Heilsuvernd ferðamanna
Malaría

5. &12. mars 2008

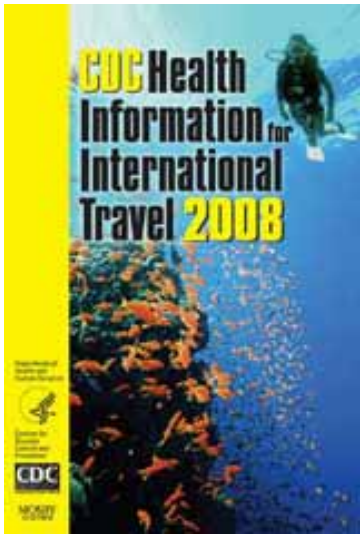
Kai Blöndal

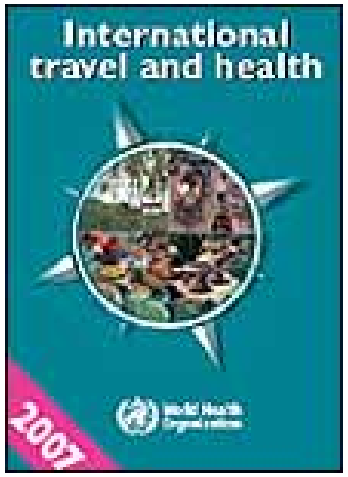
Miðstöð sóttvarna HH

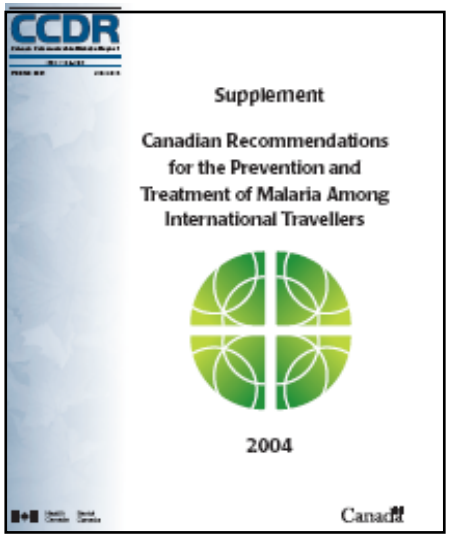
Contents

- Mosquitoes
- Epidemiology
- Transmission, Symptoms, Diagnosis
- Prevention:
  - Risk behavior
  - Prevent bites
  - Avoid bites - nets and clothing
  - Chemical barriers
  - Chemoprophylaxis
  - Pregnancy
  - Travelers' ABCD
  - Malaria vaccine
- Mosquito bites

Main publications used







What is malaria?

- **Malaria caused by one of four protozoan spieces of the genus Plasmodium:**
  - ***P. Falciparum* – *most deadly***
  - ***P. Vivax;***
  - ***P. Ovale***
  - ***P. Malariae***
- **All species are transmitted by the bite of an infected female *Anopheles* mosquito**
- **Illness and death from malaria is largely preventable**

Mosquitoes

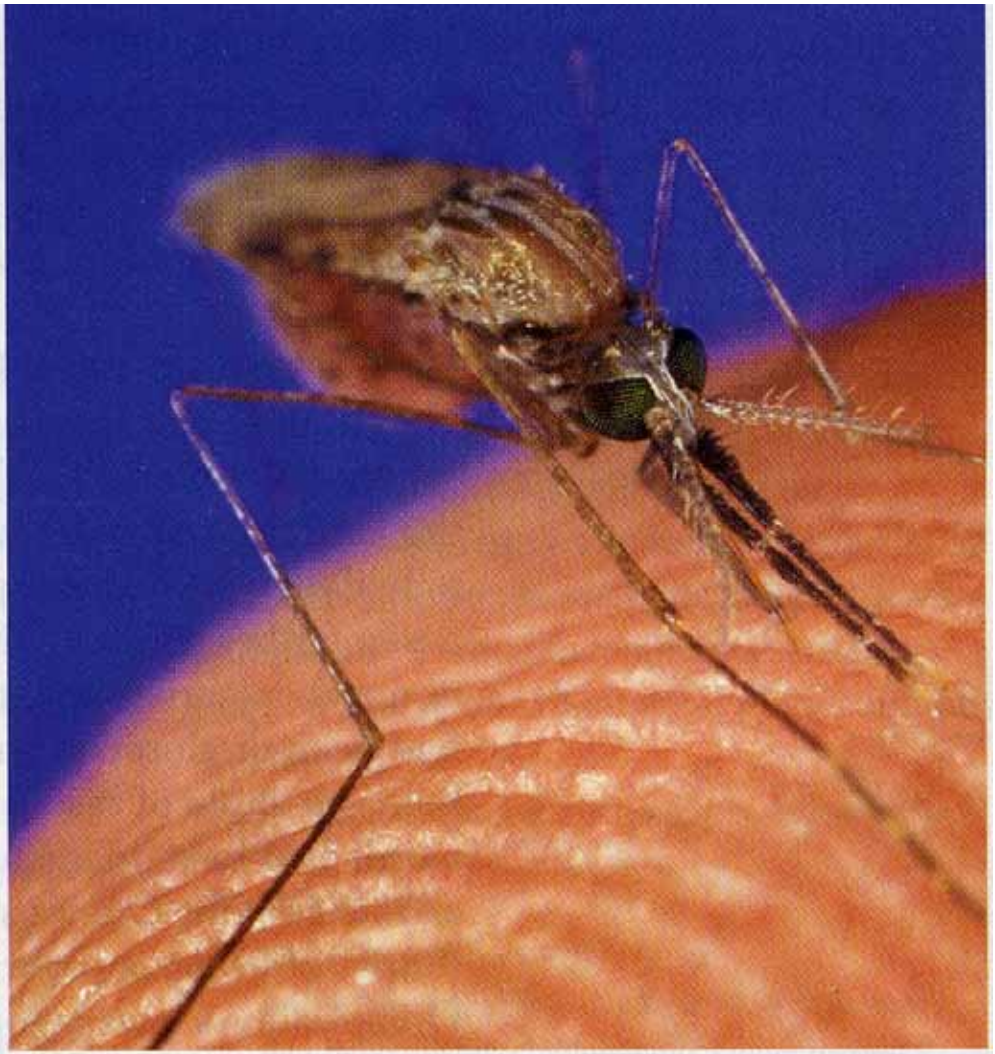
Mosquitoes in Baltic amber necklace 40 - 60 million years old

- **The females of most mosquito species suck blood from other animals**
- **Most species are dawn or evening feeders**
- **A mosquito can fly for 1 to 4 hours up to 1–2 km**
- **During the heat of the day most mosquitos rest in a cool place and wait for the evenings**

Wikipedia

http://www.malariasite.com/malaria/AnophelesMosquito.htm

Females do not require blood for survival, but for the development and laying eggs

