It's a Small World After All: Dengue and Malaria in U.S Residents - Recognizing and Treating These Mosquito-borne Diseases

Clinician Outreach and Communication Activity (COCA) Conference Call

Wednesday, June 9, 2010

2:00 – 3:00 PM (Eastern Time)

Objectives

At the conclusion of this hour, each participant should be able to:

- Describe the evolving epidemiology of the two most prevalent mosquito-borne diseases worldwide
- Compare and contrast clinical presentations of dengue and malaria
- Describe prevention strategies for dengue and malaria
- Identify key points in diagnosis and treatment for dengue and malaria
- Discuss the importance of reporting suspected cases of dengue or malaria and reporting protocol

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Today's Presenters

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Malaria and Travel

David A. Townes, MD, MPH, DTM&H

Malaria Branch, Center for Global Health
Centers for Disease Control and Prevention
Atlanta, Georgia USA

Malaria and Travel

OUTLINE

- Malaria 101
- International Travel
- Prevention
- Diagnosis
- Treatment
- Resources

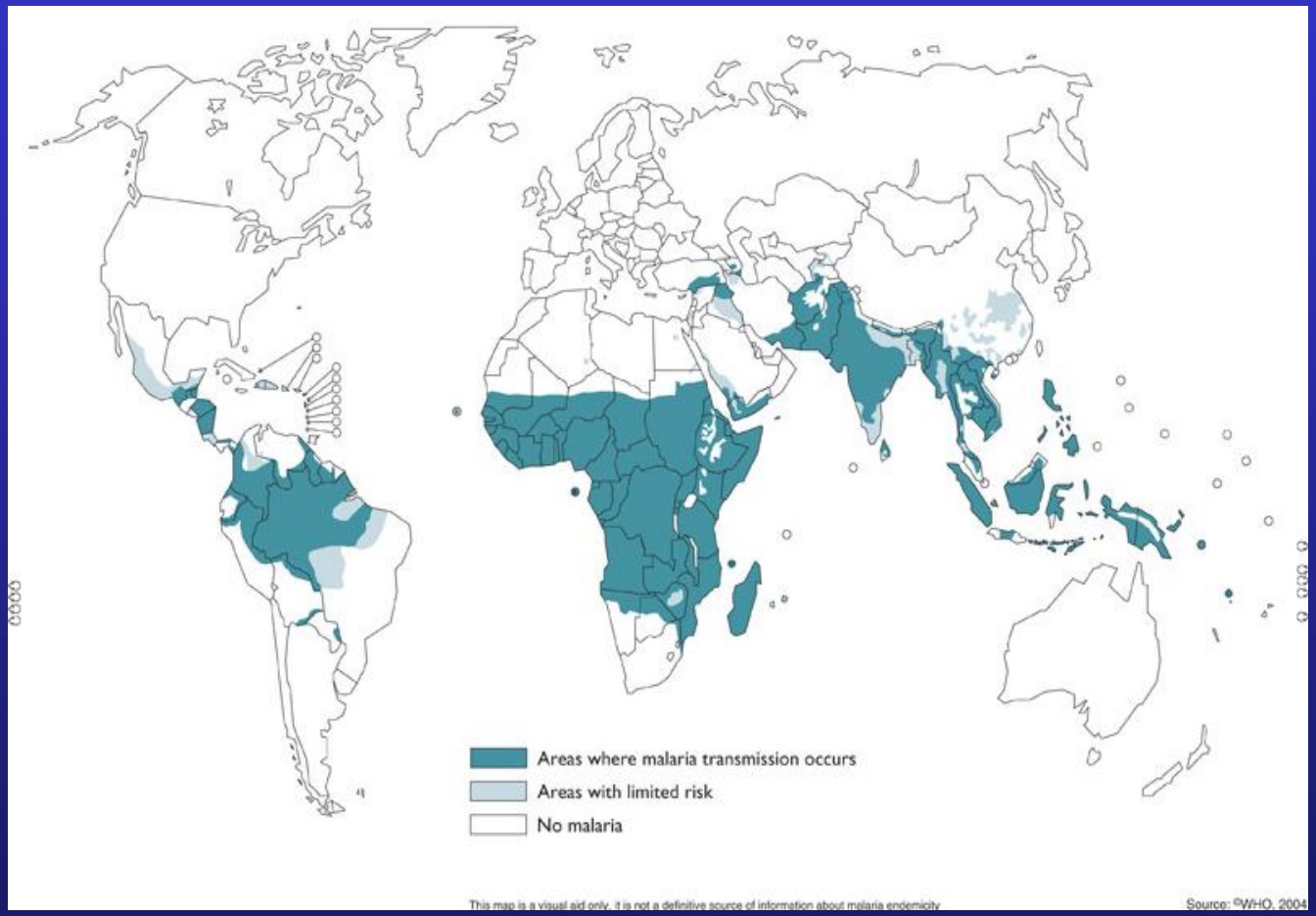
Malaria and Travel

MALARIA 101

- Parasitic infection with a protozoan
  - *Plasmodium falciparum*
  - *Plasmodium vivax*
  - *Plasmodium ovale*
  - *Plasmodium malariae*
  - *Plasmodium knowlesi*

Malaria and Travel

MALARIA 101



Malaria is Endemic in Over 100 Countries

Malaria and Travel

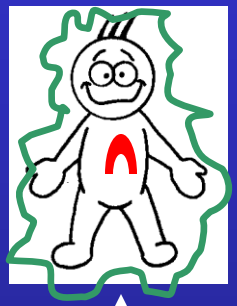
MALARIA 101

- Vector is the female anopheles mosquito
  - 400 different species
  - 30 ‘important’ species
  - Night biting
  - Rest indoors and outdoors

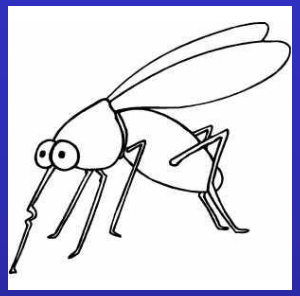
Malaria and Travel

MALARIA 101

Person infected with malaria (host)

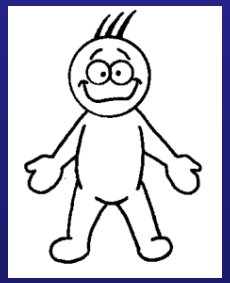


Uninfected mosquito bites infected person

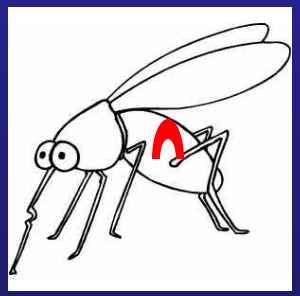


Mosquito not infected with malaria (potential vector)

Person not infected with malaria (potential host)



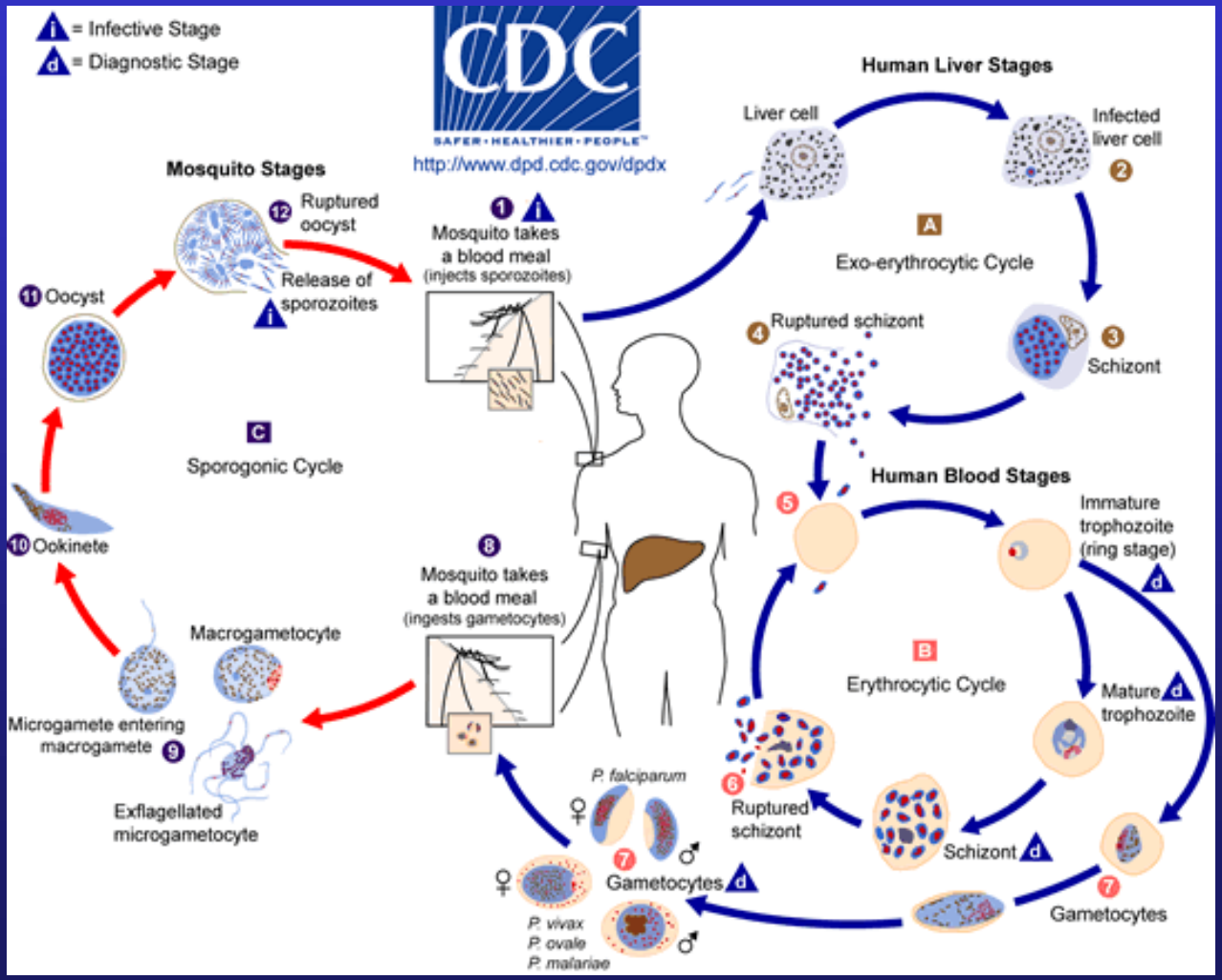
Infected mosquito bites uninfected person



Mosquito infected with malaria (vector)

