Dengue and Chikungunya: Diseases, Diagnosis, Vectors, and Threats

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California Department of Public Health

Outline

- Describe dengue and chikungunya clinical diseases, including severe dengue
- List laboratory diagnostic tests for dengue and chikungunya
- Describe epidemiology including vectors
- Discuss current threats to California and preparedness and prevention measures

California Traveler #1

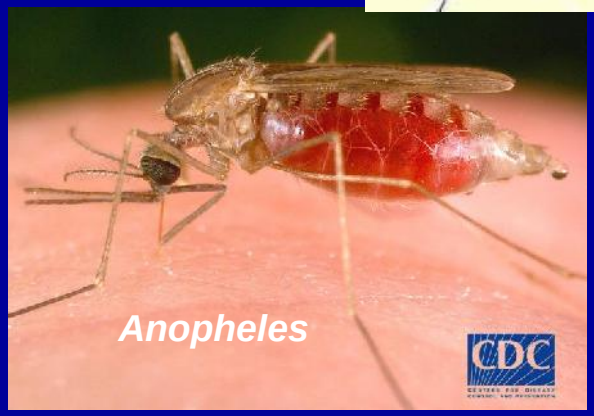
- In May 2015, a 55 y.o. male California resident presented to medical attention complaining of a week of fever, chills, night sweats, and joint pain. No headache, no eye pain, no muscle aches, no rash. Had some bleeding gums.
- He just returned from El Salvador where he had stayed for over 2 weeks. He recalled having had mosquito bites while there.
- Your guess on diagnosis?

California Traveler #2

- **In April 2015, a 44 y.o. male California resident was hospitalized for fever, headache, muscle aches, malaise, and rash. Blood tests show low WBC and low PLT.**
- **A week before illness onset, he had returned from Honduras where he had stayed for a week. Did not recall mosquito bites.**
- **Your guess on diagnosis?**

Mosquito-Borne Infectious Disease Risks to Travelers

- Chikungunya
- Dengue
- Malaria
- Zika virus disease
- Japanese encephalitis
- Yellow fever
- West Nile virus disease
- Filariasis



Mosquito Vectors of Infectious Disease Risks to Travelers

- Chikungunya: ***Aedes aegypti*, *Ae. albopictus***
- Dengue: ***Aedes aegypti* > *Ae. albopictus***
- Malaria: ***Anopheles* species**
- Zika virus disease: ***Aedes* species**
- Japanese encephalitis: ***Culex* species**
- Yellow fever: ***Ae. aegypti*, other *Aedes* spp.**
- WNV disease: ***Culex pipiens, Cx. tarsalis, Cx. quinquefasciatis*, other mosquito species**
- Filariasis: ***Anopheles, Culex, Mansonia* spp.**

Invasive *Aedes* Detected Recently in California

Aedes albopictus

(Asian tiger mosquito)

2011-15: Los Angeles County

Aedes aegypti

(Yellow fever mosquito)

2013: Madera, Fresno, San Mateo counties; **2014**: Tulare, Kern, Los Angeles, San Diego counties; **2015**: Alameda, Imperial counties.

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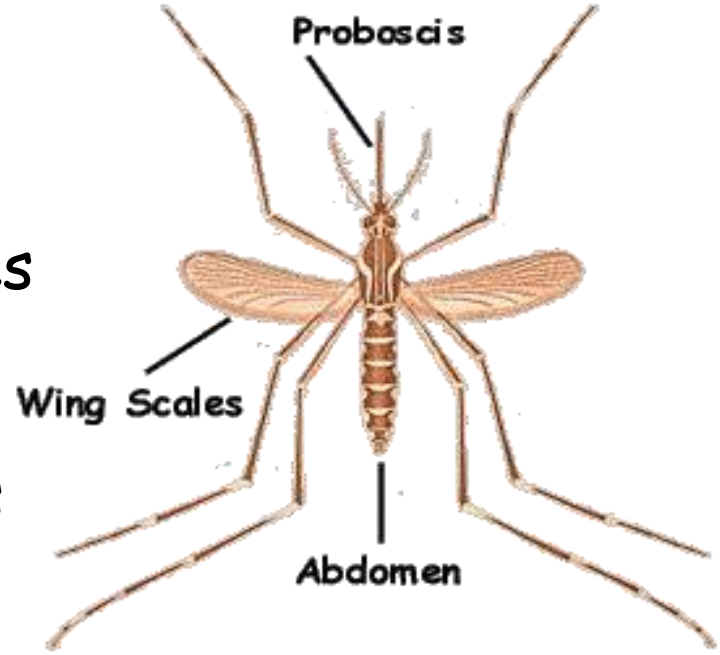
Aedes Mosquito Basics