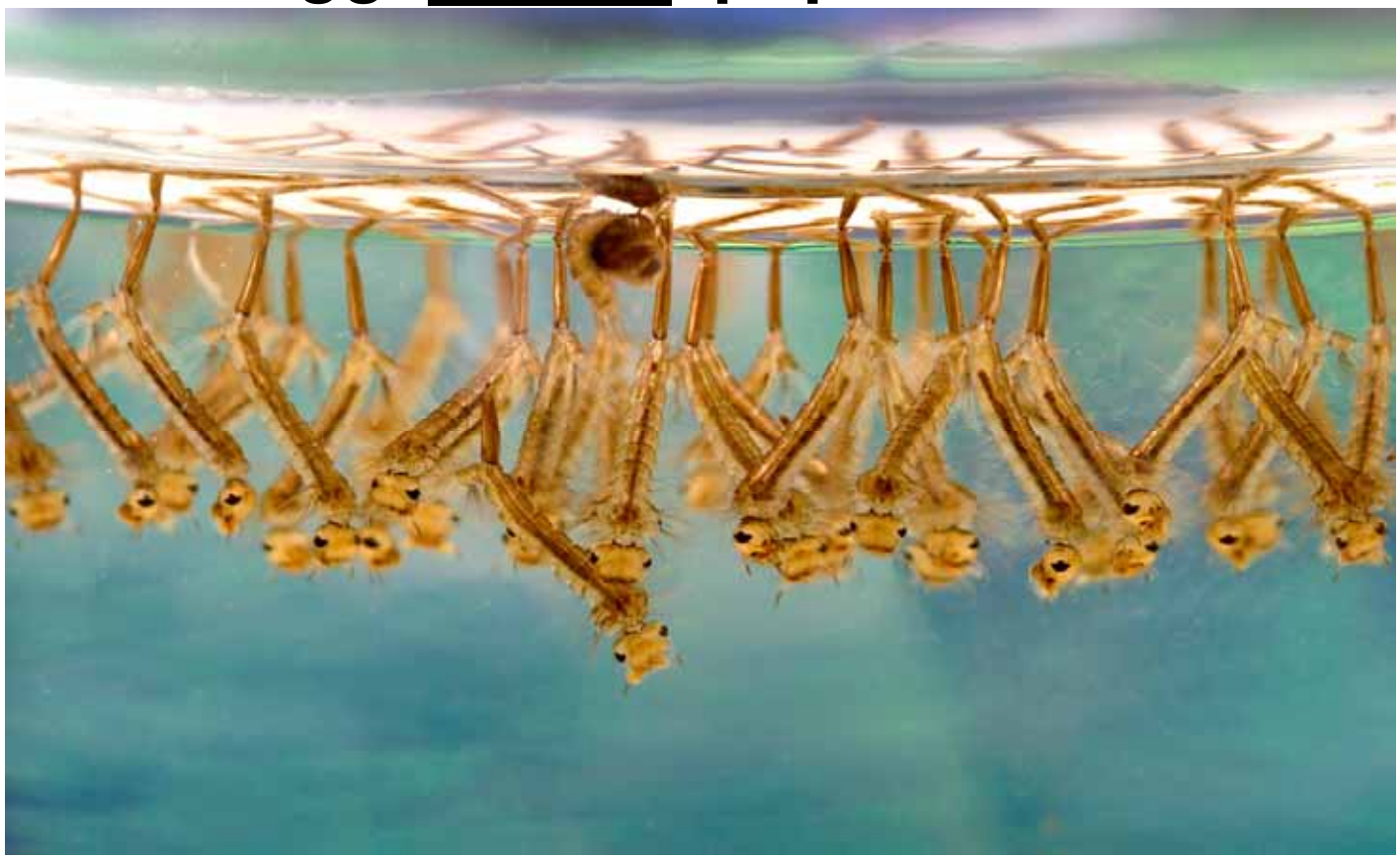


Anopheles gambiae mosquito

Prior to sucking the blood, they inject a mild painkiller and a anti-haemostatic, which numbs the host to the pain from the "bite“

Female mosquitoes lay their eggs one at a time or together in rafts of a hundred or more eggs on the surface in fresh or any stagnant water

Mosquito dvelepoment cycle:
Egg, larvae, pupa, adult



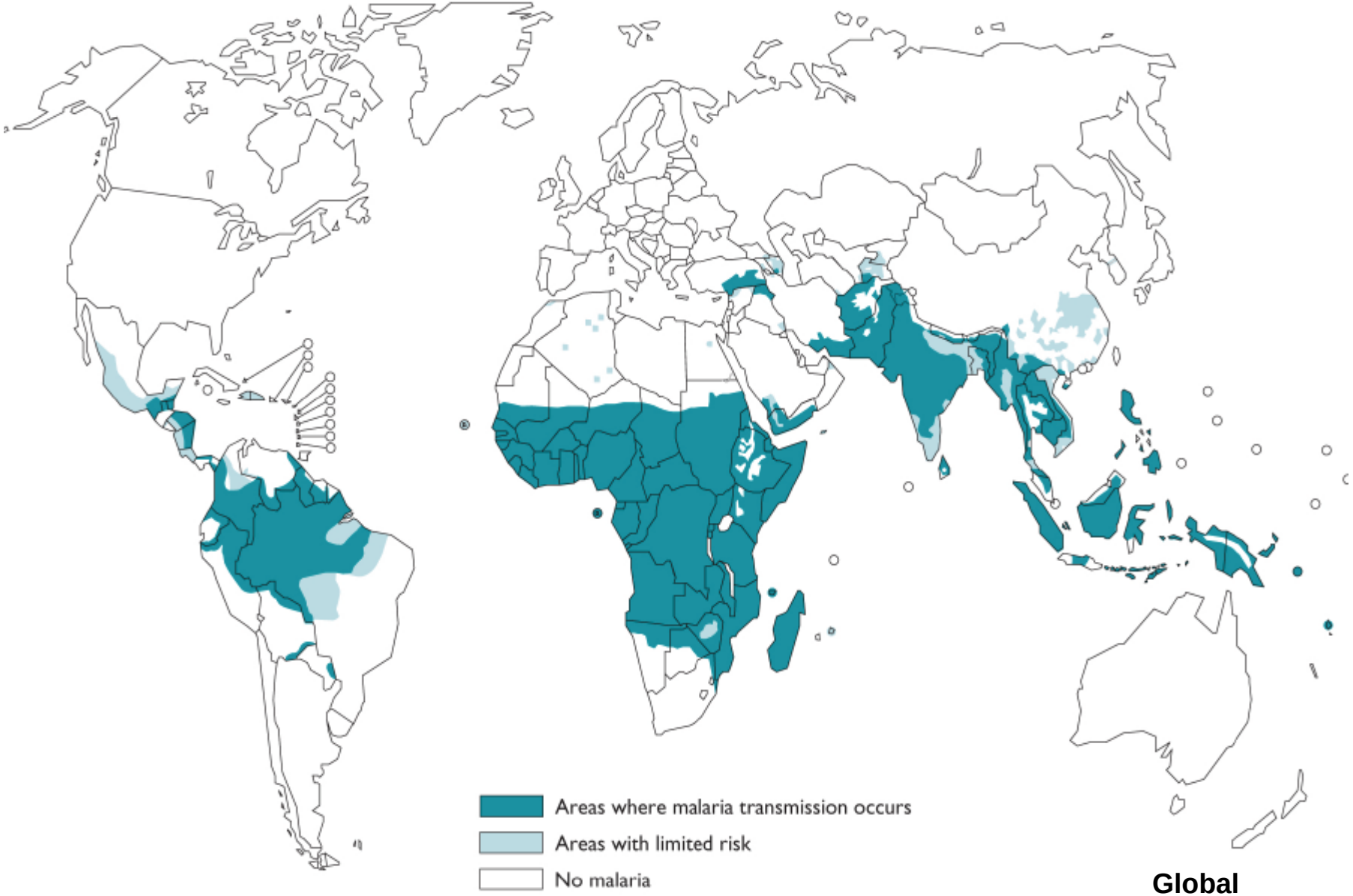
The adult mosquitoes hide themselves behind cupboards, clothes, curtains and other dark and cool corners during the day and come out to bite at night.