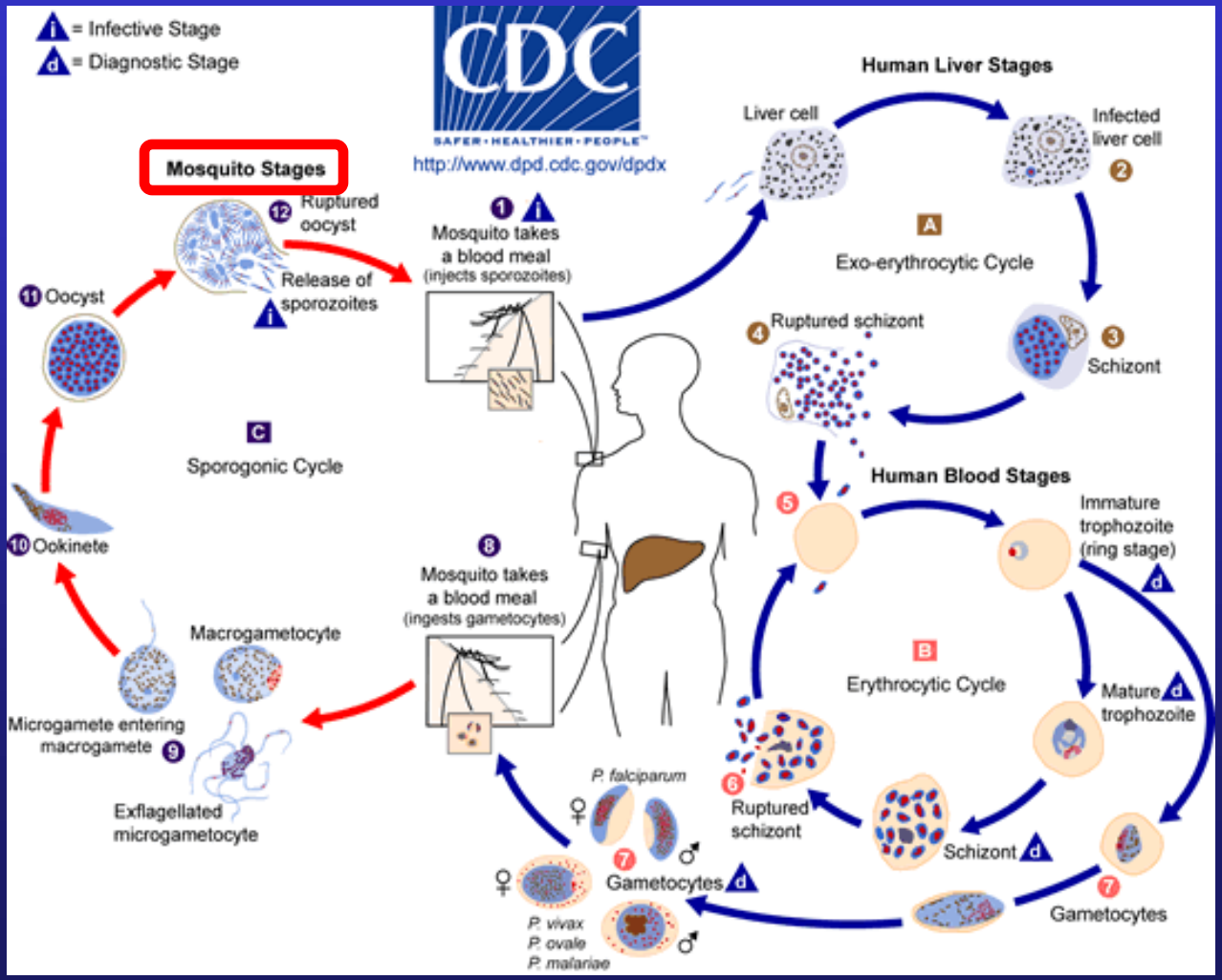
Malaria and Travel

MALARIA 101



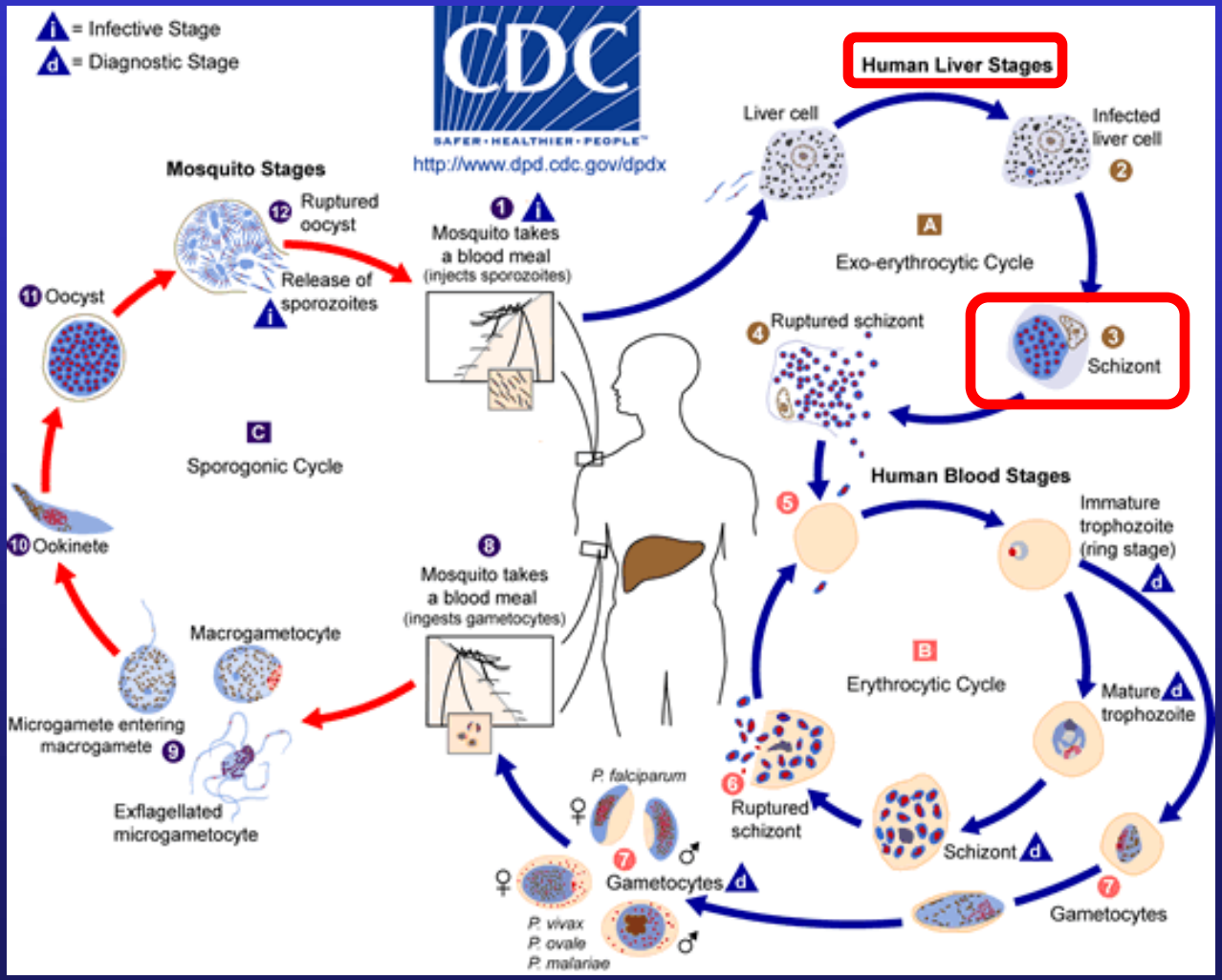
Malaria and Travel

MALARIA 101



Malaria and Travel

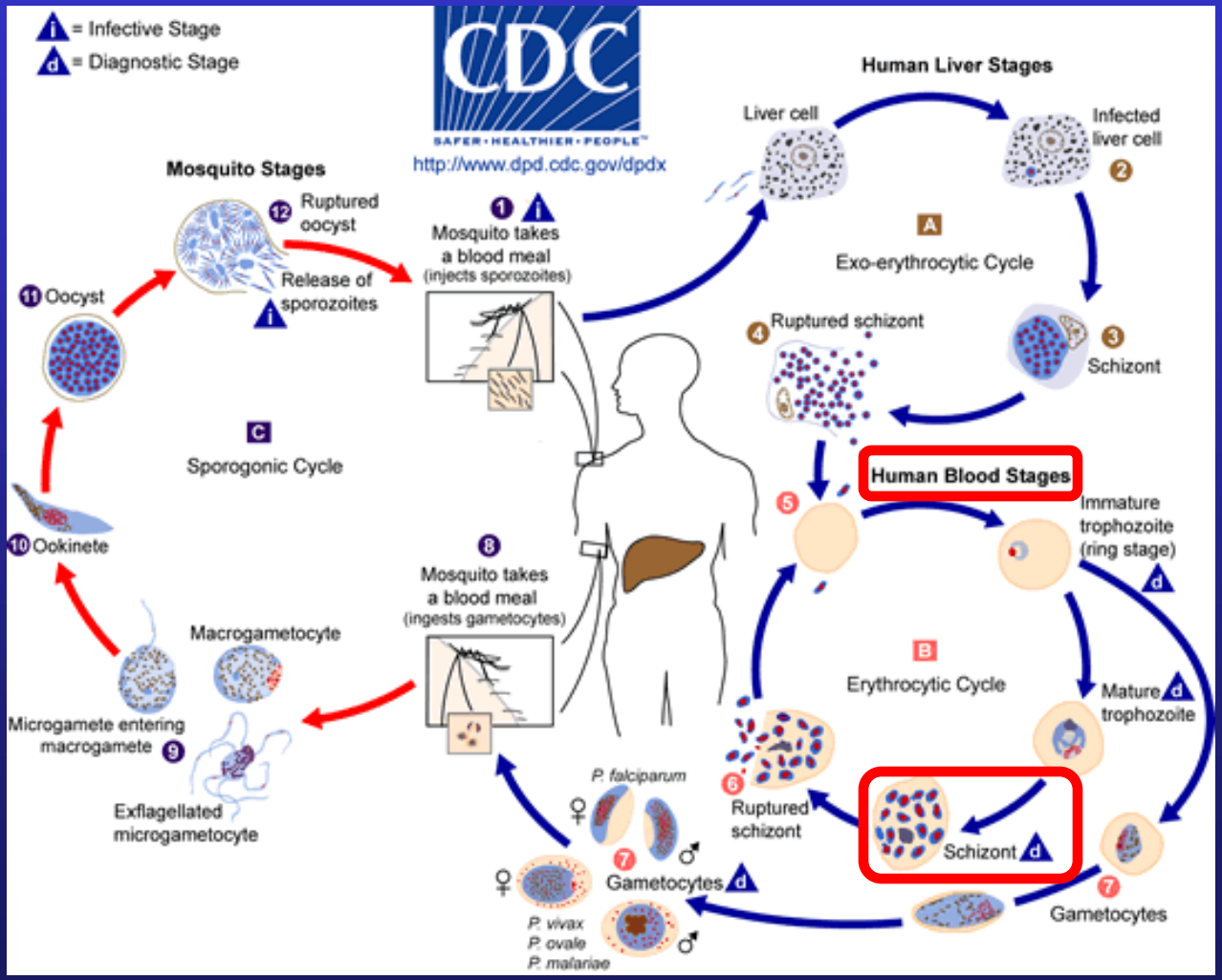
MALARIA 101



TS

Malaria and Travel

MALARIA 101



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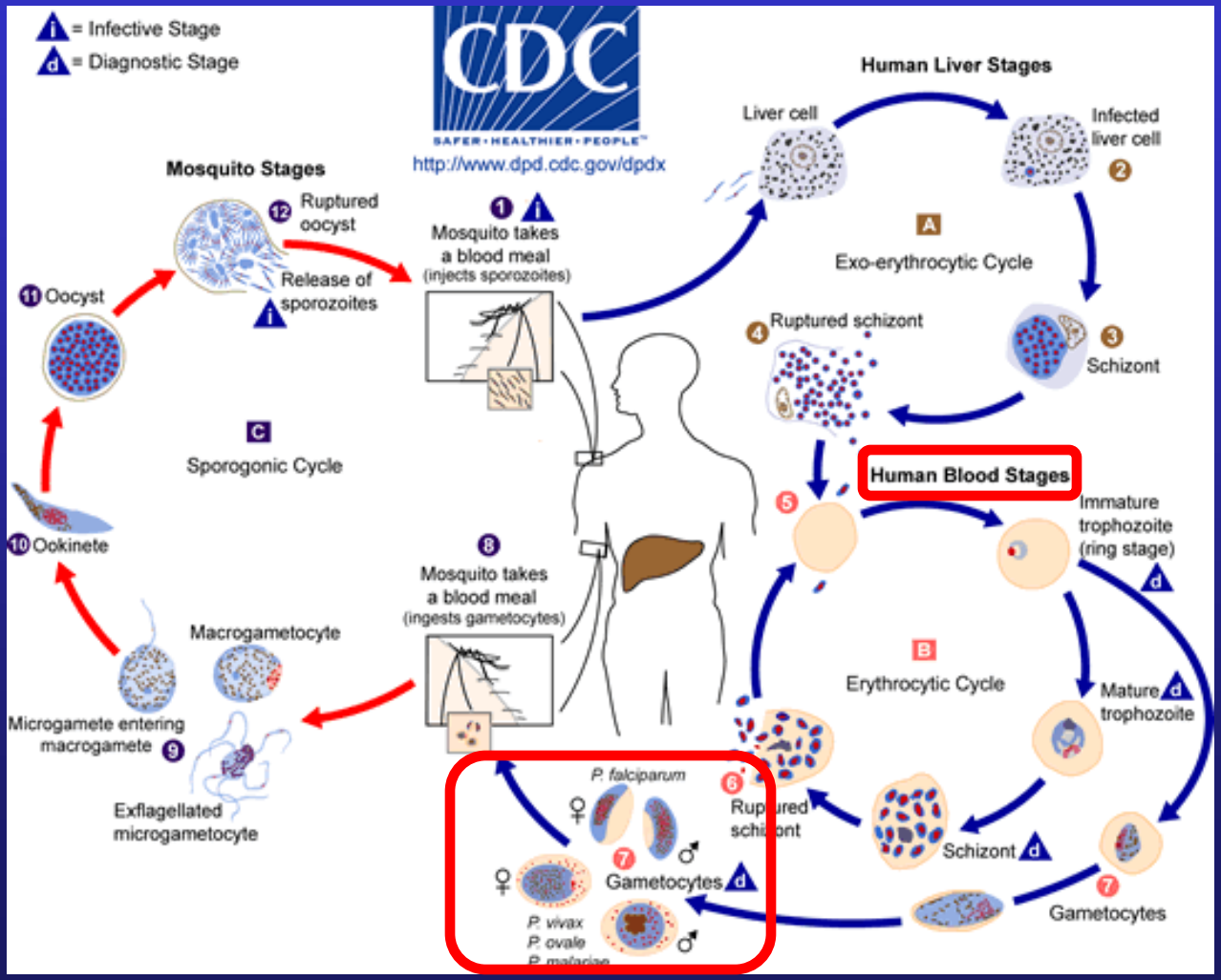
Malaria and Travel

MALARIA 101



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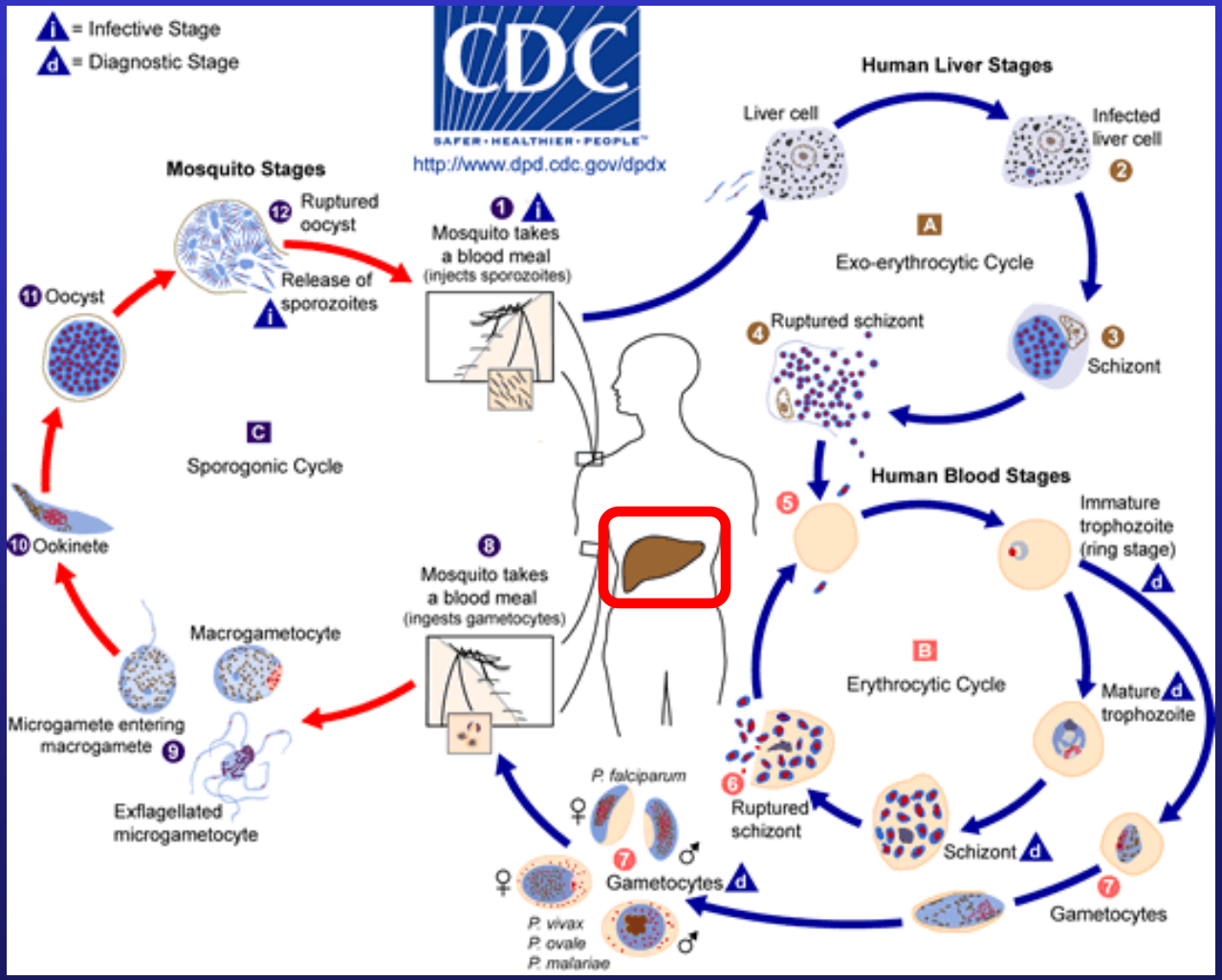
Malaria and Travel

MALARIA 101



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Malaria and Travel

MALARIA 101

- 250 million cases world wide
- 880,000 deaths
- Over 90% occur in sub-Saharan Africa

- The majority of deaths are in children under 5 years of age

WHO Annual Malaria Report, 2008

Malaria and Travel

OUTLINE

- Malaria 101
- International Travel
- Prevention
- Diagnosis
- Treatment
- Resources