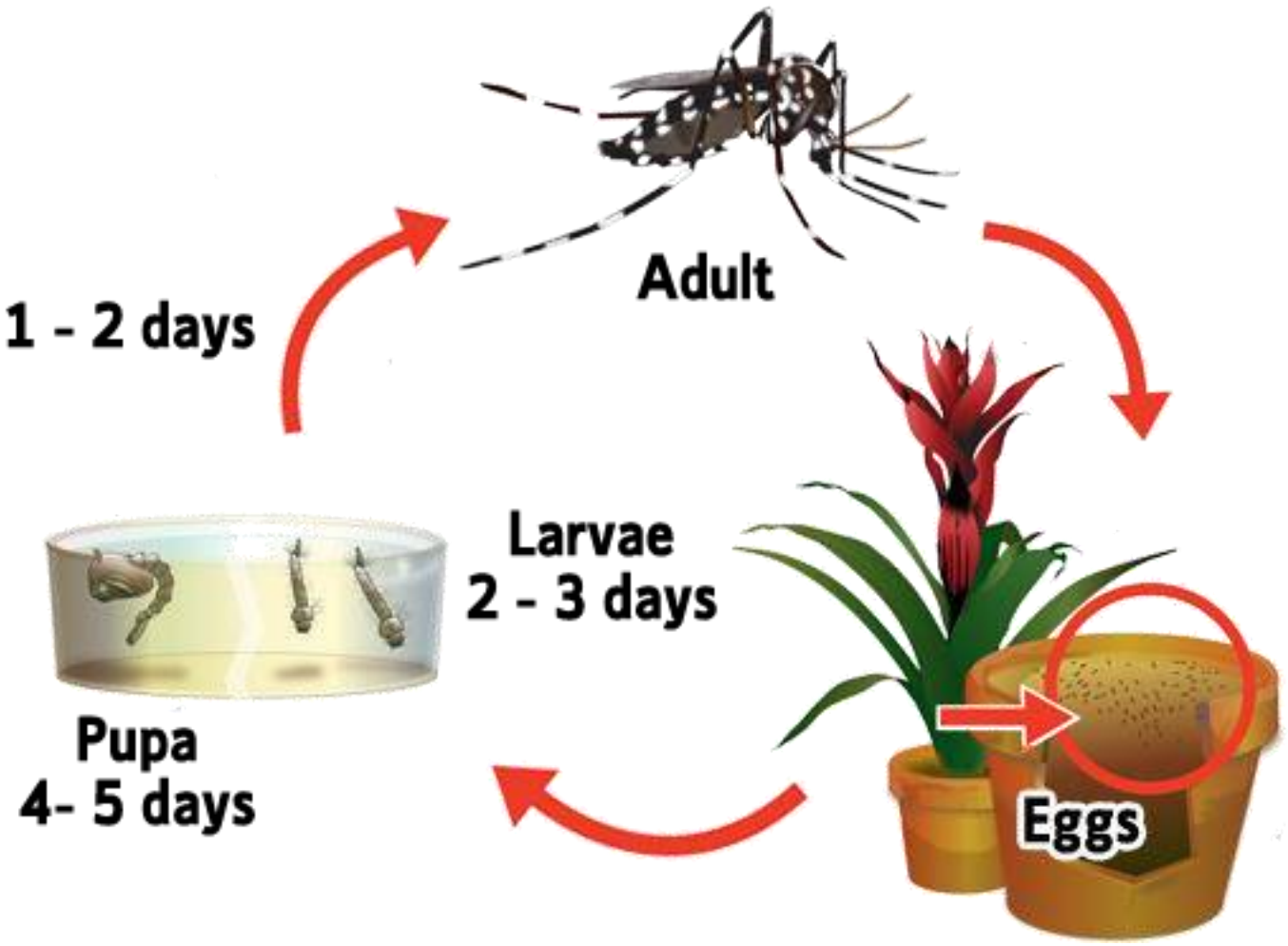
- Only the female *Aedes* mosquitoes feed on blood, because they need protein to produce eggs. Male mosquitoes feed on plant nectar.