Occurrence

- **About 40% of the worlds population are at risk from malaria**
- **350-500 million infections worldwide**
- **Main burden of disease in Africa, from there come most cases among travelers**

1 million deaths annually most of them children

Malaria, 2006



Global Malaria Programme

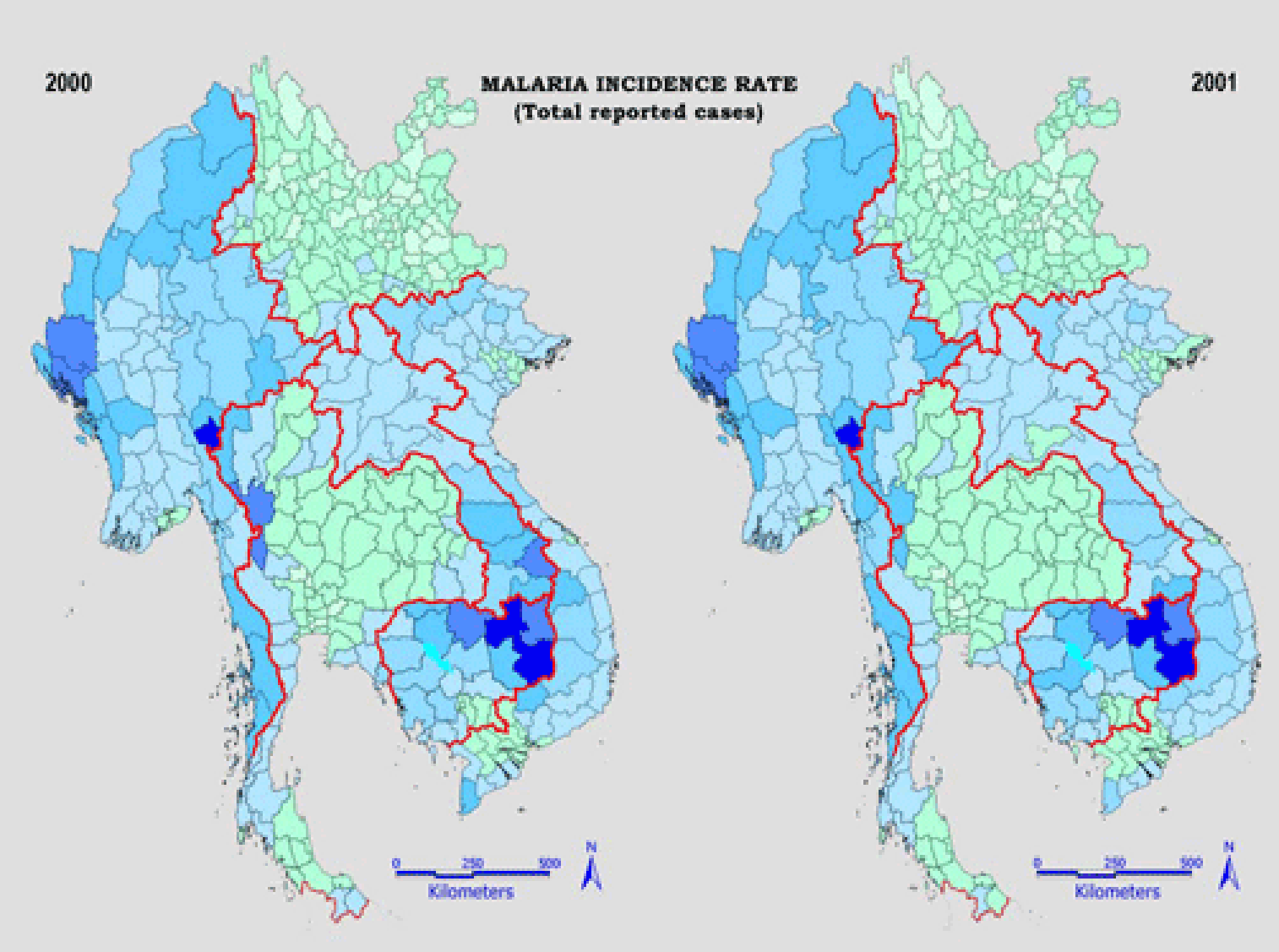
The risk of malaria changes over time