Malaria and Travel

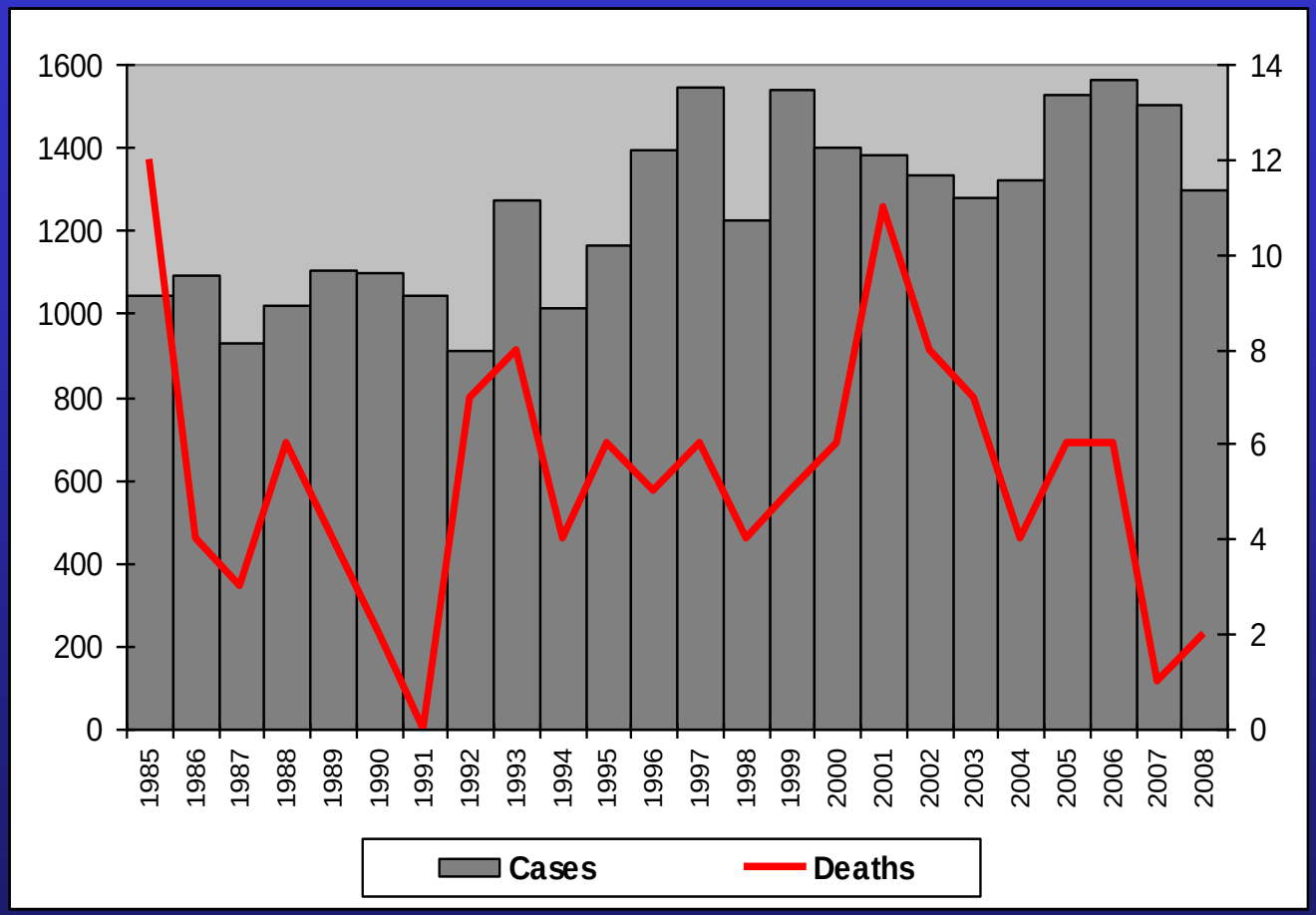
INTERNATIONAL TRAVEL

- 100,000 individuals visiting a developing country of 1 month
  - 50,000 will become ill (50%)
  - 8,000 will see a physician (8%)
  - 5,000 will stay in bed (5%)
  - 1 will die (0.001%)

Steffen R, et al. J Infect Dis 1987;156:84-91

Malaria and Travel

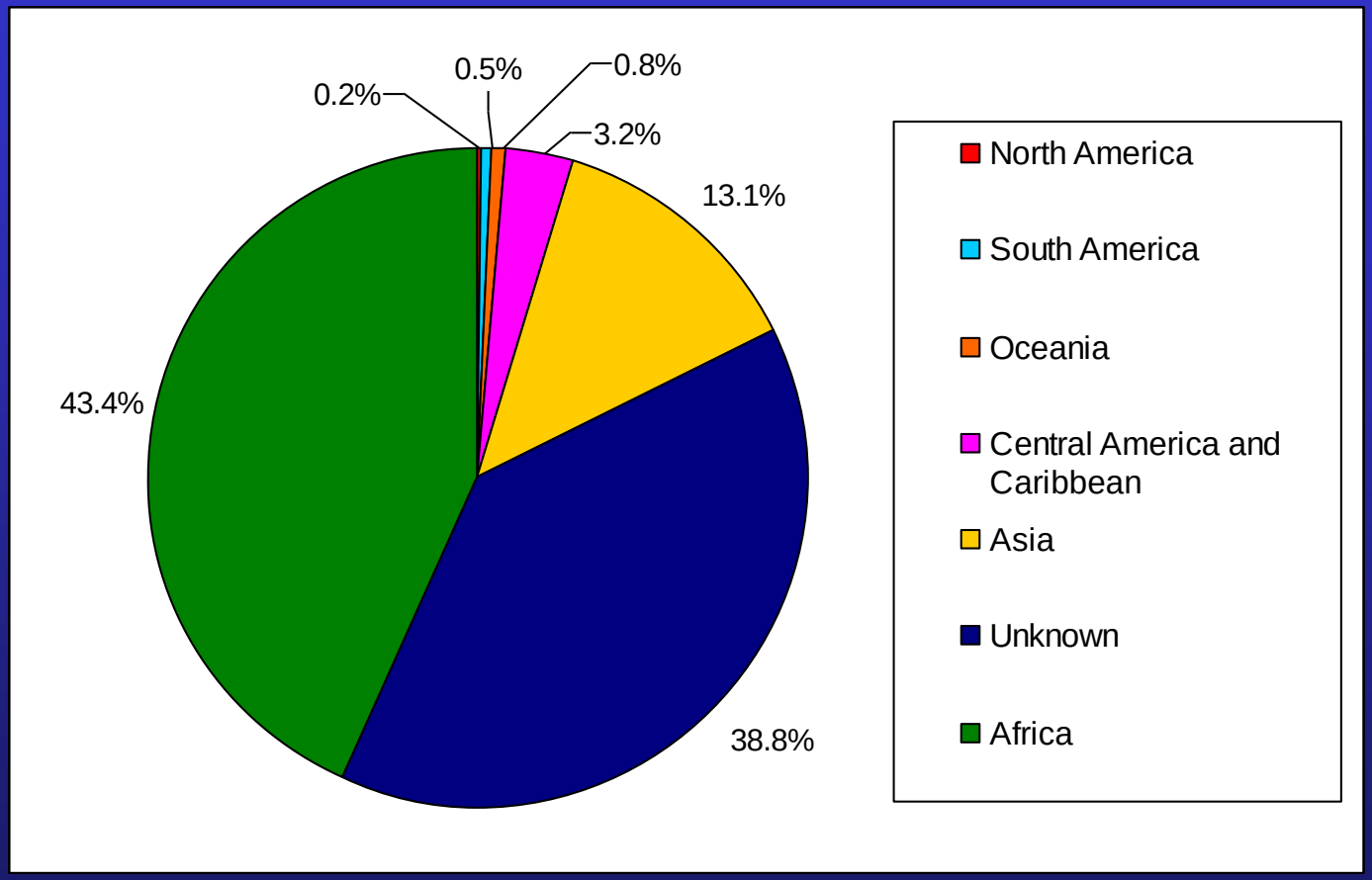
INTERNATIONAL TRAVEL



Malaria Cases and Deaths in the United States
1985 - 2008

Malaria and Travel

INTERNATIONAL TRAVEL



Geographic Area of Acquisition of Malaria Cases in the United States - 2008

Malaria and Travel

INTERNATIONAL TRAVEL

- All travel is not created equal . . . . .
  - Geography alone is not enough
  - Individual risk assessment
    - Destinations and specific itinerary
    - Type of travel, activities and accommodations
    - Season
    - Individual risk factors and ‘co-morbidities’ (pregnancy)

Malaria and Travel

OUTLINE

- Malaria 101
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Malaria and Travel

PREVENTION

- Mosquito avoidance
  - Insect repellants
  - Protective clothing
  - Insecticide treated bed nets
- Chemoprophylaxis
  - Medications

Malaria and Travel

PREVENTION

- Mosquito avoidance
  - DEET
    - No advantage to >50% concentration
    - Lower concentrations require more frequent application
  - Picaridin
    - Efficacy similar to DEET if at least 20% concentration
    - Some potential advantages
  - Others
    - Oil of lemon eucalyptus (40% concentration)
    - IR3535 / ‘Skin So Soft’ (10-20% concentration)

Malaria and Travel

PREVENTION

- Mosquito avoidance
  - Bed nets
    - INT and LLIN
  - Permethrin
    - Applied to clothing (some pre-treated)

Malaria and Travel

PREVENTION

	TS	BS	G	H
Chloroquine	TS	**BS**	G	H
Mefloquine	TS	**BS**	G	H
Doxycycline	TS	**BS**	G	H
Malarone	**TS**	**BS**	G	H
Primaquine	**TS**	**BS**	**G**	**H**

TS = tissue schizonts BS = blood schizonts G = gametocytes H = hypnozoites

Malaria and Travel

PREVENTION

- Chemoprophylaxis
  - Chloroquine (Aralen)®
    - *P. falciparum* generally resistant with limited exceptions
    - Considered safe in pregnancy
    - Start 1-2 weeks before and take weekly
    - End 4 weeks after

BS

Malaria and Travel

PREVENTION

- Chemoprophylaxis
  - Mefloquine (formerly Lariam®)
    - Reputation for psychological side effects
    - Considered safe in pregnancy
    - Start 2 weeks before and take weekly
    - End 4 weeks after

BS

Malaria and Travel

PREVENTION

- Chemoprophylaxis
  - Doxycycline
    - Least expensive
    - Potential protection against other diseases
    - Increased side effects with generic preparation
    - Contraindicated in pregnancy
    - Start 1-2 days before and take daily
    - End 4 weeks after

BS

Malaria and Travel

PREVENTION

- Chemoprophylaxis
  - Atovaquone / Proguanil (Malarone®)
    - Most expensive
    - Often best choice for short trips
    - Contraindicated in pregnancy
    - Start 1-2 days before and taken daily
    - End 7 days after

TS BS

CDC Centers for Disease Control and Prevention

PREVENTION

- Chemoprophylaxis
  - Primaquine
    - Primary prophylaxis (especially for *P. vivax*)
    - Terminal prophylaxis (*P.vivax* and *P. ovale*)
    - Possible hemolysis with G6PD deficiency
    - Contraindicated in pregnancy
    - Start 1-2 days before taken daily
    - End 7 days after

Malaria and Travel

OUTLINE

- Malaria 101
- International Travel
- Prevention
- Diagnosis
- Treatment
- Resources

Malaria and Travel

DIAGNOSIS

- Thick blood smear
  - Generally to answer the question . . . . .
    'Malaria, yes or no?'
  - Especially useful with low parasitemia
  - If negative, repeat every 12-24 hours for 36-72 hours or until 3 blood smears performed

Malaria and Travel

DIAGNOSIS

- Thin blood smear
  - To answer the question . . . . .