- On average, *Aedes* mosquitoes live 2 to 4 weeks.

- Average flight range is less than 500 meters (0.31 mile).



LIFE CYCLE OF AN AEDES MOSQUITO



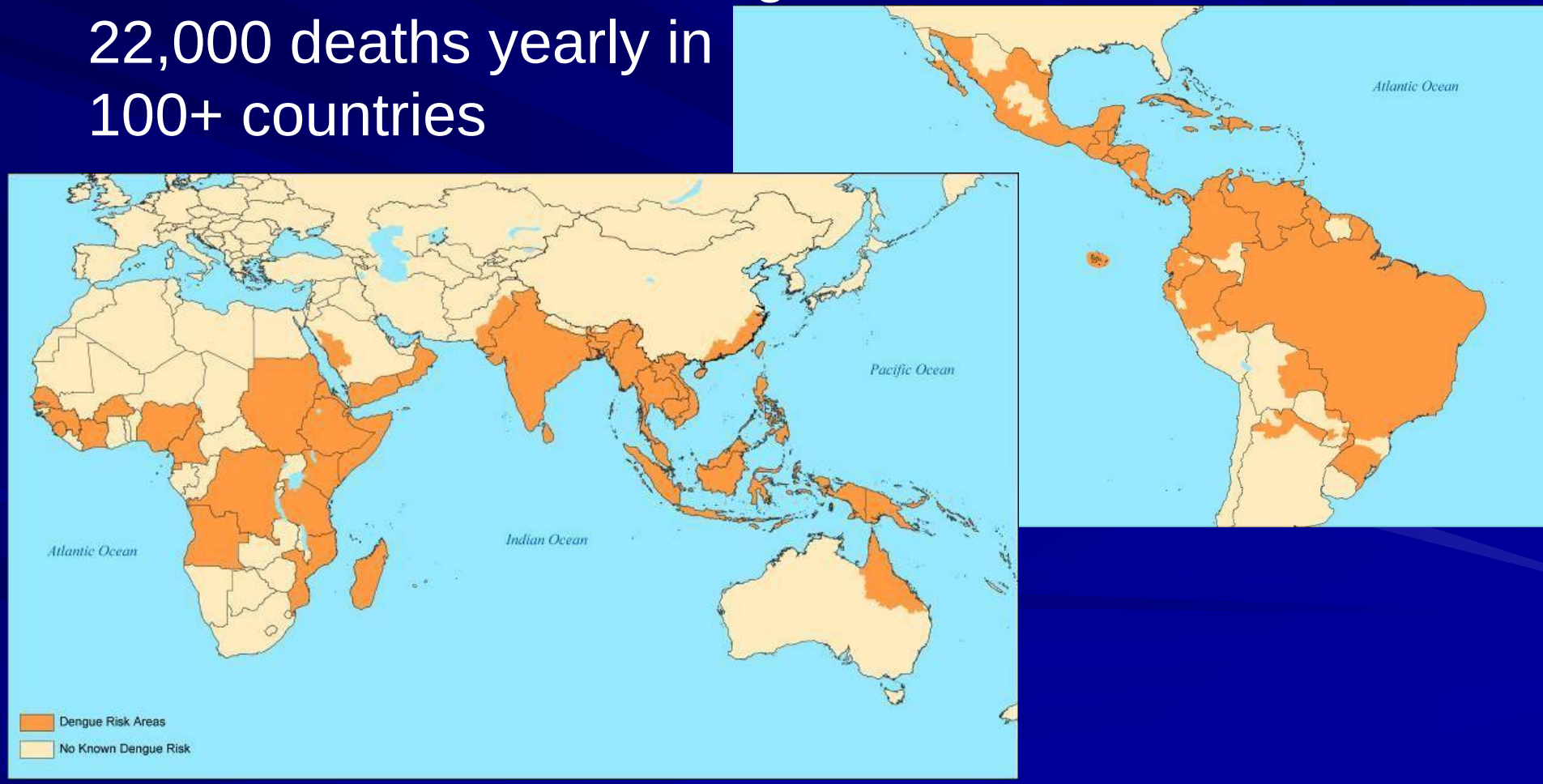
In dry conditions, eggs can survive up to a year.

