - IR3535 and KBR3023 – picaridin synthetic repellents are promising RSTMH 2004, 98,644-652
  - Oil of lemon eucalyptus works well and lasts as long as low dose DEET
- ▶ Insecticide sprays containing pyrethrum - kills on contact
  - use in living rooms / bedrooms in the evening

# Picaridin

Study	Repellent	Design/Vector	Results
AM Pretorius et al (2003) South Africa	20% picaridin lotion vs. 20% DEET lotion	Laboratory tests/ticks: <i>Amblyomma hebraeum</i> (African tick bite fever)	Protection after 1,2,3, and 4 hours; Picaridin: >85%, 56%,55%, 54%, DEET: >85%, 84%, 68%, 71%
A Badolo et al (2004) Burkina Faso	Picaridin vs DEET (varying concentrations)	Laboratory tests/mosquitoes; <i>Aedes aegypti</i> (yellow fever and dengue)	Relative potency; Picaridin at least as effective as DEET; both less effective against <i>An. Gambiae</i> than <i>Ae. Aegypti</i>
SP Frances et al (2004) Australia	19.2% picaridin vs 20% DEET and 35% DEET	Field trial;mosquitoes: <i>Culex annulirostris</i> (arbovirus) <i>Anopheles bancrofti</i> and <i>meraukensis</i> (malaria)	>95% protection; <i>Cx.</i> <i>Annulirostris</i> : Picaridin 5 hrs; DEET >7hrs <i>Anopheles</i> spp: Picaridin 1 hr, 20% DEET < 1 hr, 35% DEET 1 hr
C Costantini et al (2004) Burkina Faso	Picaridin vs DEET (varying concentrations)	Field trial/mosquitoes: <i>Anopheles</i> spp. (98.5%) (malaria)	Relative potency after 10 hr; Picaridin similar to DEET

# Precautions / Preventive measures

- ▶ Permethrin impregnated bed nets and on clothing
- ▶ "Blousy" long sleeve shirts and pants
- ▶ Stay in mosquito-free screened areas - dusk to dawn (use insecticides)
- ▶ Prophylactic drugs

# Precautions / Preventive measures

- ▶ Cover water containers
- ▶ Larvacides

# Counseling Issues

- ▶ There is no uniform approach to malaria prophylaxis
- ▶ Overseas, ignore the advice from fellow travelers and health care providers regarding prophylaxis
- ▶ No antimalarial guarantees protection
- ▶ Mosquito bite protection is extremely important
- ▶ In case of fever, seek health care advice urgently and request malarial films for diagnosis (repeated if necessary)

# The Pregnant Traveler

- ▶ Avoid travel to chloroquine resistant malaria areas
- ▶ Practice good mosquito bite prevention
- ▶ Use prophylactic medications
  - Chloroquine + Proguanil
    - ▶ Areas of low grade chloroquine resistance
    - ▶ First trimester - high grade resistance
  - > 1st trimester - Mefloquine - high grade resistance
- ▶ Treat malaria cases as for the non-pregnant

# Pregnancy and Malaria Rx

- ▶ Study of 32 pregnant with uncomplicated malaria in Eastern Sudan
- ▶ Treated with Artensunate (AS) (100 mg daily on days 0-2) and Sulfadoxine – Pyrimethamine (SP) (3 tablets of 500 mg S and 25 mg P each tablet as one dose )
- ▶ The mean gestational age during treatment was 29.7 weeks
- ▶ All patients delivered full term live babies
- ▶ One baby died on day 4
- ▶ None of the women died and there were no miscarriages, stillbirths, or congenital anomalies
- ▶ This small descriptive study failed to adverse effects to Rx of pregnant women with AS and SP

# Safety of DEET

- ▶ Annual usage - 200 million including 38% of the US population
- ▶ Adverse reports 1966-97 (30 cases)
  - CNS - 14 (13 in children < 8 yo)
  - Cutaneous - 11
  - Allergic - 4
  - Other - 1

# Prophylaxis

Malaria Chemoprophylaxis (from The Travel & Tropical Medicine Manual, 2nd Edition)		
Geographic area	Drug of choice	Alternative
Chloroquine sensitive areas located within:		
Mexico	Chloroquine	Standby treatment
Caribbean	Chloroquine	Standby treatment
Central America (north of the Panama canal)	Chloroquine	Standby treatment
Middle East (Egypt, Turkey, Syria, Iraq, UAE)	Chloroquine	Standby treatment
Chloroquine resistant areas located within:		
Central America (east and south of the Panama canal)	Mefloquine	Chloroquine + Standby treatment, Primaquine, Doxycycline or Malarone
South America	Mefloquine	Chloroquine + Standby treatment, Primaquine, Doxycycline or Malarone
South America (Amazon basin)	Mefloquine	Doxycycline, Primaquine or Malarone
Middle East (Iran, Oman, Yemen)	Mefloquine	Chloroquine + Standby treatment, Primaquine, Doxycycline or Malarone
Africa (sub-Saharan)	Mefloquine	Doxycycline, Malarone or Chloroquine + Proguanil + Standby treatment
Southeast Asia	Mefloquine	Doxycycline, Primaquine, or Malarone
Thailand (border areas along Cambodia and Burma)	Doxycycline	Proguanil + sulfa or dapsone
Oceania	Mefloquine	Doxycycline, Primaquine, or Malarone
P Vivax terminal prophylaxis		
Worldwide	Primaquine	