    'Malaria, yes or no?'
  - Also to determine species
  - Also to determine level of parasitemia
  - If negative, repeat every 12-24 hours for 36-72 hours or until 3 blood smears performed

Malaria and Travel

OUTLINE

- Malaria 101
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Malaria and Travel

TREATMENT

- Factors guiding treatment
  - *Plasmodium* species
  - Area of travel / acquisition
  - Drug-resistance
  - Parasitemia / parasite density
  - Clinical status of the patient

Malaria and Travel

TREATMENT

- Uncomplicated Malaria
  - Signs and symptoms may be non-specific
    - Fever, chills, head and body ache, vomiting, diarrhea, cough
    - Anemia, thrombocytopenia
  - Generally treated with oral therapy

Malaria and Travel

TREATMENT

- Treatment – uncomplicated malaria
  - Artemisinins
    - A group of compounds derived from sweet wormwood plant
    - Artemisinin combination therapy (ACT) is WHO first line therapy
    - Coartem® FDA approved in 2009

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Malaria and Travel

TREATMENT

- Treatment – uncomplicated malaria
  - Artemether / Lumefantrine (Coartem®)
    - *P. falciparum* or unidentified species
    - Limited data in pregnancy
    - Oral dosing
    - 3 day course

Malaria and Travel

TREATMENT

- Treatment – uncomplicated malaria
  - Atovaquone / Proguanil (Malarone®)
    - *P. falciparum* or unidentified species
    - Contraindicated in pregnancy
    - Oral dosing
    - 3 day course

TREATMENT

- Treatment – uncomplicated malaria
  - Quinine plus either doxycycline, tetracycline, or clindamycin for 7 days
    - *P. falciparum* or unidentified species
    - Quinine considered safe in pregnancy
    - Clindamycin considered safe in pregnancy
    - Oral dosing
    - 3 day course / 7 days for SE Asia

Malaria and Travel

TREATMENT

- Treatment – uncomplicated malaria
  - Mefloquine (formerly Lariam®)
    - *P. falciparum* or unidentified species not acquired in SE Asia (resistance)
    - Contraindicated in pregnancy
    - Oral dosing
    - 2 doses at time 0 and 6-12 hours

Malaria and Travel

TREATMENT

- Treatment – uncomplicated malaria
  - Chloroquine (Aralen®)
    - *P. vivax* generally sensitive with limited exceptions
    - *P. malariae* and *P. ovale* generally sensitive
    - *P. falciparum* generally resistant with limited exceptions
    - Considered safe in pregnancy
    - Oral dosing
    - 4 doses at time 0, 6, 24, 48 hours

Malaria and Travel

TREATMENT

- Treatment – uncomplicated malaria
  - Primaquine
    - Eradication of hypnozoites in *P.vivax* and *P. ovale*
    - Possible hemolysis with G6PD deficiency
    - Contraindicated in pregnancy
    - Oral dosing
    - 14 day course

Malaria and Travel

TREATMENT

- Severe Malaria
  - Anemia, hypoglycemia, DIC, acidosis, renal failure, ARDS, hemolysis, shock, cerebral malaria, hyperparasitemia (parasite density > 5%)
  - Generally treated with

    IV therapy

TREATMENT

- Treatment – severe malaria
  - Quinidine plus either doxycycline, tetracycline, or clindamycin
    - Requires cardiac monitoring (anti-arrhythmic)
    - Quinidine considered safe in pregnancy
    - Clindamycin considered safe in pregnancy
    - IV loading dose then daily dosing or continuous infusion

Malaria and Travel

TREATMENT

- Treatment – severe malaria
  - Artemisinins
    - A group of compounds derived from sweet wormwood plant
    - Artesunate available in US through the CDC via an Investigational New Drug Protocol

Malaria and Travel

TREATMENT

- Treatment – severe malaria
  - Artesunate
    - Limited data in pregnancy
    - 3 day course followed by one of the following
      - atrovaquone / proguanil for 3 days (oral)
      - doxycycline for 7 days (oral or IV)
      - clindamycin for 7 days (oral or IV)
      - mefloquine for 2 doses (oral)

Malaria and Travel

OUTLINE

- Malaria 101
- International Travel
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Malaria and Travel

RESOURCES

CDC Malaria Webpage
www.cdc.gov/malaria

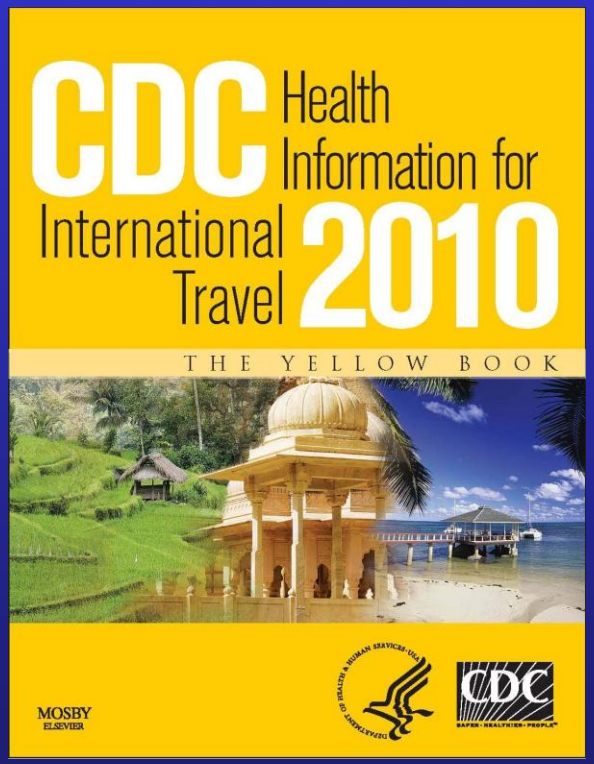
CDC Travelers Health Webpage
wwwnc.cdc.gov/travel/default.aspx

Malaria Map Application
www.cdc.gov/malaria/map/index.html

CDC Surveillance / Reporting Form
www.cdc.gov/malaria/report.html

Malaria and Travel

RESOURCES



Country	Areas with Malaria	Estimated relative risk of malaria for US travelers	Drug Resistance	Malaria Species	Recommended Chemoprophlaxis	Helpful links for Select Countries
Pakistan	All areas (including all cities) at altitudes below 2,500m (<8202 ft).	Moderate	Chloroquine	*P. falciparum* 70% *P. vivax* 30%	Atovaquone/ proguanil, doxycycline, or mefloquine	
Palau	None	None	Not Applicable	Not Applicable	Not Applicable	
Panama	Present in rural areas of the provinces of Bocas Del Toro, Darién, Veragaus, San Blas and San Blas Islands. None in Panama City or in the former Canal Zone.	Low	Chloroquine	*P. vivax* 90-95% *P. falciparum* 5-10%	Bocas Del Toro: Atovaquone/ proguanil, chloroquine, doxycycline, mefloquine, or primaquine Darién, San Blas, and Veragaus provinces: Atovaquone/ proguanil, doxycycline, mefloquine, or primaquine	**Provinces in Panama** **To determine if a city is within a certain province**
Papua New Guinea	Present throughout at altitudes below 1,800m (<5,906ft).	High	Chloroquine (both P. falciparum and P. vivax)	*P. falciparum* 65-80% *P. vivax* 10-30% *P. malariae* and *P. ovale* rare	Atovaquone/ proguanil, doxycycline, or mefloquine	**Altitude information** for Papua New Guinea
Paraguay	Present in the departments of Alto Paraná, Caaguazú, and Canendiyú.	Very Low	None	*P. vivax* 95% *P. falciparum* 5%	Atovaquone/ proguanil, chloroquine, doxycycline, mefloquine, or primaquine	**To determine if a city is within a certain department** **Departments of Paraguay**
	All departments below 2000m (6,561ft) **except** none in			*P. vivax* 70% *P. falciparum*	Lima, coastal areas south of Lima, or the highland tourist areas (Cuzco, Machu Picchu, and Lake Titicaca):	

www.cdc.gov/travel/contentYellowBook.aspx

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Malaria and Travel

RESOURCES

Guidelines for Treatment of Malaria in the United States

(Based on drugs currently available for use in the United States)

CDC Malaria Hotline: (770) 488-7788 Monday-Friday 8 am to 4:30 pm EST
(770) 488-7100 after hours, weekends and holidays (ask to page the malaria person on-call)

Clinical Diagnosis/ *Plasmodium* species	Region Infection Acquired	Recommended Drug and Adult Dose[1,8]	Recommended Drug and Pediatric Dose[1,8] *Pediatric dose should NEVER exceed adult dose*
Uncomplicated malaria/ *P. vivax* or *P. ovale*	**All regions**[8] Note: for suspected chloroquine-resistant *P. vivax*, see row below	**Chloroquine phosphate plus Primaquine phosphate**[7] **Chloroquine phosphate:** Treatment as above **Primaquine phosphate:** 30 mg base po qd x 14 days *2nd line alternative for treatment:* **Hydroxychloroquine plus Primaquine phosphate**[7] **Hydroxychloroquine:** Treatment as above **Primaquine phosphate:** 30 mg base po qd x 14 days	**Chloroquine phosphate plus Primaquine phosphate**[7] **Chloroquine phosphate:** Treatment as above **Primaquine phosphate:** 0.5 mg base/kg po qd x 14 days *2nd line alternative for treatment:* **Hydroxychloroquine plus Primaquine phosphate**[7] **Hydroxychloroquine:** Treatment as above **Primaquine phosphate:** 30 mg base po qd x 14 days
Uncomplicated malaria/ *P. vivax*	**Chloroquine-resistant**[8] (Papua New Guinea and Indonesia)	**A. Quinine sulfate**[2] **plus either Doxycycline or Tetracycline plus Primaquine phosphate**[7] **Quinine sulfate:** Treatment as above **Doxycycline or Tetracycline:** Treatment as above **Primaquine phosphate:** Treatment as above	**A. Quinine sulfate**[2] **plus either Doxycycline**[4] **or Tetracycline**[4] **plus Primaquine phosphate**[7] **Quinine sulfate:** Treatment as above **Doxycycline or Tetracycline:** Treatment as above **Primaquine phosphate:** Treatment as above
		B. Mefloquine plus Primaquine phosphate[7] **Mefloquine:** Treatment as above **Primaquine phosphate:** Treatment as above	**B. Mefloquine plus Primaquine phosphate**[7] **Mefloquine:** Treatment as above **Primaquine phosphate:** Treatment as above
Uncomplicated malaria: alternatives for pregnant women[9,10,11,12]	**Chloroquine-sensitive**[12] (see uncomplicated malaria sections above for chloroquine-sensitive *Plasmodium* species by region)	**Chloroquine phosphate:** Treatment as above *2nd line alternative for treatment:* **Hydroxychloroquine:** Treatment as above	Not applicable
	Chloroquine resistant *P. falciparum*[9,10,11] (see uncomplicated malaria sections above for regions with known chloroquine resistant *P. falciparum*)	**Quinine sulfate**[2] **plus Clindamycin** **Quinine sulfate:** Treatment as above **Clindamycin:** Treatment as above	Not applicable
	Chloroquine-resistant *P. vivax*[9,10,11,12] (see uncomplicated malaria sections above for	**Quinine sulfate** **Quinine sulfate:** 650 mg[3] salt po tid x 7 days	Not applicable

[7] Primaquine is used to eradicate any hypnozoite forms that may remain dormant in the liver, and thus prevent relapses, in *P. vivax* and *P. ovale* infections. Because primaquine can cause hemolytic anemia in persons with G6PD deficiency, patients must be screened for G6PD deficiency prior to starting treatment with primaquine. For persons with borderline G6PD deficiency or as an alternate to the above regimen, primaquine may be given 45 mg orally one time per week for 8 weeks; consultation with an expert in infectious disease and/or tropical medicine is advised if this alternative regimen is considered in G6PD-deficient persons. Primaquine must not be used during pregnancy.