Dengue

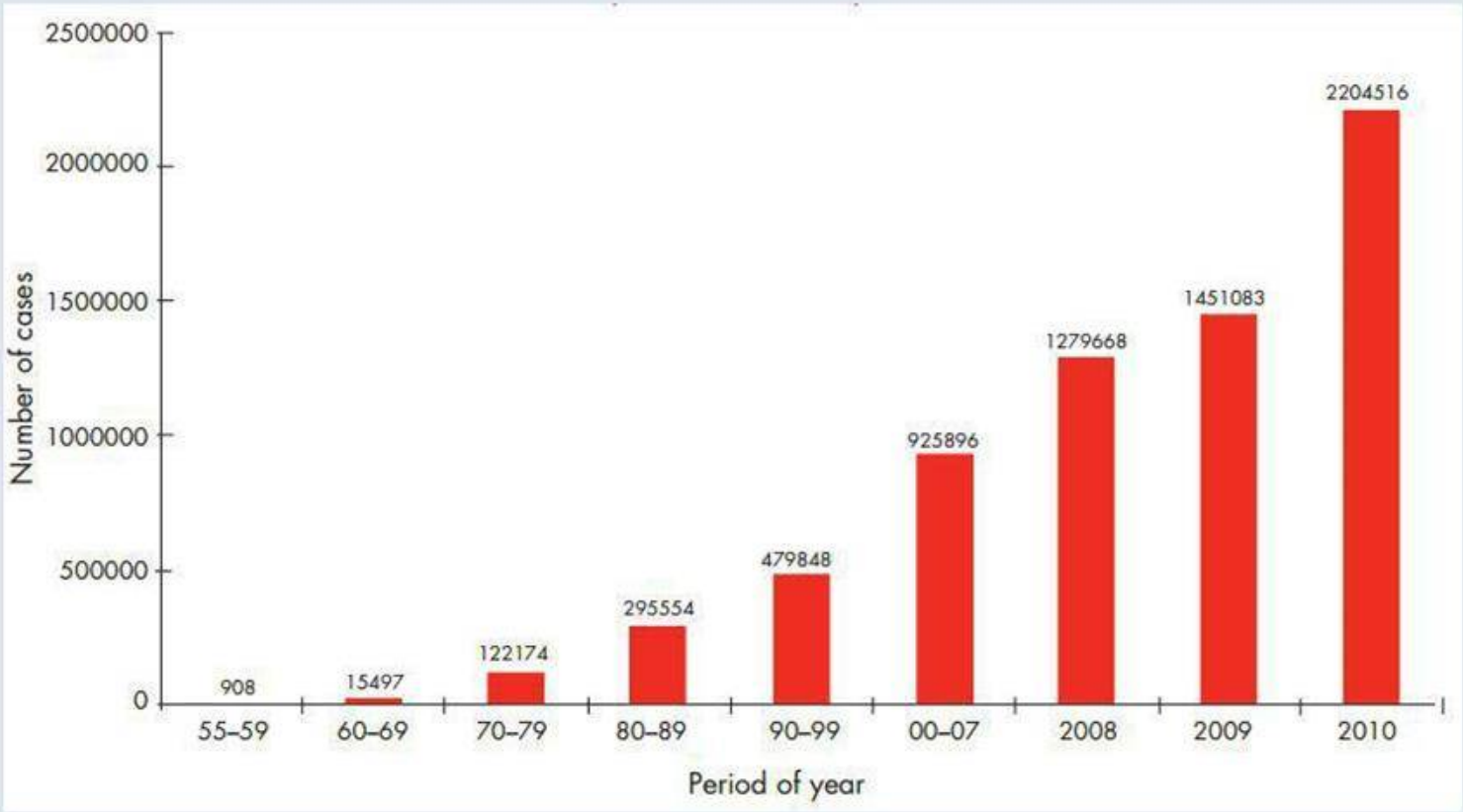
- Pathogen: Dengue virus (flavivirus) serotypes 1-4
- Diseases: Inapparent infection (up to 66-75%), Dengue Fever (DF), Severe Dengue (DHF, DSS)
- Mosquito vectors: *Aedes aegypti, Aedes albopictus*

