Malaria

Jarmila Kliescikova, MD, Department of Tropical Medicine, 1st Faculty of Medicine, UK
300-500 mil cases each year
(1-3 millions of deaths – children in subsahar Africa)

25-30 millions of people travelling each year to tropical countries;

10 – 30 thousands of travellers infected by malaria
Distribution of malaria, 2005
Malaria

*Plasmodium falciparum*
*Plasmodium ovale*
*Plasmodium vivax*
*Plasmodium malariae*

**Vector:** mosquito – *Anopheles spp.*
Anopheles spp.

- Female
- Biting at **dawn and during night**
- Like lowland areas with clean water (**swamps, paddyfields, rain puddles**)
- Appropriate temperature for development of plasmodium **16-33°C**
- Salivary glands
Life cycle of plasmodia

Sexual phase of Plasmodium life cycle takes place inside mosquito — gametes fuse to form zygotes, meiosis takes place, sporozites are produced and migrate to salivary gland.

Female Anopheles mosquito bites human infected with malaria and picks up Plasmodium gamete cells.

Infected mosquito bites another human, injecting saliva that contains Plasmodium sporozoites.

Plasmodium sporozoites infect liver cells and multiply asexually.

Infected liver cells burst, releasing Plasmodium cells called merozoites that infect red blood cells.

Merozoites reproduce asexually inside red blood cells.

Infected red blood cells burst, releasing merozoites that infect other red blood cells. Some cells release gametes that can infect mosquitoes.
Stages of life cycle

- **Sporozoityes**
  - (mosquito) infectious for human
  - Asexual replication in hepar

- **H Y P N O Z O I T E S!!!**
  - *(P. vivax, P. ovale)*

- **Merozoites**
  - (infectious for erythrocytes)

- **Gametocytes**
  - (infectious for the mosquito)
Intrahepatic development (exoerythrocytic) asymptomatic
(circulation in blood before the entering into hepatocyte: 15-60 min)
Development in the hepatocyte: *Pl. Falciparum*: 5.5 days, *Pl. Malariae*: 15 days

Intraerythrocytic development malaria
development in ery: *Pl. Falciparum, vivax, ovale* - 48 hrs; *Pl. Malariae*: 72 hrs
Infected ery:
*Shape changes* $\Rightarrow$ reduced flexibility

Membrane knobs
(*Pl. falciparum, malariae*)

„Glueing“ to the endothelium
(*Pl. falciparum*) tzv. knobs – sequestration
**Rosetting**
Adherence between erythrocytes (infected and non-infected)
altered function of the microcirculation

**Sequestration**
Adherence to venules of vital organs (HRP, sequestrin/CD36, ICAM)
(brain, heart, liver, kidney, intestine)
altered function of the microcirculation

Cerebral malaria
anaerobic glycolysis, lactate acidosis
Plasmodia
degradate Hb in affected ery (production of hemozoin), utilise glucose, produce of lactate

Preference of ery:

*P. falciparum*: no preference
*P. vivax*: young ery (Duffy+)
*P. malariae*: old ery
PATHOGENESIS OF TROPICAL MALARIA

Intra-erythrocytic merogony

**Disintegration of ery**
- Paratic Ag
- GPI
- Activation
- IL-4, 5, 6
- B-lymfo
- Antibodies
- Elimination of parasite

**Sequestration of ery**
- Activation
- T lympho
- IL-1
- Activation of macrophages
- NO
- Microcirculation obstruction
- Tissue hypoxo
- Inner organs damage
- Escape from immunity