[8] NOTE: There are two options (A or B) available for treatment of uncomplicated malaria caused by chloroquine-resistant *P. vivax*. High treatment failure rates due to chloroquine-resistant *P. vivax* have been well documented in Papua New Guinea and Indonesia. Rare case reports of chloroquine-resistant *P. vivax* have also been documented in Burma (Myanmar), India, and Central and South America. Persons acquiring *P. vivax* infections outside of Papua New Guinea or Indonesia should be started on chloroquine. If the patient does not respond, the treatment should be changed to a chloroquine-resistant *P. vivax* regimen and CDC should be notified (Malaria Hotline number listed above). For treatment of chloroquine-resistant *P. vivax* infections, options A and B are equally recommended.

[9] For pregnant women diagnosed with uncomplicated malaria caused by chloroquine-resistant *P. falciparum* or chloroquine-resistant *P. vivax* infection, treatment with doxycycline or tetracycline is generally not indicated. However, doxycycline or tetracycline may be used in combination with quinine (as recommended for non-pregnant adults) if other treatment options are not available or are not being tolerated, and the benefit is judged to outweigh the risks.

[10] Because there are no adequate, well-controlled studies of atovaquone and/or proguanil hydrochloride in pregnant women, atovaquone-proguanil is generally not recommended for use in pregnant women. For pregnant women diagnosed with uncomplicated malaria caused by chloroquine-resistant *P. falciparum* infection, atovaquone-proguanil may be used if other treatment options are not available or are not being tolerated, and if the potential benefit is judged to outweigh the potential risks. There are no data on the efficacy of atovaquone-proguanil in the treatment of chloroquine-resistant *P. vivax* infections.

[11] Because of a possible association with mefloquine treatment during pregnancy and an increase in stillbirths, mefloquine is generally not recommended for treatment in pregnant women. However, mefloquine may be used if it is the only treatment option available and if the potential benefit is judged to outweigh the potential risks.

[12] For *P. vivax* and *P. ovale* infections, primaquine phosphate for radical treatment of hypnozoites should not be given during pregnancy. Pregnant patients with *P. vivax* and *P. ovale* infections should be maintained on chloroquine prophylaxis for the duration of their pregnancy. The chemoprophylactic dose of chloroquine phosphate is 300 mg base (=500 mg salt) orally once per week. After delivery, pregnant patients who do not have G6PD deficiency should be treated with primaquine.

Malaria Hotline / Clinician on Call

(770) 488-7788 (9-5 M-F)

(770) 488-7100 (after hours, weekends and holidays)

CDC Centers for Disease Control and Prevention

Dengue Update for US Clinicians

Christopher J. Gregory, MD, MPH
EIS Officer, Dengue Branch
Centers for Disease Control and Prevention
San Juan, Puerto Rico, USA

Dengue Overview

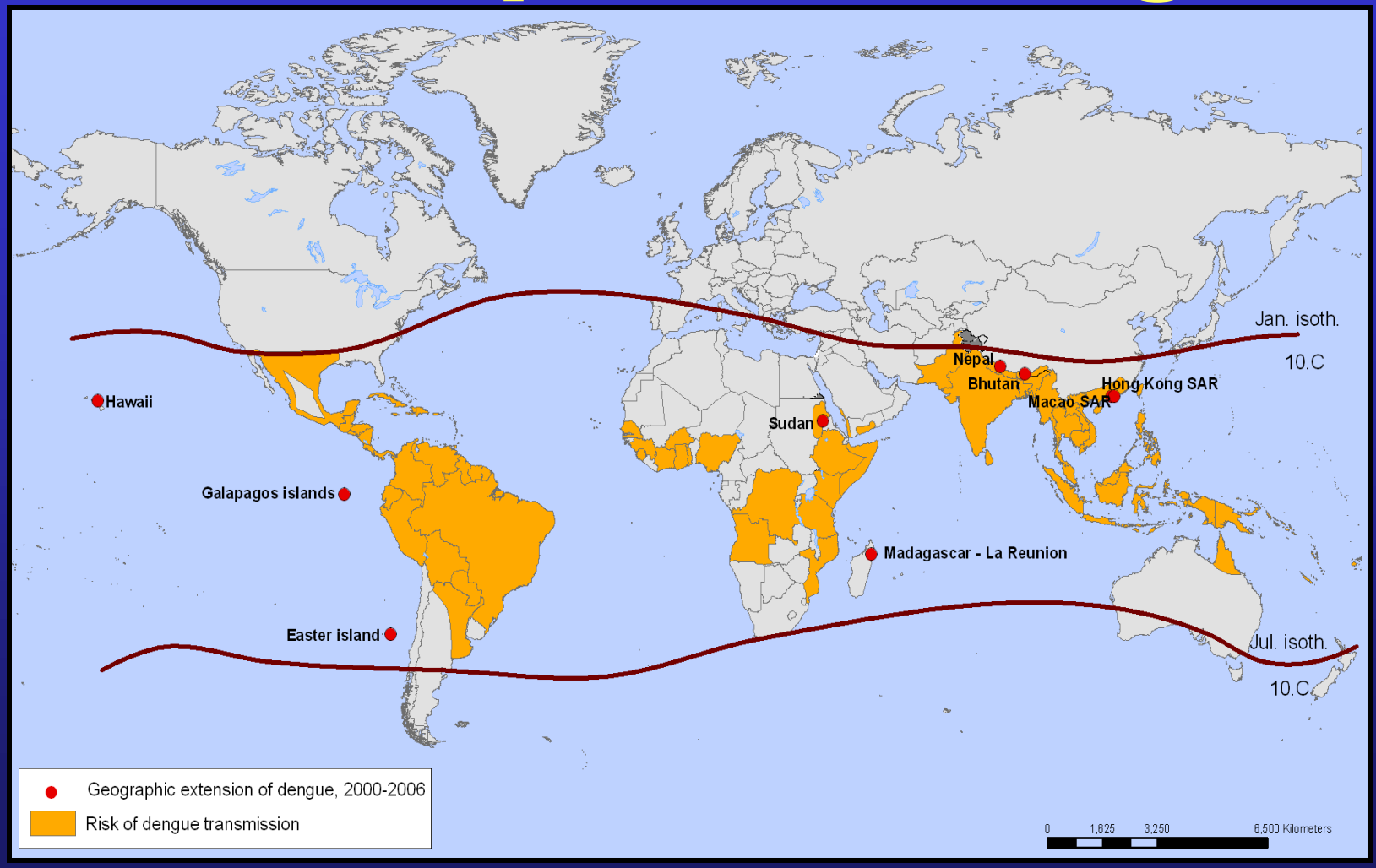
Dengue Virus

- Single stranded RNA virus
  - Flaviviridae family: West Nile virus (WNV), Japanese encephalitis virus (JEV), and yellow fever virus (YFV)
- Four serotypes: Dengue virus (DENV)-1, -2, -3, -4
  - All capable of causing full spectrum of disease from undifferentiated fever to severe disease with shock and/or hemorrhage
  - Infection confers lifelong serotype-specific immunity

Burden of Disease

- 40% of world at risk of infection; at least 4 million U.S. citizens live in dengue-endemic areas
- 50 - 100 million cases of dengue occur annually
  - Five fold increase in cases in Americas in 20 years
- Leading cause of febrile illness in U.S. travelers returning from Asia, South America, Caribbean

Global Impact of Dengue

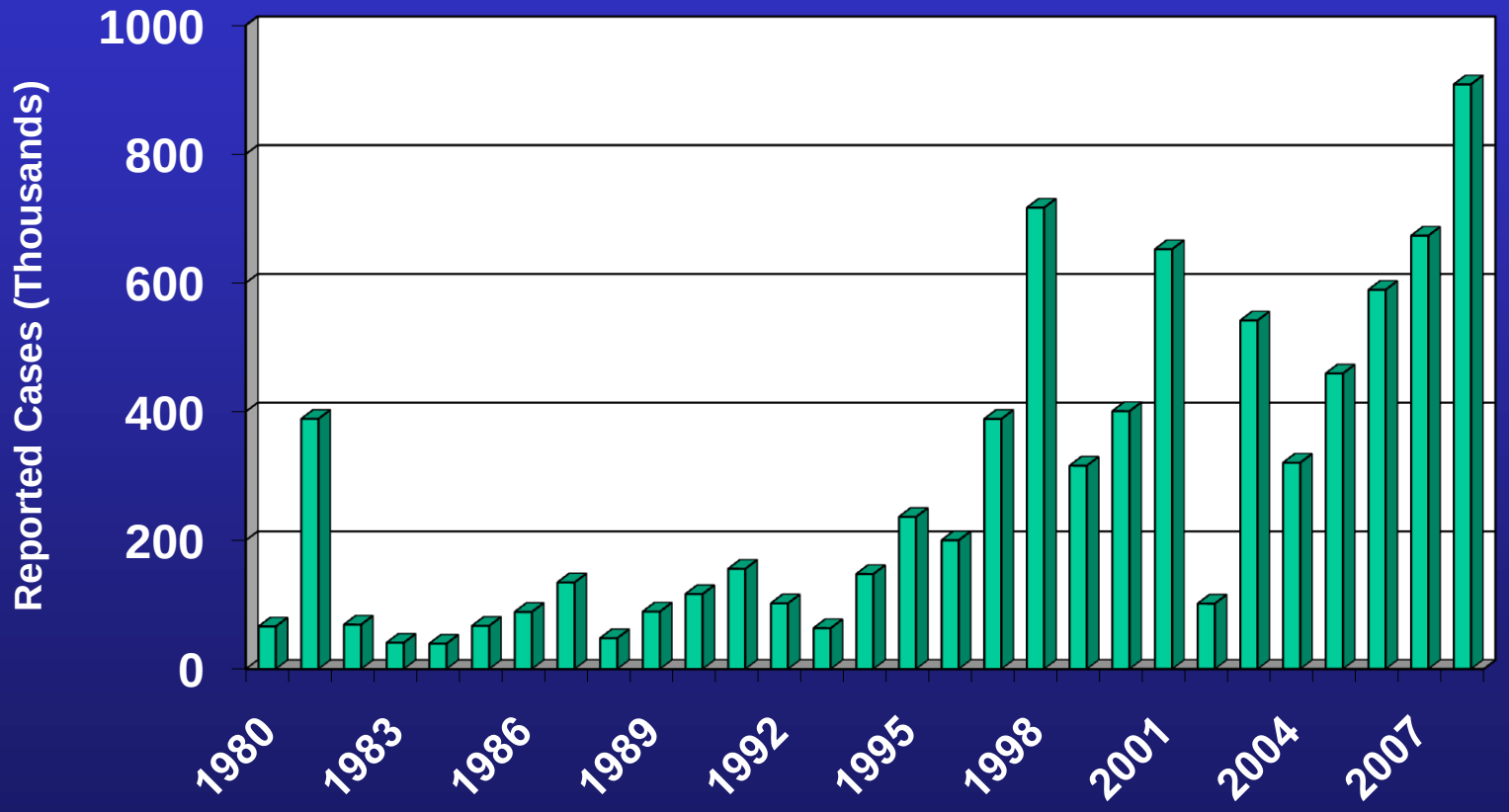


WHO graphic from 2006

Modern History of Dengue

- After WWII, increased dengue transmission
  - Industrialization and first plastic containers
  - Rapid population growth and new urbanizations
  - Increase in travel and over-seas commerce
- Emergence of DHF epidemics
  - 1st description of DHF—Manila epidemic, 1953-54
- By 1970s, DHF was leading cause of hospitalization and death among children in SE Asia