Dengue Risk Areas and Burden

W.H.O. estimates 50-100 million infections including 22,000 deaths yearly in 100+ countries

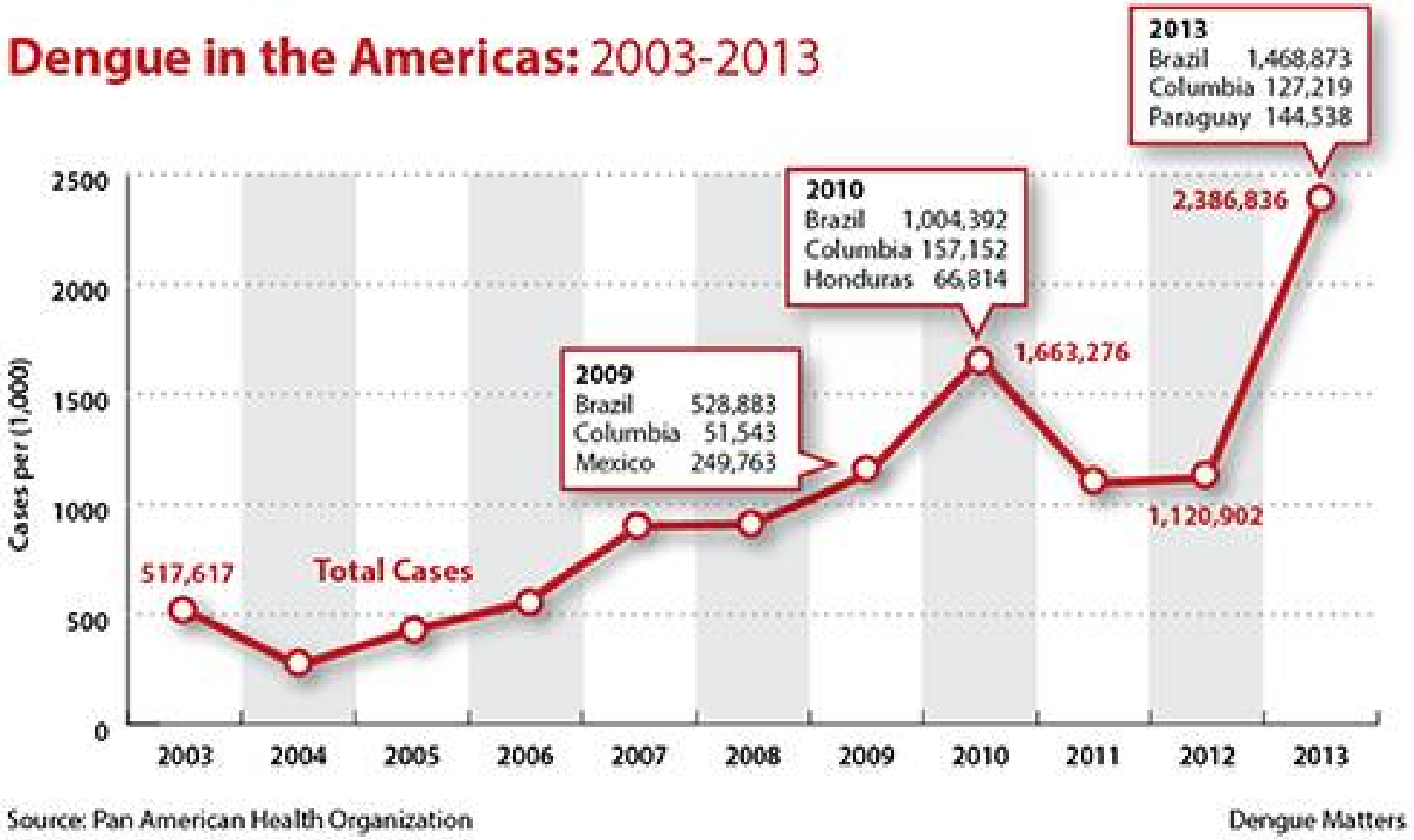


Average number of dengue and severe dengue cases reported to WHO annually in 1955–2007 and number of cases reported in recent years, 2008–2010