**Activation of macrophages**
- IFNγ
- IL-6
- TNFα
- IL-1

**Activation of coagulation**
- Activation of coagulation
- Complement activation

**Antibodies**
- Elimination of parasite

**Prostaglandins**
- Vasodilatation

**Kinis**
- Increased capillary permeabilisation

**Hypovolaemia**

**Hypoperfusion of organs**

**Fever**
- Malaria
# Malaria aetiology

<table>
<thead>
<tr>
<th>Species</th>
<th>Disease</th>
<th>Development</th>
<th>Distribution</th>
<th>Relapses</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. falciparum</em></td>
<td>Tropical malaria, malignant tertian</td>
<td>24-48 hrs</td>
<td>Africa, SE Asia, India, S and Str. Amerika</td>
<td>No</td>
</tr>
<tr>
<td><em>P. vivax</em></td>
<td>Benignant tertian vivax</td>
<td>48 hrs</td>
<td>Tropics, subtropics</td>
<td>Yes</td>
</tr>
<tr>
<td><em>P. ovale</em></td>
<td>Tertian, ovale</td>
<td>48 hrs</td>
<td>Tropical western Africa</td>
<td>Yes</td>
</tr>
<tr>
<td><em>P. malariae</em></td>
<td>Quartan</td>
<td>72 hrs</td>
<td>Tropics, subtropics – some parts</td>
<td>No</td>
</tr>
</tbody>
</table>
Symptomatology

**Prodromal Symptoms**

Nausea, anorexia, headaches, myalgia

- **Adults:**
  - Fever — typical malaria paroxisms
  - Anaemia — lack of reticulocytosis = suppression of bone marrow
  - Splenomegaly — very early sign
  - Icterus — absent or very mild, elevation of HE

- **Children:**
  - Fever, cough, vomiting, diarrhoea, anaemia
  - Faster progression (1-2 days)
  - Pulmonary oedema
  - Renal failure very rare
Course of the disease

Incubation period: malignant tertian: 11 days
tertian: 12 days
quartan: 13-28 days

FEVER: 3 phases: chills (temperature increase) myalgia and headache 10-30 min
fever
sweating
(vasodilatation, ortostatic hypotension – 4-8 hrs)
Temperature curves:

Tertian

Quartan

Malignant malaria
Anaemia

Hepatosplenomegaly
<table>
<thead>
<tr>
<th>Species</th>
<th>Disease</th>
<th>Parasitaemia</th>
<th>IP (days)</th>
<th>Compl.</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. falciparum</em></td>
<td>Tropical malaria/ Malignant tertian</td>
<td>- 30%</td>
<td>7-14</td>
<td>Malignant malaria</td>
</tr>
<tr>
<td><em>P. vivax</em></td>
<td>Benign tertian</td>
<td>- 2%</td>
<td>12-17</td>
<td>Anaemia, splenomegaly</td>
</tr>
<tr>
<td><em>P. ovale</em></td>
<td>Tertian ovale</td>
<td>- 1-(2)%</td>
<td>15-18</td>
<td>Anaemia, splenomegaly</td>
</tr>
<tr>
<td><em>P. malariae</em></td>
<td>Quartan</td>
<td>- 1%</td>
<td>18-40</td>
<td>Glomerulonephritis, nephrotic sy</td>
</tr>
</tbody>
</table>
COMPLICATIONS OF MALIGNANT MALARIA

• Cerebral malaria
• Renal failure
• Pulmonary oedema
  • Bleeding disorders
  • Hepatic failure
  • GIT complications
• Circulation colapsus – algid malaria
• Hypoglycaemia, ion dysbalance
CEREBRAL MALARIA

- Severe consciousness disorder, unconsciousness, coma
- Focal neurologic deficiency uncommon
- In children - seizures, paresis of oculomotoric nerves
- Meningeal irritation signs usually negative
- 30-50 % mortality
- CT normal
- Oedema of the brain - terminally
- Pathogenesis not completely understood: NO and lactate production, malfunction of microcirculation
unconsciousness, cerebral malaria

Oedema of brain, cerebral malaria

Cerebral malaria

Multiple petechias, cerebral malaria
Pulmonary oedema- ARDS

Adherence of neutrophils to the endothelium of pulmonary capillaries
Activation of neutrophils and macrophages

Increased permeability of pulmonary capillaries
- Oedema of endothelium and interstitium, hyalinous membranes formation
- Increased hydration of patient
RENAL FAILURE