Map courtesy Health Protection Agency, Advisory Committee on Malaria Prevention

GOA

http://www.nathnac.org/ds/c_pages/country_page_IN.htm

South East Asia



Brazil

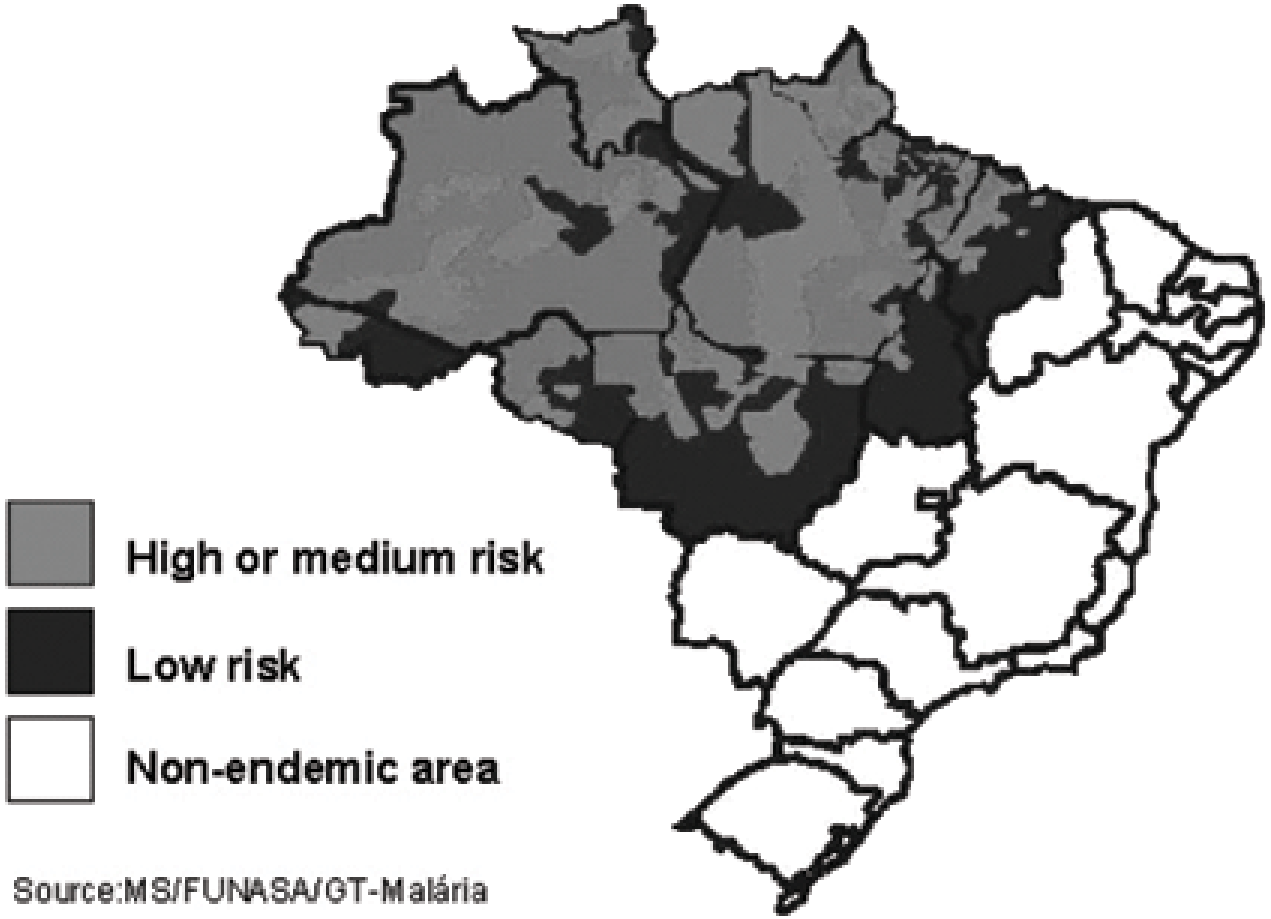
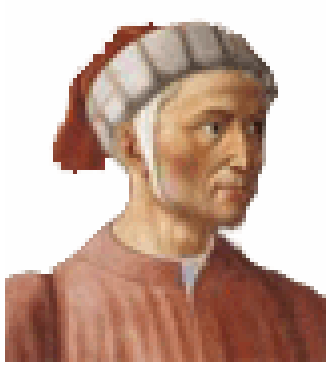
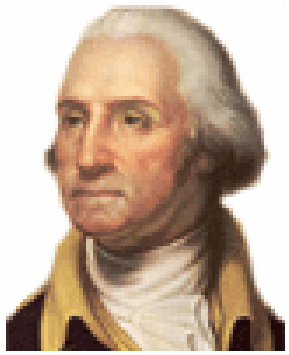


Fig. 1 – Malaria risk areas in Brazil.

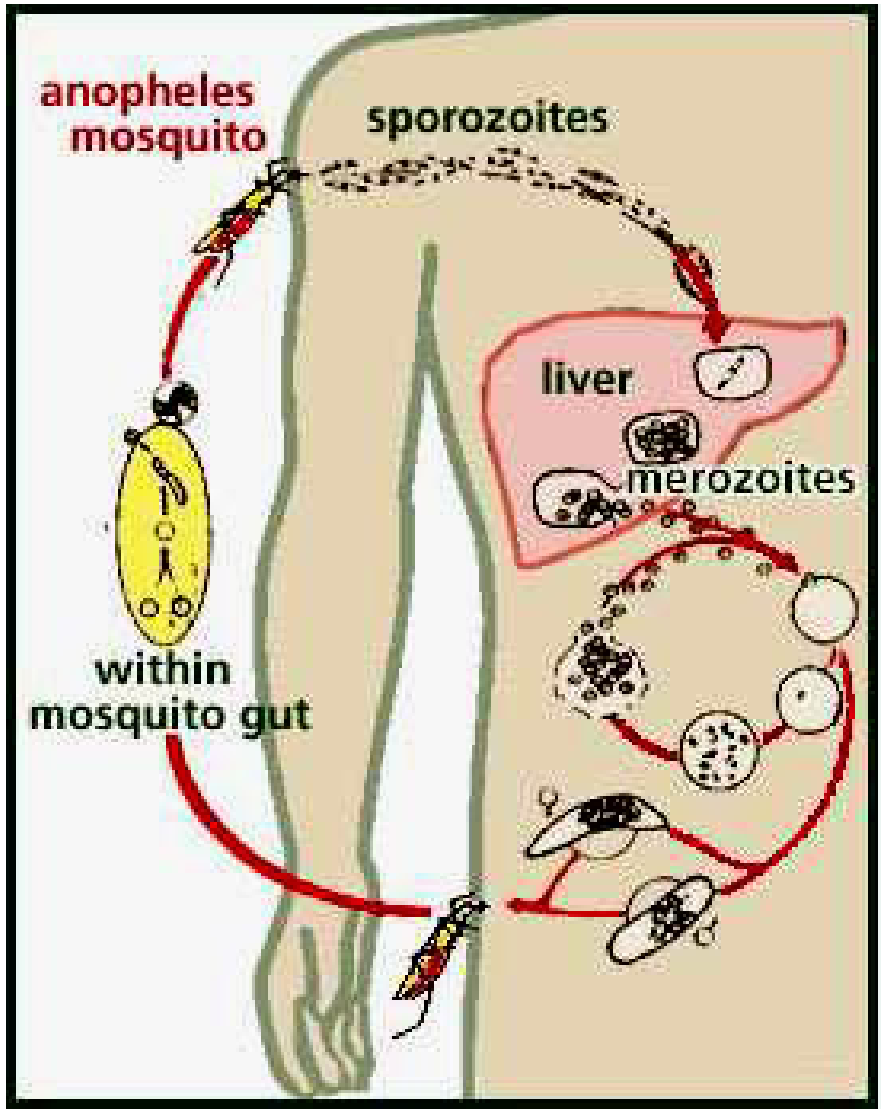
Gandhi, Livingstone, Mother Teresa, Kennedy, Dante, Washington