Reported Cases of Dengue in the Americas, 1980 – 2008*



*Note: Reported cases as of January 27,2009 from Pan American Health Organization (PAHO)

Dengue Transmission

Transmission

- Dengue is mosquito-borne disease
  - *Aedes aegypti*, *Aedes albopictus*
- Virus replicates within mosquito for 8 to 12 days (extrinsic incubation period)
  - mosquito remains infected for life
- Mosquito bites human and transmits DENV with as little as 10^2 viral particle per secretion*

* **Kraiselburd E et al. Trans R Soc Trop Med Hyg 1985; 79:248-51**

Transmission

- Virus replicates within human for 3 to 14 days (intrinsic incubation period) before symptom onset
- Viremia begins slightly before onset of symptoms and is thought to last 5 to 6 days*
- Majority of infected people remain asymptomatic**
  - Especially children and those with primary infections
  - Viremia in asymptomatic blood donors can be as high as in symptomatic patients ($10^5 - 10^9$ viral copies per mL)

* Infected persons can transmit virus as early as 1 to 2 days before symptoms develop. Nishiura & Halstead, 2007.

** 53-87% of infected individuals are asymptomatic. Rodriguez L et al. Am J Trop Med Hyg 1995; 52(6):496; and Endy TP et al. Am J Epid 2002; 156:40, Burke DS et al. Am J Trop Med Hyg 1988; 38:172.

Other Routes of Transmission

- Evidence of transmission of dengue through receipt of donor organs or tissue[1]
  - Bone marrow transplant and renal transplant
- Transmission of dengue documented via receipt of blood products (RBC transfusion)[2,3]
  - (1/600 to 1/1300 units in PR with detectable dengue virus)
- Seven reports of transmission after occupational exposure in a healthcare setting[1]

[1] Wilder-Smith A, et. al. Threat of Dengue to Blood Safety in Dengue-Endemic Countries. EID 2009; 15(1):8-11.
[2] Chuang et al. Review of dengue fever cases in Hong Kong during 1998 to 2005. Hong Kong Med J 2008;14:170-177.
[3] Tambyah et al.Dengue hemorrhagic fever transmitted by blood transfusion. N Engl J Med 2008;359:1526-1527.

Other Routes of Transmission

- DENV can be transmitted from mom to the fetus *in utero* or to neonate at parturition (vertical transmission), however may be rare, only 35 cases reported in literature*
- Rates of vertical transmission vary and may depend on severity of maternal infection
- Described cases of symptomatic congenital DENV infections had symptomatic mom with infection late in pregnancy or at delivery

*** Pouliot S.H., et. al. Maternal dengue and pregnancy outcomes: a systematic review. Obstetr Gynecol Survey 2010.**

Mosquito Vectors

- *Aedes aegypti* is most efficient vector
  - Lives around human habitation; rests in dark areas
  - Primarily a daytime feeder; bites indoors
  - Lays eggs preferentially in artificial, water-holding containers, also occasionally bromeliads and tree holes

Breeding sites: plants, pools, water-filled buckets, used tires, empty oil drums, water storage containers etc.

Mosquito Vectors

- *Aedes albopictus* less efficient
  - Feeds on other animals as well
- No effective, sustainable way to eliminate mosquito and breeding sites

Mosquito Vectors

Aedes albopictus

Aedes aegypti

Both have white markings on legs

Dengue in the U.S.

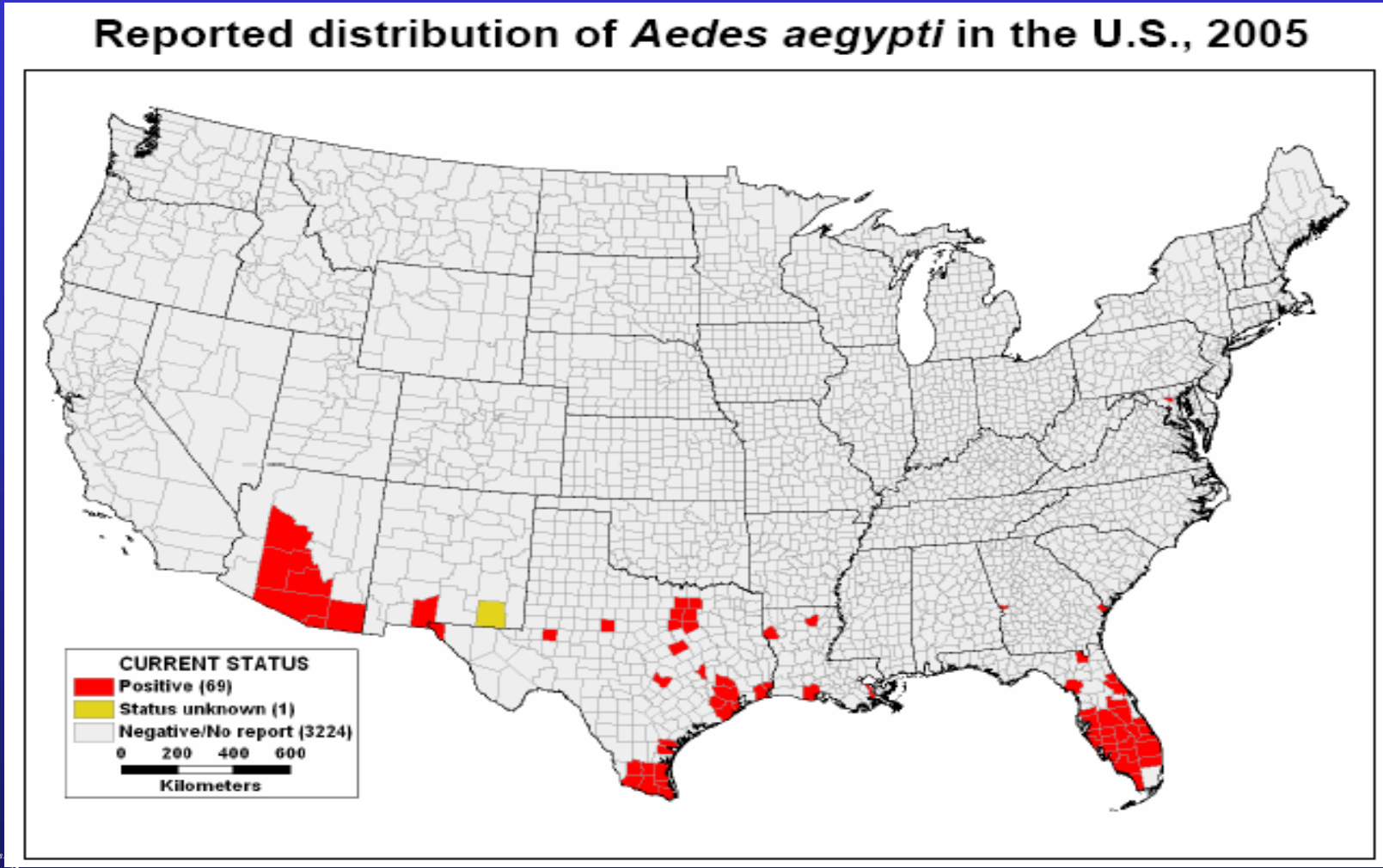
Dengue Transmission in U.S.

- For dengue transmission need:
  - Susceptible population
  - Ample vector population
  - Virus introduction
  - Sufficient interaction between vector and people
- All factors present in many parts of U.S.

Dengue in the Continental U.S.

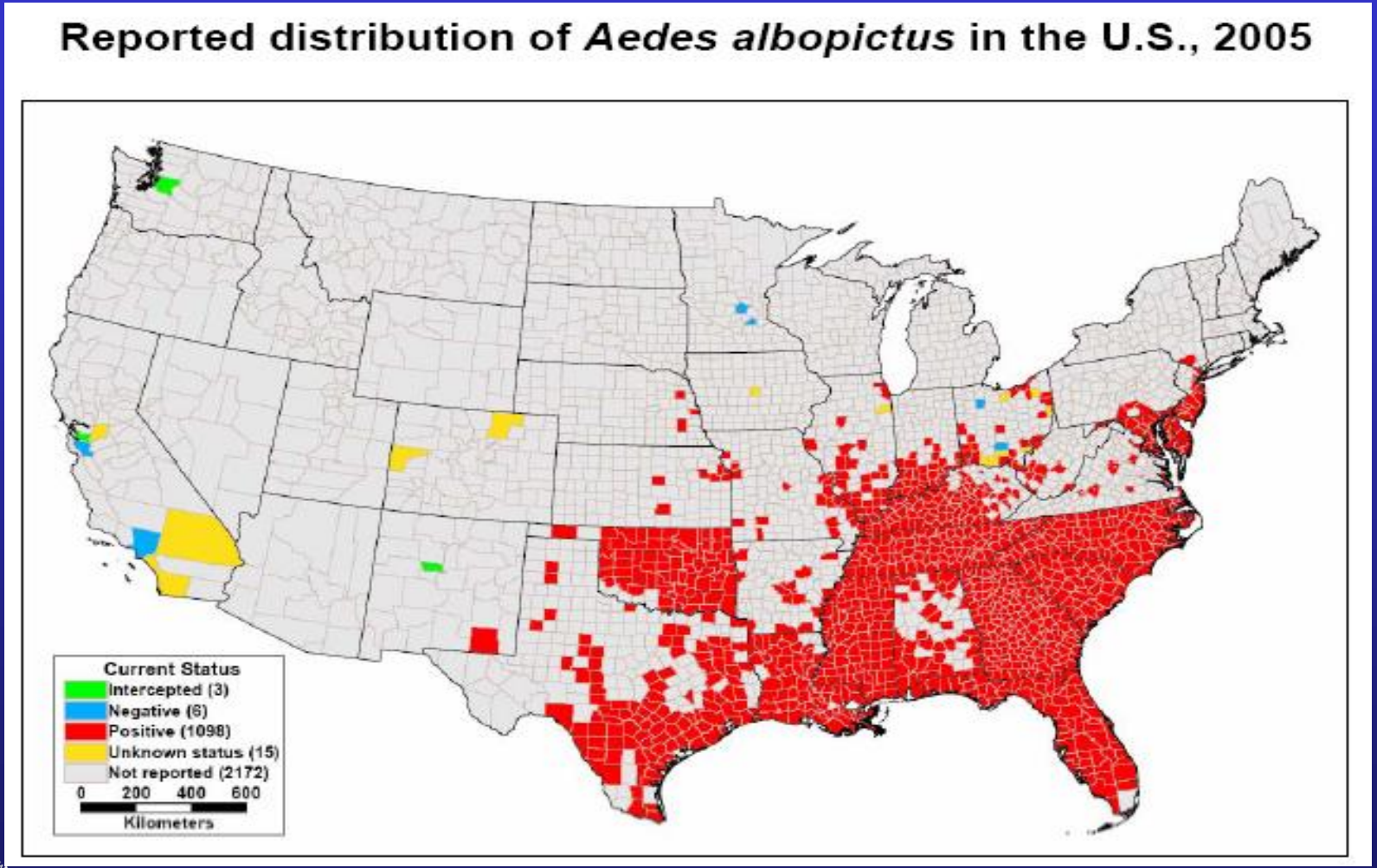
- Locally-acquired outbreaks in U.S.
  - Texas: 7 since 1980 (1st since 1940)
  - Hawaii: 2001 (1st since 1945)
  - Florida: 2009 (1st since 1935)
- *Aedes aegypti* present in AZ,LA,GA,TX,NM,FL
  - *A. albopictus* widespread through southeastern US
- Increased international travel and immigrant population with ties to endemic country of origin
  - 2006-08: >1000 travel-associated cases