• Malfunction of microcirculation
• Hypovolemy and hypoperfusion of ren
• Acute tubular necrosis
• Anuria, asotaemia and ureamia
• Hemoglobinuric fevor
• Formation of haemoglobin cylinders
Nephrotic sy/Blackwater fever

- *Pl. Malariae*; immunocomplex format.
- Deficiency of G6PD
- Quinine
- Urine of Coca-cola colour
Hepatic failure

- **Uncommon** in malaria
- Hyperbilirubinaemia, elevation HE
- Defect of **glukoneogenesis and glycogenolysis**
- Defect in utilisation of lactate
- Hypoalbuminemia
- Decreased **synthesis of lipoproteins**
PANCYTOPENY

- Anaemia
  - Defect of erythropoiesis in bone marrow
  - Intravascular hemolysis, hypersplenism
- Thrombocytopeny
  - Decreased production and survival of thrombocytes
- Leucopeny

Malaric pigment in lien
Malaric pigment in monocyte
Defects in the inner environment

**Hypoglycaemia**
- Increased utilisation of glucose – hyperparasitaemia
- Defect of gluconeogenesis
- Hyperinsulinemia

**Lactate acidosis**
- Tissue hypoxia
- Defect of hepatic function

Increased Kalium, Decreased Natrium and Chlorides
Clinical criteria of the malignant tropical malaria

- **Hyperpyrexia > 24 hrs**
- **Cerebral malaria**: unconciousness – coma, seizures, focal neurological deficiency
- **Oliguria** (< 400 ml/24 hrs.)
- Macroscopic haematuria
- **Pulmonary oedema**
- Shock, hypotension
- Fast progressing icterus
- Fast progressing anaemia
- Hemorrhagia, DIC
- Very severe vomiting
DIC, malignat tertian

Hepatic failure, hemozoin

Cerebral malaria, hemozoin

Icterus
Malignant malaria should be treated in the ICU
Laboratory criteria of malignant tropical malaria

Serum concentration of creatinin < 265 μmol/l (3 mg/dl)
Bilirubin > 50 μmol/l
Hematocrit < 20 %
Haemoglobin < 75 g/l
Severe thrombocytopenia (< 20 000/μl)
Haemoglobinuria
Acidosis (bicarbonate < 15 mmol/l)
Hypoglycaemia (< 2.2 mmol/l)
Parasitaemia before treatment initiation > 5%
MALARIA in pregnancy

- Increased risk of abortion, premature birth, decreased birth weight and neonatal mortality, hypoglycaemia!!!!!

- Increased maternal morbidity and mortality
  - Parasitaemia higher and anaemia more severe
  - Increased risk of hypoglycaemia and pulmonary oedema

- Congenital transmission very rare, more common in non-immune and infections with *P. vivax, P. malariae*
Infiltration of placenta, sequestration of ery
Relapses

*P. vivax; P. ovale*

**Hypnozoites in hepar**
- Time periods longer in subtropical (*vivax*) than in tropical relapses (*ovale*)

**Onset of the disease faster,**
- Paroxyzmys synchronised from the start
- Primachin destroys about 80% of present hypnozoites
MALARIA: important

- Incubation period- **min 8 days**
- No lymphadenopathy
- No exantema
- Hepatosplenomegaly; mild elevation of HE
- Relative lymphocytosis and thrombocytopenia, anaemia not present in acute phase
- Fatal complication of the disease can occur within first 48 hours
- **NO protective immunity!!!!**
– Newborns protected first 6 months
– Repeated exposition: immunita in 5 years = nonsterile immunity
– Partial immunity disappears after five years of no exposition
Natural partial resistance against malaria

Disorders in the shape of ery
(sickle cell anaemia, thalassemia, ovalocytosis)

Enzymatic defects: deficiency of G6PD

Variability of surface ery antigens
(Duffy in *P. vivax*)