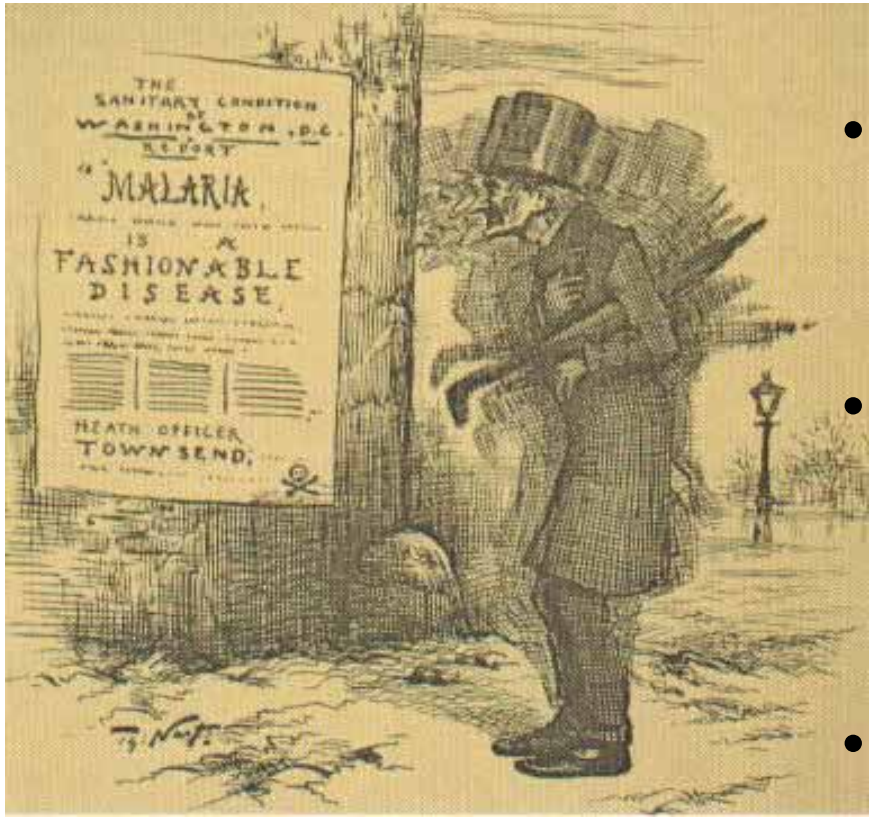


Lord Byron in Death Bed

Transmission



Symptoms



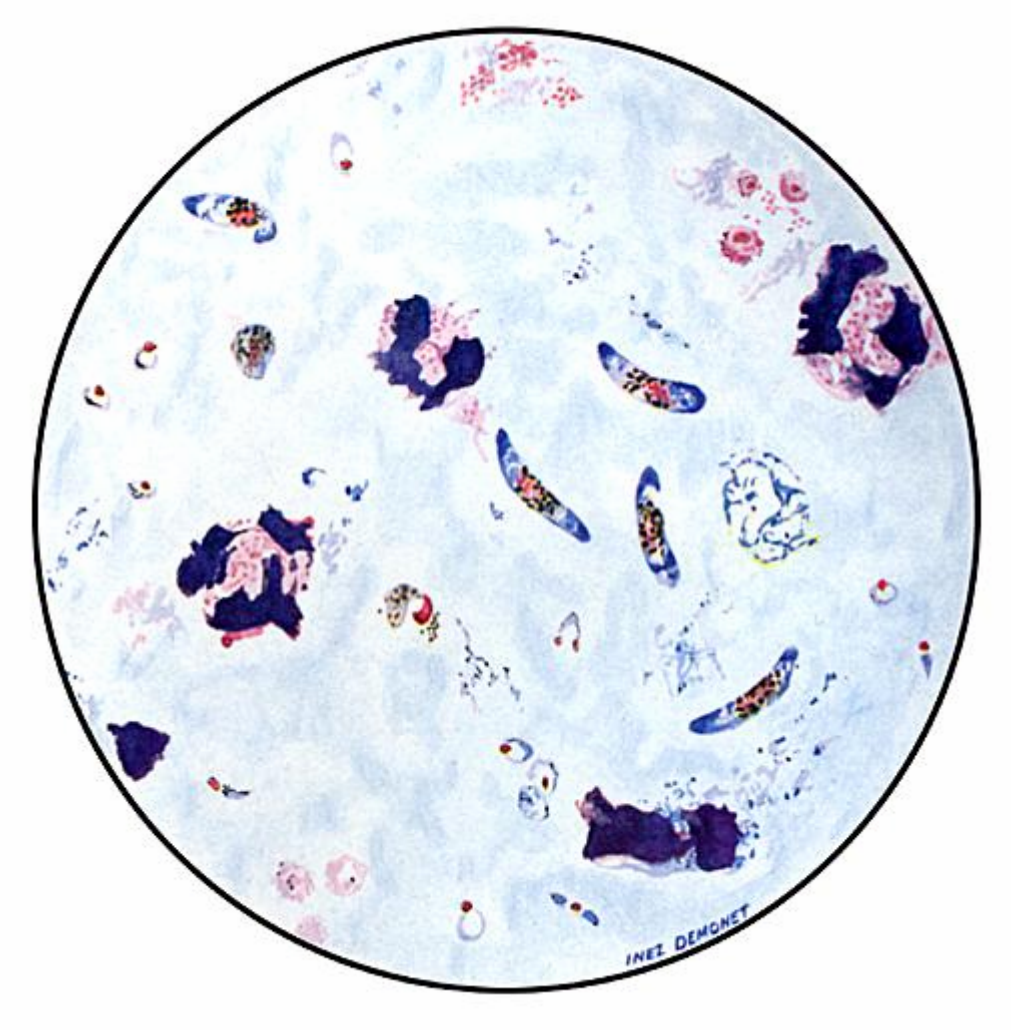
- **Surgeons from both sides of the Civil War called malaria *"ague","shakes"*, or *"intermittent fever"***
- **Started with shivers down the spine, then fluctuating fevers for days**
- **Doctors used a variety of treatments for malaria, but *whiskey and quinine* were the standard treatment**
- **Some were given so much quinine that their teeth became loose**

UK penguins struck by avian malaria

Diagnosis

- **Exposure to malaria and a history of fever in the previous (24h) 3 days**
- **Parasitological confirmation by light microscopy and rapid diagnostic tests (RDTs)**

Plasmodium Falciparum
thick smear



Prevention

- **Risk reduction behavior:**
  - **<u>avoid</u> mosquitoes, e.g., by staying in an insect-proof area during the period of the day when mosquitoes bite**
  - **<u>prevent</u> the bites of mosquitoes through:**
    - **physical barriers, e.g., clothing, bed nets**
    - **chemical barriers, e.g., repellents, insecticides**

Avoid mosquitoes

- doors and windows that close properly and tightly; and walls and roof that are “without holes”
- staying in a mosquito-protected area during the time(s) of the day when local mosquitoes are actively biting
- not traveling to an area at risk during the season

Prevent bites

- **Clothing: light-colored long-sleeved shirts and long pants (tucked into socks)**
- **Mosquito net: Sleeping under a mosquito net**
  - **The treatment of mosquito netting with insecticide (e.g. permethrin) substantially increases the protection**

http://www.safariquip.co.uk/acatalog/Mosquito_Nets.html

- **Travel Safe Net Cap**

Mosquito Net - Permethrin Treated

Outdoors spraying

Bed nets – Permetherin treated

Reality

World Health Organsization (WHO) Preventing malaria – nets and housing

- **The free distribution of insecticide treated bed nets halfed child death in Kenya***
- **Selling the nets does not work among the African populations but mass distribution will do**
- **Fewer than 7% of he housholds had an insecticide treated net in surveys conducted from 1999 to 2006.**
- **WHO would like to see 80% of the target groups (young children, pregnant mothers) sleeping under nets by 2010**

BMJ 2007;335:17

Permethrin Treatment Kit

Applications,1 mixing bag,1 pair disposable gloves, outer tub for water measurement plus instructions

<u>Effective for 3 month</u>

Comparative efficacy of pyrethroid insecticides for use on nets*

Active ingredient	Formulation	Brand**	Duration of efficacy† (mos)	Level of evidence
Permethrin EC 55%	Emulsified concentrate	Peripel	6	A I
Deltamethrin SC 1%	Suspension concentrate	K-Orthrine	12	A I
Deltamethrin 400 mg	Tablet	K-O Tab	12	A I
Lambda-Cyhalothrin CS 2.5%	Capsule suspension	Icon	9	A I
Cyfluthrin EW 0.05%	Water emulsion	Solfac	6-9	A I
Alpha-Cypermethrin SC 10%	Suspension concentrate	Fendona	6-9	A I