WHO, 2012

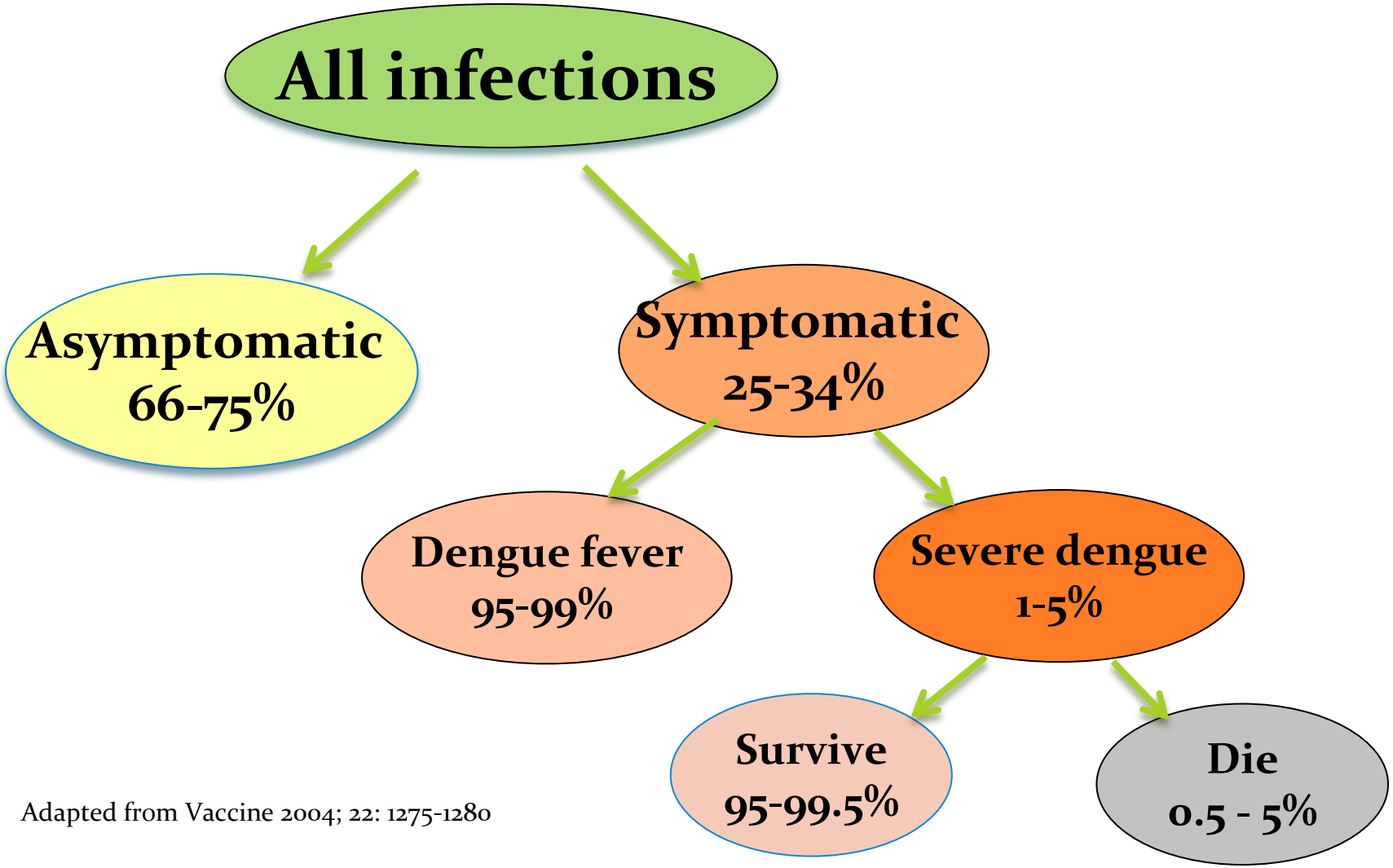
Dengue in the Americas: 2003-2013



Source: Pan American Health Organization

Dengue Matters

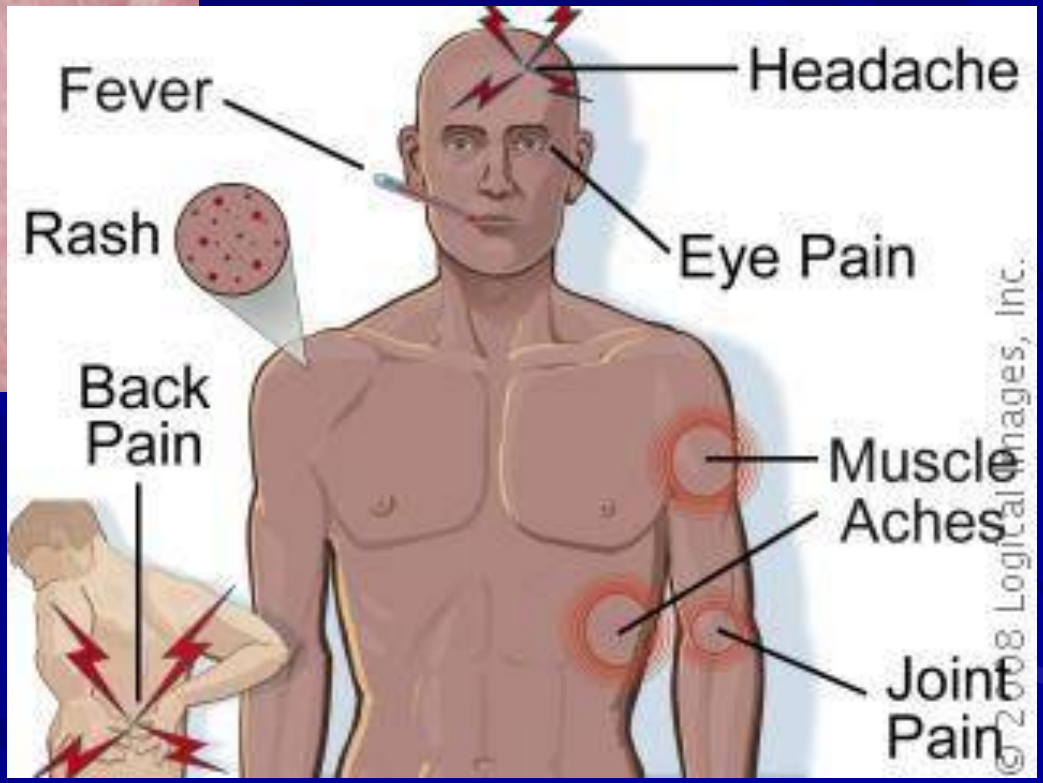
Dengue Infections



Adapted from Vaccine 2004; 22: 1275-1280

Dengue Fever

- Incubation period: 3 – 10 days
- **Dengue Fever:**
  - High fever ≥ 102 F/ 39 C for 2 – 7 days, AND
  - two or more of: severe headache, pain behind eyes, muscle and bone pain, joint pain (without effusion), rash, easy bruising or mild bleeding (e.g., nose or gums bleed), low WBC
- Critical period 24 – 48 hours after defervescence


Fever
Headache
Rash
Eye Pain
Back Pain
Muscle Aches
Joint Pain
©2008 Logical Images, Inc.

Severe Dengue

- **Dengue Hemorrhagic Fever (DHF):**
  - Warning signs during critical period 24-48 hrs after defervescence:
  - Abdominal pain or persistent vomiting, red spots on skin, bleeding from nose or gums, tarry stools, drowsiness, clammy skin, difficulty breathing
- **Dengue Shock Syndrome (DSS):**