Variability in immune system (HLA)
MALARIA IN CR

NRL for diagnostics of tropical parasitic infections – Dr. Nohýnková

1994 – 2004: IMPORTED MALARIA

Together: 216 cases
46 foreigners

- import from 1997 stabil (!)
- ~ 20-25 cases treated in CR/year

Foreigners since 2000 low number of cases
Diagnostics of the malaria

- Thick and thin blood smear – „golden standard“ of the diagnostics
- Smears of the periferal blood, repeat in specific time intervals (after 12 – 24 hrs.); also in the case of afebrilia
- Always important to know the parasitaemia – response to the treatment
- Sensitivity of the thick blood smear: 50/μl ~ 0,001% parasitaemia

Thick and thin blood smear, stained with Giemsa
Diagnostics of the malaria

Thick and thin blood smear/film
Therapy of malaria
LIFE CYCLE AND ANTIMALARIALS

**Sporontocidal:**
*(Radical prophylaxis)*
Proguanil, pyrimethamin, atovachon

**Gametocidal:**
*(Radical prophylaxis)*
8-aminochinolins.
Chinin, meflochin, chlorochin - *No effect against P.falciparum*

**Blooid schizontocidal:**
*(Supresive therapy)*
Chlorochin, chinin, meflochin, artemisinin, atovachon, tetracykliny, klindamycin, pyrimethamin, sulfonamidy

**Sporozoity**
Zygota (ookinet)
Lumen střeva

**Gametocyty**
Hepatocyty:
Tissue schizontocidal:
*(Causal prophylaxis)*
8-aminochinoliny, proguanyl, atovachon
Tetracykliny, azitromycin

**Gametocyta**
Erytrocytární merogonie
Hypnozoitocidal (antirelaps) therapy:
*(Radical therapy)*
8-aminochinolins

**Erytrocytární merogonie**
Gametocyta
Hypnozoity (P.vivax, ovale)

**Střevo**
Slinné žlázy

**Anopheles**
Human
4-AMINOCHINOLINS

- Chlorochin = 4-(4-diethylamino-1-methylbutylamino)-7-chlorchinolin (DELAGIL, tbl. 150 mg báze)
- Hydroxychlorochin (PLAQUENIL)
- Amodiachin
4-AMINOCHINOLINES

- **Mechanism of effect:** interference with detoxification of free hem while degrading Hb
- **Indications**
  - *Plasmodium sp.:* schizontocide, gametocide (*Pl. vivax, ovale, malariae*), prophylaxis of malaria
  - Extraintestinal amebiasis
- **Side effects:** pruritus, headache, GIT problems, exfoliative dermatitis; retinopathy and keratopathy in high doses
- **Contraindication:** severe malfunction of hepar and ren, neurologic disorders (epilepsy), retinopathy, porphyria, careful with psoriasis
- **Drug interaction:** increasing the plasma levels of digoxin and methotrexate; inhibitors of MAO increase the toxicity
8-AMINOCHINOLINY

• Primachin = 8-(4-amino-1-methylbutylamino)-6-methoxychinolin (PRIMAQUINE, tbl. 7,5 mg báze)
• Pamachin
• Tafenochin
8-AMINOCHINOLINES - PRIMACHIN

- **Mechanism of effect:** activation to form toxic aminocholins, interference with redox reactions
- Fast absorption from GIT, $T_{1/2} = 5$ hrs.
- **Indication:** gametocide in all plasmodia, antirelapses treatment of *Pl. vivax* and *ovale* (destroys hepatic hypnozoites)
- **Side effects:** GIT (anorexia, nausea, abdominal pain), methemoglobinemia, leucopenia; haemolytic anaemia in patients with G-6-P DH deficiency
- **Contraindications:** defects of haemopoiesis, pregnancy, lactation
- **Drug interactions:** increase in plasma levels of meflochim
- **Doses:** 0.25 (0.33) mg/kg/day, 14 days
Effective substances from plants