Health Canada. CCDR2004;30S1:1-62. Canadian recommendations for the prevention and treatment of malaria among international travelers

Doses of commonly used insecticides (in mg of insecticide per square metre of material – polyester)	
Compound and formulation	**Dose (mg of active ingredient/square metre)**
Permethrin EC	200-500
Deltamethrin SC	15-25
Deltamethrin tablet	1 tablet per net
Lambda-cyhalothrin CS	10-15
Cyfluthrin EW	30-50
Alpha-cypermethrin SC	20

Health Canada. CCDR2004;30S1:1-62. Canadian recommendations for the prevention and treatment of malaria among international travelers

- **Expedition 100 Spray Lifesystems 100ML CONTAINS 100% DEET:**
- **long lasting protection**
- **suitable for impregnating cotton and wool clothing.**
- **can be applied to skin in small quantities, very concentrated !**

- **Clothing Treatment: 0.5% Permethrin w/w**

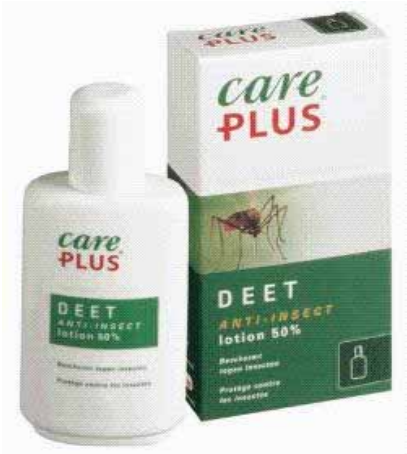
- **Effcetive for 2 weeks**

Prevent bites: Chemical Barriers

- **Repellents: DEET (N,N-diethyl-3-methylbenzamide, also known as N,N-diethyl*m*-toluamide) is generally acknowledged as the most effective of the currently available repellents**

- **"Natural-based" repellents: Most repellents containing "natural" products are effective for shorter durations than DEET**

The smell of the active ingredient (i.e. DEET or a natural active ingredient) is highly unpleasant for the insect however hardly noticeable and not harmful for humans



U.S. Environmental Protection Agency (EPA) registration:

- **DEET (N,N-diethylmetatoluamide)**
- **Picaridin (KBR 3023)**
- **IR 3535**
- **p-menthane 3,8-diole (PMD or oil of lemon eucalyptus)**
- **Oil of citronella**
- **MGK-326**
- **MGK-264**

Active ingredient	Formulation	Brand*	Duration of efficacy† (hrs)	Level of evidence
DEET < 10%	Pump spray, aerosol, gel, lotion	Cutter Skedaddle Skintastic (OFF)	1-3	A I
DEET 10%-30%	Pump spray, aerosol, lotion, stick	Cutter Backwoods Cutter Backyard Cutter Outdoorsman Deep Woods OFF! Muskol OFF!	4-6	A I
DEET 20%-35%	Lotion (microencapsulated slow release)	Sawyer Ultrathon	8-12	A I
Citronella oil 5%-15%	Pump spray, lotion, oil, towelette	Buzz Away Green Ban Herbal Armor Natrapel	0.3-0.5 (20-30 min)	E II
Lemon eucalyptus oil 10%-30%	Lotion	OFF! Botanicals Lotion Insect Repellent 1	2-5	A II
Soybean oil 2%	Oil	Bite Blocker	1-4	A II
Bayrepel 10%-20% (Picaridin/ Hepidanin)	Pump spray, aerosol	Autan	3-5 (10%) 8-10 (20%)	A II

*NOTE : These products are presented as examples only and are not necessarily endorsed by Health Canada.

Based on a 2002 study

(Fradin and Day, 2002.):

- **A product containing 23.8% DEET provided an average of 5 hours of protection from mosquito bites.**
- **A product containing 20% DEET provided almost 4 hours of protection**
- **A product with 6.65% DEET provided almost 2 hours of protection**
- **Products with 4.75% DEET were both able to provide roughly 1 and a half hour of protection.**

How to apply mosquito repellents?

- **Apply during the *biting time* - dusk to dawn.**
- ***Avoid contact with mucous membranes* (eyes, nostrils, mouth, lips)**
- **Do not allow *young children* to apply this product;**
- **Do not apply to sensitive, *sunburned* or damaged skin or deep skin folds.**
- **Use just enough repellent to cover exposed skin and/or clothing; *do not use under the clothing*.**
- **Avoid over-application.**
- ***Wash the hands* after applying the repellent.**
- **After returning indoors, *wash* treated skin with soap and water; wash treated clothing before wearing it again.**

Spray

- **In case of repellents formulated as sprays:**
  - **Do not spray in enclosed areas.**
  - **Do not spray directly onto face; spray on hands first and then rub on face.**
- **Repeated applications (every 3–4 hours) may be needed, especially in hot and humid climates.**
- **Strictly adhere to the manufacturers' instructions and do not exceed the dosage, especially for young children.**

Moscquito coil

Repellent stick

Mosquito Repellent Mats

Liquid Vaporizer

Ineffective personal protective measures against insects:

- These include electronic (ultrasonic) devices,
- *Wristbands*/neckbands/ankle bands impregnated with repellents
- Electrocuting devices (i.e., “bug zappers”), odor-baited mosquito traps,
- The Citrosa plant (i.e., geranium houseplant)
- *Oral vitamin B1*
- Avon Skin-So-Soft

Chemoprophylaxis

- **A strategy that uses medications**
  - **Before**
  - **During**
  - **And after**

  the exposure period to prevent the disease caused by malaria parasites
- **Compare *travel itinerary* with the information on areas of risk in the given country**
- **If there is a risk - decide if a anti-malarial drug *resistance* has been reported?**