Distribution of Aedes aegypti



Source: Chester G. Moore, Ph.D., Colorado State University

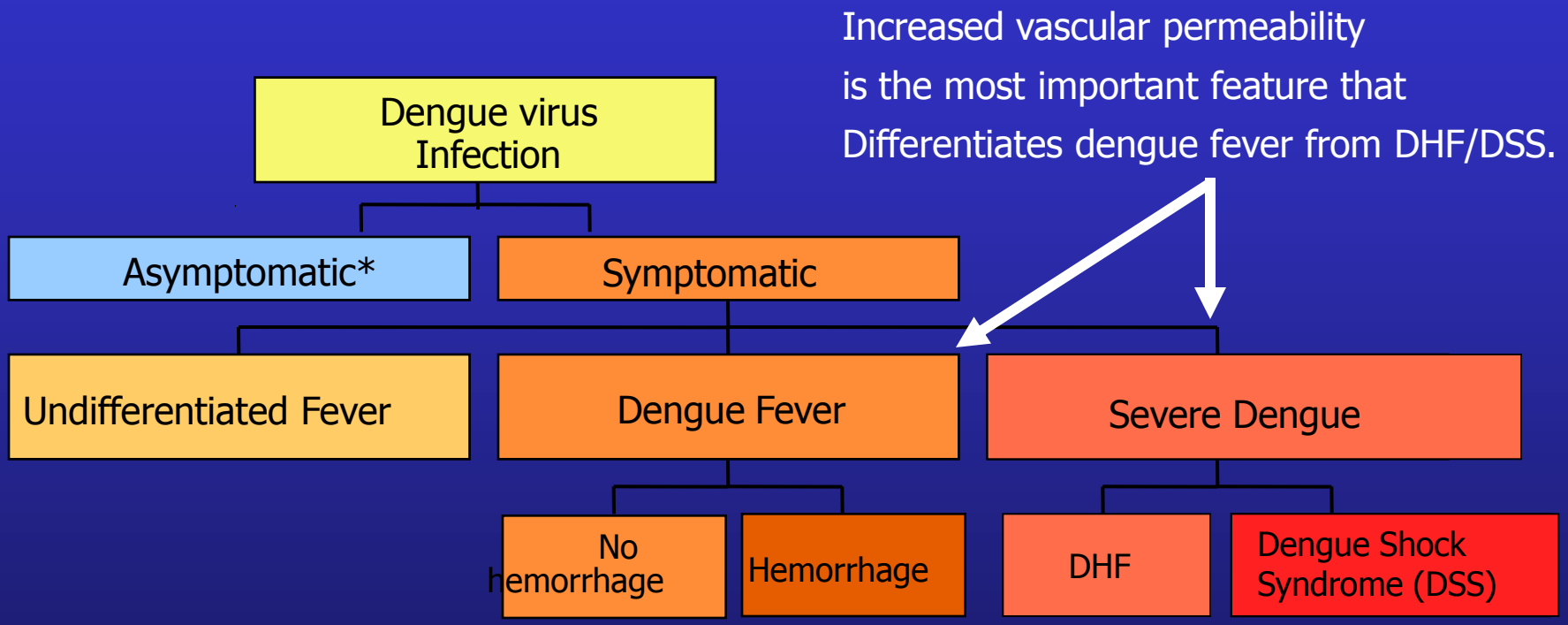
Distribution of Aedes albopictus



Source: Chester G. Moore, Ph.D., Colorado State University

Dengue Clinical Presentation

Dengue – Clinical Spectrum



*** Rodriguez L et al. Am J Trop Med Hyg 1995; 52(6):496; Endy TP et al. Am J Epid 2002; 156:40, Burke DS et al. Am J Trop Med Hyg 1988; 38:172**

Dengue – Treatment

- Standard of care is supportive management (appropriate IV fluid therapy)
- No curative treatment or vaccine available
- Can be fatal but proper treatment can reduce case-fatality rate to <1%[1]

[1] Dengue hemorrhagic fever: diagnosis, treatment, prevention and control. 2nd edition. Geneva; World Health Organization. 1997.

Clinical Course of Dengue

- Dengue is a systemic and dynamic disease.
- After the incubation period, the illness begins abruptly and will be followed by 3 phases:
  - Febrile phase
  - Critical phase
  - Recovery phase

Febrile Phase

- Fever usually lasts 2 – 7 days
- Around the time of defervescence, patients can either improve or deteriorate. Those who deteriorate will manifest warning signs.
- Monitoring for defervescence & warning signs are crucial to recognise progress to critical phase
- Fever > 7 days relatively uncommon
  - Incorrect initial diagnosis
  - Co-infection (malaria); second infection

Critical Phase

Onset phase usually can be identified by:

- Defervescence
- Drop in platelet count with rise in hematocrit (onset of leukopenia ~ 24 hrs. before platelet drop)
- Development of warning signs

Warning Signs

- **Severe abdominal pain**
- **Persistent vomiting**
- **Clinical fluid accumulation (ascites, pleural effusion)**
- **Mucosal bleed**
- **Lethargy; restlessness**
- **Liver enlargement >2cm**

Critical Phase

- May deteriorate to severe dengue during this phase
- Warning signs are result of plasma leakage due to vascular permeability
- Clinically significant plasma leakage usually lasts 24 to 48 hours from time of defervescence
- Must monitor carefully for resolution of plasma leak and start of recovery phase to avoid fluid overload

Recovery Phase

- Gradual re-absorption of extravascular fluid takes place in 48–72 hours.
- General well being improves, hemodynamic status stabilises and diuresis ensues.
- Laboratory
  - HCT stabilises or may lower due to dilutional effect of reabsorbed fluid (hemodilution).
  - WBC usually starts to rise soon after defervescence.
  - Recovery of platelet count is typically later than WBC.

Clinical Problems

- Febrile phase: dehydration; febrile seizures in young children; neurological disturbances
- Critical phase: shock from plasma leakage; severe hemorrhage; organ impairment
- Recovery phase: hypervolemia and acute pulmonary edema may occur if intravenous fluid therapy has been excessive and/or extended into this period

Common Laboratory Findings

- **WBC** – initially WBC normal then at end of febrile phase, WBC (neutrophils) decrease and lymphocytes (atypical lymphocytes too) increase
- **Platelets** – initially normal with rapid decrease shortly before/simultaneous with increase in HCT at defervescence
- **Hematocrit**: ≥20% above baseline
- **Liver function tests** – may have elevated aspartate aminotransferase (AST); usually AST is 2 times the level of alanine aminotransferase (ALT)

Dengue Diagnosis and Reporting

Differential Diagnosis of Dengue

- Leptospirosis
- Influenza
- Malaria
- Typhoid fever
- Measles
- Rubella
- Rickettsial infections (typhus, scrub typhus)
- Enterovirus
- Meningococcemia
- Bacterial sepsis
- Chikungunya
- West Nile Virus
- Other viral hemorrhagic fevers

Dengue Diagnostic Testing

- Laboratory tests should be done to confirm diagnosis
  - Clinical Diagnosis alone unreliable
- Acute management of dengue infection should be based on clinical evaluation and not await laboratory confirmation.

Dengue Diagnostic Testing

- Virus can be detected for up to 5 days post onset
  - Viremia coincides with fever
  - Acute phase (≤5 days after onset) – detect DENV via polymerase chain reaction (PCR) OR non-structural protein-1 (NS1)
- Convalescent phase (>day 5) – detect antibody via enzyme-linked immunosorbent assay (ELISA)
  - IgM antibodies detected for up to 3 months
- IgG antibodies elevated for lifetime; not useful for diagnosis
  - Anti-dengue antibodies cross react with antibodies against other flaviviruses

Dengue Diagnosis and Reporting

- Dengue added as nationally notifiable condition in June 2009; 32 states currently mandate reporting
  - Dengue is not reportable in 7 states that have competent mosquito vectors
- Should be reported to CDC via state and local health departments
- Recent outbreak in Florida detected by report of New York State physician

Resources

Contact information:

Dengue Branch:

Tele: 787.706.2399

Fax: 787.706.2496

Websites: CDC Dengue: **www.cdc.gov/dengue**

CDC's Traveler's Health webpage: wwwnc.cdc.gov/travel

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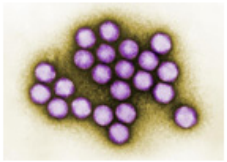

Photo/CDC

A colorized transmission electron micrograph of adenovirus. This issue of MMWR includes a report on an outbreak of adenovirus 14 respiratory illnesses in Alaska.

January 15, 2010 / Vol. 59 / No. 1

"Choking Game" Awareness and Participation Among 8th Graders — Oregon, 2008

In 2008, CDC reported 82 deaths attributed to the "choking game" and other strangulation activities during the period 1995–2007; most victims were adolescent males aged 11–16 years. To assess the awareness and prevalence of this behavior among 8th graders in Oregon, the Oregon Public Health Division added a question to the 2008 Oregon Healthy Teens survey concerning familiarity with and participation in this activity. This report describes the results of that survey.

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