• Mostly alkaloides
• One of the most effective antiinfectious drugs from plants
  – Extrakt from qing hao (*Artemisia annua*) – was used in China for fever treatment since 430 AC („Handbook of Prescriptions for Emergency Treatments“)
  – Cinchona was used by Indians as antimalarial and antipyretic treatment in Peru
Effective substances from plants

• Quinine – alcaloid of *(Cinchona succirubra)* isolated by Pelletier at the beginning of 19th century (1820 n. 1834)

• Artemisinin = qinghaosu – qing hao (*Artemisia annua*)

• Emetin – alcaloid from *(Cephaelis ipecacuanha)* used for treatment of amebiasis
  
  – Less toxic derivate dehydroemetin is still used

• Konesin – alcaloid from *Holarrhena antidysenterica* was used in India for treatment of *Entamoeba histolytica* a *Trichomonas vaginalis*
DERIVATES OF QUININE

- Quinine = 8-(4-amino-1-methylbutylamino)-6-methoxychinolin
- Quinidine = D-isomer of quinine
- Meflochin = 4-chinolinemethanol (LARIAM, MEPHAQUIN, tbl. 250 mg báze)
MEFLOCHIN

- **Mechanism of effect:** inhibition of Hb detoxification in a food vacuole
- Fast absorption from GIT, 98% binds to plasma proteins, $T_{1/2} = 21$ days, elimination by bile
- **Indication:** *Plasmodium sp.:* schizontocide (uncomplicated malignant malaria resistant to chloroquine), gametocide (*Pl. vivax, ovale, malariae*), prophylaxis of malaria
- **Side effects:** GIT (nausea, vomiting, diarrhoea), headaches, defects of coordination, vertigo, hallucinations; rash, pruritus, bradycardia, nightmares
- **Contraindication:** epilepsy, psychic disorders, retinopathy, pregnancy, lactation; severe malfunction of liver and ren
- **Drug interactions:** increased effect of peroral anticoagulants and cardioglycosides, primachine increasing its plasma levels; increased risk of sinus bradycardia when treating with quinine, quinidine, halophantrine, beta-blocators, Ca$^{2+}$ blocators
QUININE

- **Mechanism of effect**: inhibition of Hb detoxification in a food vacuole
- **Indication**:
  - *Plasmodium sp.*: schizontocide, gametocide (*Pl. vivax, ovale, malariae*), prophylaxis of malaria
  - Complicated malignant malaria resistant to chloroquine
  - Babesiosis
- **Side effects**: hypoglycaemia, vertigo, tinnitus, visual disturbances
- **Contraindications**: bradycardia, AV blockage, decompensated heart insufficiency, intoxication with digoxine, pregnancy (except for vital indication)
- **Drug interactions**: increase effect of peroral antikoagulans and peripheral myorelaxans, increase plasma levels and toxicity of digoxine a meflochine, ritonavir increase its plasma levels and toxicity
- **Dosage**: 20 mg/kg in a first dose, after 10 mg/kg á 8 h.
DERIVATES OF ARTEMISINES

- Dihydroartemisinine
- Artemether
- Arteether
- Artesunate
DERIVATES OF GUANIDINE

- Proguanil = 1-(4-chlorfenyl)-5-isopropylbiguanid (PALUDRINE, tbl. 100mg)
- Cykloguanil
- Chlorproguanil
• **Mechanism of effect**: inhibition of dihydrophalate dehydrogenase

• Good absorption from GIT, $T_{1/2} = 12-16$ hrs., metabolised in liver, eliminated by bile

• **Indication**: prophylaxis of malaria

• **Side effects**: GIT, stomatitis, granulocytopeania, hrombocytopeania

• **Contraindication**: severe nephropathy

• **Drug interactions**: increasing the effect of peroral anticoagulans
HYDROXYNAFTOCHINONY