- **Which chemoprophylaxis is appropriate???**

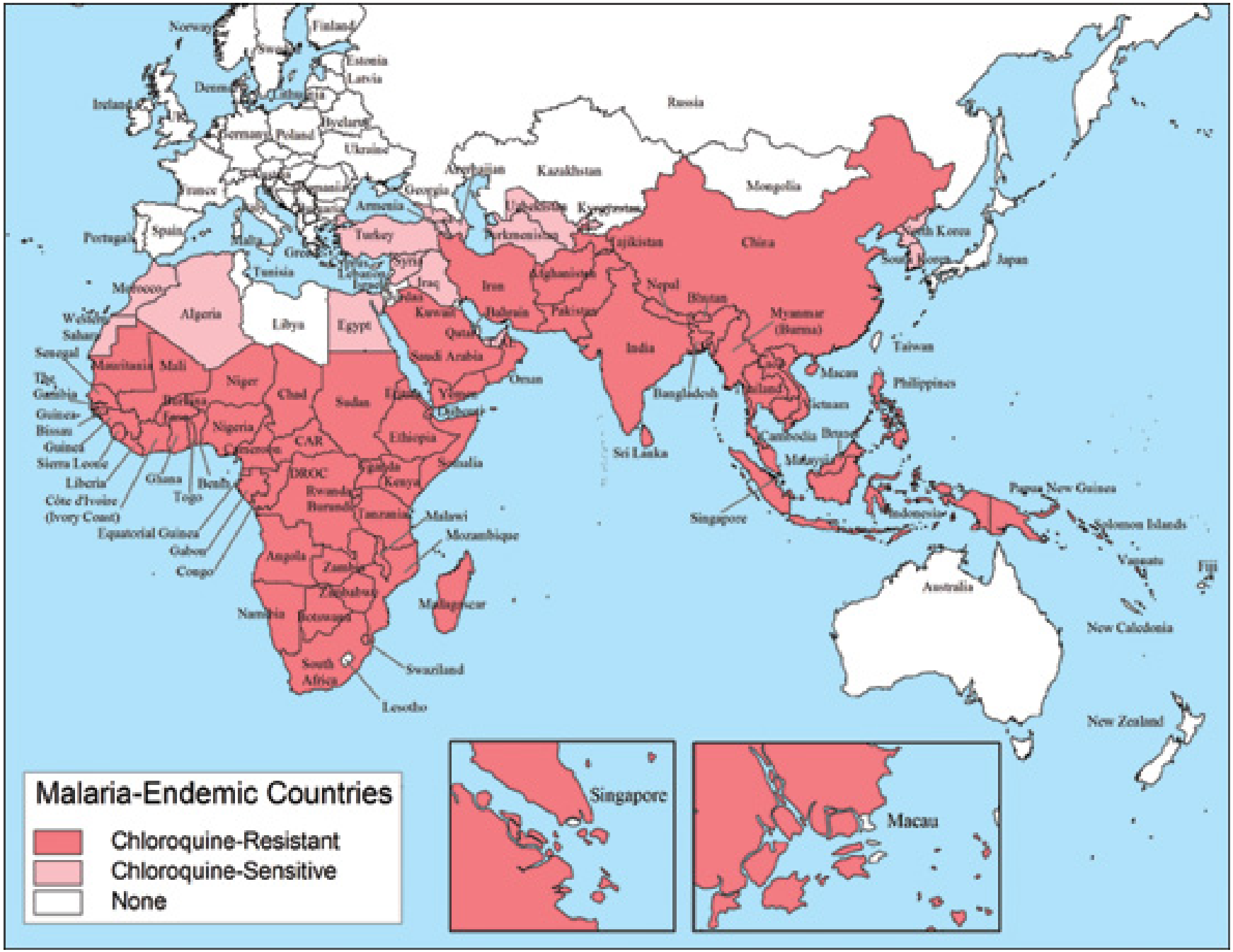
Chloroquine

Prophylaxis only in areas with chloroquine sensitive *P. Falciparum*

- **500 mg orally once / week. Begin 1-2 weeks before traveling to malarious areas, continue during stay, and for 4 weeks after leaving such areas**

- **May exacerbate psoriasis**

MAP 4-08 Malaria-endemic countries in the Eastern Hemisphere.



MAP 4-07 Malaria-endemic countries in the Western Hemisphere.

Mefloquine (Lariam)

- Begin 1-2 weeks before risk area
- Take all stay at risk
- Continue 4 weeks after leaving the risk area
- 1 tablet (250 mg) per week
- SIDE EFFECTS !!!!

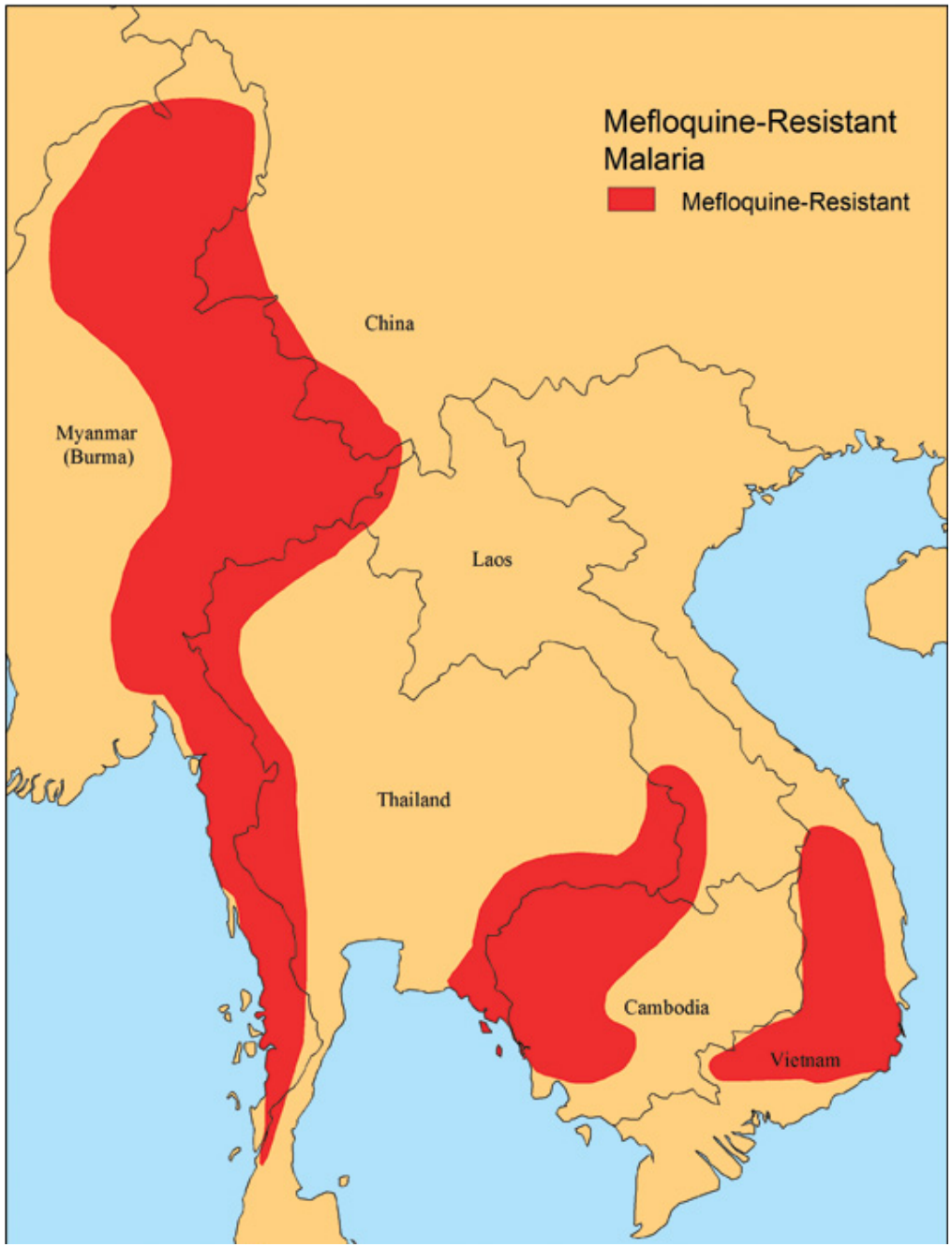
Contraindications: quinine allergy, active depression, psychosis, seizures, generalized anxiety disorder

Lariam: long term travellers (>6 mo)

- **N=1192, self-reported long term travelers**
- **Compliance 60%**
- **54% changed the regimen (2/5 because of side effects)**

Health Canada. CCDR2004;30S1:1-62. Canadian recommendations for the prevention and treatment of malaria among international travelers

MAP 4-09 Geographic distribution of mefloquine-resistant malaria.