# General Prophylaxis Comments

- ▶ Generally start prophylaxis 1 week prior to travel to an endemic area and continue for 4 weeks after leaving for non-causal prophylaxis drugs (eg Chlorquine, Doxycycline, and Mefloquine)
- ▶ For causal prophylaxis drugs start 1 day prior to travel and continue for 7 days after leaving endemic areas (eg Primaquine, Malarone)

# New Prophylactic drugs

## ▶ Primaquine

- Take with food
- Start 1 day before travel and continue for 1 week after travel
- Side effects - GI upset, met Hb
- Contraindication - G6PD, Pregnancy

## ▶ Malarone

## ▶ Tafenaquine (WR238605, Etaquine)

- 250 mg / week

## ▶ Azithromycin

- 250 mg / day

# Malarone - Causal Prophylaxis

- ▶ Atovaquone and proguanil have activity against liver stages
- ▶ 16 volunteers given M 1 day prior to 6 days after challenge with PF
- ▶ 0 volunteers vs 100% placebo developed clinical malaria
- ▶ M may be discontinued 7 days after leaving malarial area

TRSTMH 2001;95:429-432

# Prophylaxis Efficacy

## ► Variable

- Mefloquine - 77-91%
- Chloroquine / proguanil - 54-72%
- Chloroquine - 10-42%
- Doxycycline - 84-100%
- Primaquine - 74-95%
- Malarone - 100% (Kenya, Gabon)
- Azithromycin - 72-83%

# Adverse Reactions

- ▶ Mefloquine - 18.8%
- ▶ Chloroquine - 17.1-18.6%
- ▶ Chloroquine + Proguanil - 30.1%
- ▶ Fansidar = 11.7% (occasionally life threatening)

# Mefloquine side-effects

- ▶ Nausea - 12.3 %
- ▶ Headache - 6.2%
- ▶ Dizziness - 7.6%
- ▶ Visual problems - 2.2%
- ▶ Depression - 1.8%
- ▶ Insomnia - 4.2%
- ▶ Mouth ulcers - 1.2% (7.9% with chloroquine + proguanil)
- ▶ Pruritis - 2.7%
- ▶ Other skin problems - 5.5%

# Mefloquine side-effects

- ▶ 1:200 - 1:500 have neuropsychological problems : insomnia, nightmares, anxiety, irritability, and depression
- ▶ 1:10,000 - 1:13,000 develop psychosis or seizures (usually a previous history)
- ▶ 1:100 - 1:1500 develop psychosis or seizures when used for treatment

Weimeke T, et al. AJTMH 1991;45:86-89

# Mefloquine Contraindications

- ▶ History of epilepsy or psychiatric disorder
- ▶ No longer contraindicated
  - Beta- and calcium channel-blocker
  - Tasks involving fine coordination
  - Children < 5 kg
  - Pregnancy
    - ▶ Safe > 1st trimester
    - ▶ No increased teratogenicity or abortions when used in the 1st trimester

# Mefloquine dosing

- ▶ Weekly dosing: steady state in 7 weeks
- ▶ Loading dose; steady state in 4 days
  - 250 mg / day X 3 days
  - Well tolerated (depression initially)
  - Adverse events seen in the first week vs at 3-7 weeks
  - Start 2 weeks prior to departure

# Prevention is 98% effective

- ▶ Insect repellents from dusk to dawn
- ▶ Insecticide sprays containing pyrethrum
- ▶ Treated bednets and clothing
- ▶ "Blousy" long sleeve shirts and pants
- ▶ Stay in mosquito-free screened areas - dusk to dawn (use insecticides)
- ▶ Prophylactic drugs
- ▶ Cover water containers

# Permethrin Application

- ▶ Use "4 Week Tick Killer 13.3% solution"
- ▶ Pour 2 oz into a large plastic bag with 12 oz water to make a final concentration of 2%
- ▶ Place rolled fabric in the bag and gently shake 2 times then let it rest for 2.5 hours.
- ▶ Remove the roll
- ▶ Hang to dry for at least 3 hours
- ▶ Do not let the liquid come in contact with bare skin