Atovaquon

Ubichinin
ATOVAQUON

- Mechanism of effect: blocking the transport of electrons in respiratory chain
- Good absorption from GIT
- Indication: therapy and prophylaxis of malaria resistant to chloroquine, toxoplasmosis (effective in tissue cysts?); pneumocystosis
- Side effects: GIT (nausea, vomiting, diarrhoea); rash (20%); headache; anemia, neutropenia, hypotension
- Contraindication: pregnancy, careful in people above 65 years
- Drug interactions: metoclopramide and rifampicin are decreasing its plasma levels
ANTIBIOTICS WITH ANTIMALARIAL EFFECT

• Tetracyclines
  – Doxycycline (DEOXYMYKOIN, DOXYBENE)

• Makrolides
  – Spiramycin (ROVAMYCIN)
  – Azitromycin (SUMAMED)

• Clindamycine (DALACIN)

• Rifampicine
ENDOSYMBIOTIC THEORY

[Diagram showing the process of endosymbiosis, with labels for prokaryote, N^1, N^2, P, N^3, and N'].

A primary endosymbiosis is depicted, followed by a secondary endosymbiosis.
APICOPLAST – EM (gold labeling)
APICOPLAST morphology during life cycle of *P. falciparum* in RBC
ANTIPHOLATES

PABA

SULPHONAMIDES
SULPHONES

Dihydropteroate synthase

Dihydropteroate

Dihydropholate synthase

Dihydropholate (H$_2$F)

ANTIFOLÁTY

DHFR

Metyl-H$_4$F

dUMP

-CH$_3$

dTMP

Thymidilát syntáza

INHIBITORY DHFR:

Trimethoprim
Pyrimethamin
Trimetrexát Piritrexim

SULFONAMIDY, SULFONY:

Sulfametoxazol
Sulfadiazin
Sulfadoxin
Dapson
Effect of antiphololates

**Toxoplasma**
- Syntéza kys. listové
- Dihydrofolát reduktáza
- Folic acid

**Člověk**
- Syntéza kys. listové
- Dihydrofolát reduktáza
- Folic acid

- Sulfonamid
- Pyrimethamin

- Nuclei acid synthesis

- Folinová k.

- +

- -
Therapy of malaria

<table>
<thead>
<tr>
<th>Species</th>
<th>Antiparoxysmal</th>
<th>Antirelapses</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. vivax</em></td>
<td>Chloroquinn basis</td>
<td>Primaquin basis</td>
</tr>
<tr>
<td></td>
<td>10 mg/kg and 5 mg/kg after 12, 24 a 36 hrs.</td>
<td>0.25 mg/kg (0, 375 mg/kg) daily, 14 days</td>
</tr>
<tr>
<td><em>P. ovale</em></td>
<td>Same</td>
<td>No</td>
</tr>
<tr>
<td><em>P. malariae</em></td>
<td>Same</td>
<td>No</td>
</tr>
<tr>
<td><em>P. falciparum</em> chloroquinum sensitive</td>
<td>Same</td>
<td>No</td>
</tr>
<tr>
<td><em>P. falciparum</em> Chloroquinum resistant</td>
<td>Quinine, mefloquin, Fansidar, Malarone, Artemisinins, doxycyclins, Clindamycin</td>
<td>No</td>
</tr>
<tr>
<td>Therapy of tropical malaria</td>
<td>Non-complicated</td>
<td>Complicated</td>
</tr>
<tr>
<td>----------------------------</td>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td><strong>Mefloquin (LARIAM)</strong></td>
<td>750 – 500 – 250 mg every 8 hrs</td>
<td>Quinine</td>
</tr>
<tr>
<td><strong>Atovaquone + proguanil (Malarone)</strong></td>
<td>4 tbl./day for 3 dni</td>
<td><strong>Artesunat</strong></td>
</tr>
<tr>
<td><strong>Quinine sulfate + doxycyclin or clindamycin</strong></td>
<td>10 mg/kg po 8 hrs</td>
<td><strong>Artemether</strong></td>
</tr>
<tr>
<td><strong>Pyrimethamin + sulfadoxin (FANSIDAR)</strong></td>
<td>2 - 3 tbl. once</td>
<td></td>
</tr>
</tbody>
</table>
# Development of resistance against antimalarial treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Therapy since</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinine</td>
<td>1632</td>
<td>1970</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>1945</td>
<td>1957</td>
</tr>
<tr>
<td>Proguanil</td>
<td>1948</td>
<td>1949</td>
</tr>
<tr>
<td>Pyrimethamine/sulfadoxine</td>
<td>1967</td>
<td>1967</td>
</tr>
<tr>
<td>Meflochine</td>
<td>1977</td>
<td>1982</td>
</tr>
<tr>
<td>Atovaquon</td>
<td>1996</td>
<td>1996</td>
</tr>
<tr>
<td>Artemisinins</td>
<td>China ancient era</td>
<td>2009</td>
</tr>
</tbody>
</table>
Resistency of plasmodia against antimalarial treatment