Doxycyclin (Doxýtab)

- **Prophylaxis in areas with chloroquine resistant or mefloqunie resistant *P. falciparum***

- **100 mg orally, daily. Begin 1-2 days before traveling to a malarious area, continue during travel, stop 4 weeks after travel**

- **Contraindications: Children < 8 years, and pregnant women**

Malarone

- **Prophylaxis in areas with chloroquine resistant or mefloqunie resistant *P. falciparum***
- **250/100 mg once a day. Start 1-2 day before traveling to a malarious area, continue during travel, stop 7 days after travel**
- **Contraindications: Severe renal impairment. Not recommended for children < 5 kg, pregnant women, and women breastfeeding infants < 5kg**

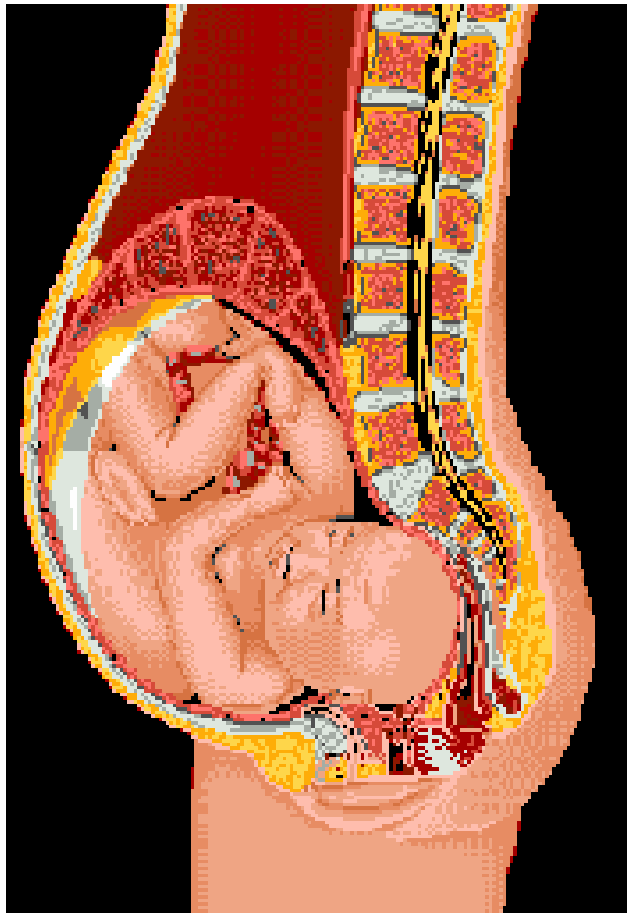
Malaria chemoprophylaxis regimens for at-risk individuals[a] according to presence of drug resistance

Region	Drug(s) of choice[b]	Alternatives
Chloroquine sensitive	Chloroquine	Atovaquone/proguanil, doxycycline, mefloquine
Chloroquine resistant	Atovaquone/proguanil, doxycycline, or mefloquine	Primaquine[c]
Chloroquine and mefloquine resistant	Doxycycline[d]	Atovaquone/proguanil

Changing medications during Chemoprophylaxis

- **Started mefloquine or doxycycline and changes to Malarone (atovaquone & proguanil hydrochloride)**
  - **If the change *3 weeks or more* before departure from the risk area: Malarone all remainder of the stay plus 7 days after**
  - **If the change *less than 3 weeks* before departure: Malarone all remainder and 4 weeks after**
  - **If the change occurs *following departure* from the risk area: Malarone 4 weeks after the date of departure**

Anti malarials in pregnancy:



- ***All trimesters:*** Chloroquine; Quinine; Artesunate / Artemether / Arteether
- ***2nd trimester:*** Mefloquine; Pyrimethamine / sulfadoxine
- ***3rd trimester:*** Mefloquine; ?Pyrimethamine / sulfadoxine
- ***Contra indicated:*** Primaquine; Tetracycline; Doxycycline; Halofantrine

Risk assessment for travelers

Higher risk

- Adventure travelers
- Peace corps volunteers
- Staying in rural areas (close to water)
- Poor adherence to prophylactic drug regimen, wrong regimen

Lower risk

- Hotel dwellers
- Cruise ship passengers if at sea
- Using anti-mosquito measures
- Dwelling in air conditioned houses

Travellers ABCD*

- **A - be aware of the risk, incubation period, main symptoms**
- **B – mosquitoes bite particularly between dusk and dawn**
- **C – chemoprophylaxis to prevent infection developing into disease**
- **D – diagnosis and treatment if a fever develops 1 week or more after entering malaria risk area or up to 3 months after**

* ***WHO 2007***

FUTURE: Candidate malaria vaccine

- **No vaccine available**
- **Candidate malaria vaccine - ongoing testing, efficacy 66%**
  - **A study of 214 babies in Mozambique given three doses of the new vaccine by 18 weeks or Engerix B, in addition to their routine diphtheria, tetanus, whole cell pertussis, hemophilus influenzae type b; and oral poliovirus**

BMJ 2007;335:851

Mosquito bites

- **Visible, irritating bites are due to an immune response from the binding of IgG and IgE antibodies to antigens in the mosquito's saliva**

Clements, A.N. 2000. The Biology of Mosquitoes. Volume 1: Development, Nutrition and Reproduction. CABI Publishing, Oxon. ISBN 0ö85199-374-5

http://scienceweek.com/2004/sb040416-6.htm; Budiansky S. Creatures of Our Own Making. Science. 2002; 298:80-86

Anti-itch medications

- **Anti-itch medications orally or topically applied *antihistamines* for more severe cases, *corticosteroids* such as hydrocortisone and triamcinolone.**

Contains chlorpheniramine

Corticosteroids:

Fucidin-Hydrocortison

Triamcinolone:

Pevisone, Kenalog

Histasín, Postafen, Aerius, Kestine, Clarytin, Lóritín, Periactin

- **Bite and Sting Relief *Spray***
- **A combination of menthol and bisabolol to help cool and soothe the skin.**
- **Can be used from the age of 3 years.**
- **Apply directly to the affected area.**

Patch **- reduce the itch and relieve the bite**

Mosquito bites

- ***Home remedies*** **are effective against itching, including calaming lotion, baking soda, rubbig alcohol, and vinegar.**

- ***Ammonia*** **is another ingredient in commercial mosquito bite treatments (e.g. Afterbite). Ammonia has been clinically demonstrated to be an effective treatment.**

- **It is also possible to temporarily stop the itching by rubbing a fresh clove of *garlic* against the bite.**

- **Another proven remedy for the itch is applying *heat* directly to the bite. Common methods for applying heat treatment include running hot water from a faucet over the irritated skin or heating a mug of water in a microwave for 1 to 2 minutes and then holding the hot mug against the bite for at least 1 minute.**

Maibach, Howard I. "Mosquito Bite Therapy: Evidence-Based". Exogenous Dermatology 3 (6): 332-338

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