- **Pl. falciparum**
  - Chloroquine: sensitive only in the meso America
  - Fansidar: Asia, Africa (especially eastern), South America; sensitivity – Arabian peninsula
  - Meflochin: SE Asia (Thailand, Cambodia, Barma, Vietnam), Amasonia only some parts
  - Quinine: decreased sensitivity in SE Asia, subsaharan Africa and Amasonia
  - Artemisinins: resistency described in january 2009 in SE asia

- **Pl. vivax**
  - Chloroquine: Oceania, PNG, some parts of Indonesia, SE Asia, Brasilia, Guayana, Peru, Columbia
  - Primachine: Indonesia, PNG, Western Pacific

- **Pl. malariae**
  - Chloroquine: occasionally Sumatra
Antimalaric prophylaxis I.

• Depending on the presence and resistency of *Pl. falciparum*

• Always combine with expositional prophylaxis

• Efficiency never 100%, protects from fatal course of the disease

• In the highly endemic areas better inadequate prophylaxis than none prophylaxis
ANTIMALARIAL PROPHYLAXIS – WHO ZONES
Antimalaric prophylaxis II

• Zone A:
  – Meso America, North Africa, Middle East, N. China
  – Chloroquine (DELAGIL) – 2 tbl./week
    • Begin 1 week before travel, continue 4 weeks after return

• Zone B:
  – India, Indonesia
  – Chloroquine + proguanil (PALUDRINE) - 2 tbl./day
    • proguanil: begin 1-2 days before and continue 4 weeks after return

• Zone C:
  – Trop. Africa, S America, SE. Asia, Oceania
  – Meflochine (LARIAM) – 1 tbl./week
    • Begin week before travel, continue 4 weeks after return
  – Atovaquon + proguanil (MALARONE) - 1 tbl./day
    • Begin 1 day before travel, continue 7 days after return
  – Doxycycline (DEOXYMYCOIN) – 1 tbl./day
    • SE. Asia – begin 1-2 days before and continue 4 weeks after return
Non-specific prophylaxis

- Mosquito nets
- Repelents
- Insecticides
# Recommended repellents

<table>
<thead>
<tr>
<th>Name</th>
<th>Active compound</th>
<th>Conc</th>
<th>Form</th>
<th>Producer</th>
</tr>
</thead>
<tbody>
<tr>
<td>REPELENT R 378</td>
<td>DEET</td>
<td>15%</td>
<td>water, spray</td>
<td>Astrid, CR</td>
</tr>
<tr>
<td>AUTAN</td>
<td>DEET</td>
<td>20%</td>
<td>water, spray, milk,</td>
<td>Bayer, Germany</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>nebulizer</td>
<td></td>
</tr>
<tr>
<td>SKIN TASTIC</td>
<td>DEET</td>
<td>16%</td>
<td>spray, milk, nebulizer</td>
<td>SC Johnson, Italy</td>
</tr>
<tr>
<td>DIPTEROL</td>
<td>DEET</td>
<td>20%</td>
<td>spray, napkin, stick</td>
<td>Pliva, Croatia</td>
</tr>
</tbody>
</table>