  - Increased vascular permeability / plasma leakage → pleural effusions, ascites, hypotension, shock → death (1-5%)

Meta-Analysis of Signs/Symptoms Predictive of Severe Dengue*

- Bleeding (OR: 13.6; 95% CI: 3.3-56.5)
  - Hematemesis (OR: 6.2; 95% CI: 2.7-14.3)
  - Melena (OR:10.4; 95% CI: 3.1-35.0)
- Abdominal pain (OR: 2.3; 95% CI: 1.6-3.2)
- Skin rashes (OR: 2.0; 95% CI: 1.3-3.3)
- Hepatomegaly (OR: 4.8; 1.8-12.6)

**Zhang H, et al. BioMed Research International 2014*

Risk of Severe Dengue in Second Infection with Different Serotype

- Documented in several studies in different countries, with most serotypes.
- Postulated to be due to antibody-dependent enhancement (ADE) from heterotypic antibodies from first infection.
- However, recent studies found antibodies from first infection protective up to 2 years; and risk of severe dengue increases if second dengue infection acquired >2-3 years after first infection.
- Third and fourth infections milder clinically.

Dengue: Laboratory

- Tests:
  - RT-PCR
  - Serology: IgM & IgG IFA, IgM antibody-capture ELISA (MAC-ELISA), IgG ELISA
  - Neutralizing antibody for confirmation
- Availability:
  - CDPH Viral and Rickettsial Disease Laboratory (VRDL)
  - CDC

Dengue Treatment & Prevention

- Treatment:
  - Supportive, fluid (oral rehydration solution or isotonic solutions), acetominophen (avoid aspirin and NSAIDs which may increase risk of bleeding)
- Prevention:
  - Avoid mosquito bites in risk areas
- Vaccine:
  - No commercial vaccine yet
  - Some in clinical trials

Selected Dengue Vaccine Candidates

- Live attenuated tetravalent chimeric YF-DEN (Sanofi Pasteur) _ Phase III
- Live attenuated tetravalent , licensed NIH (Butantan, Brazil) _ Phase II
- Live attenuated tetravalent chimeric (Takeda acquired Inviragen)(eng. at CDC) _ Phase II
- Recombinant E subunit protein (Merck) _ Phase I
- Tetravalent formulation (NIH) _ to begin Phase II

Efficacy and Safety of one Dengue Vaccine Candidate*

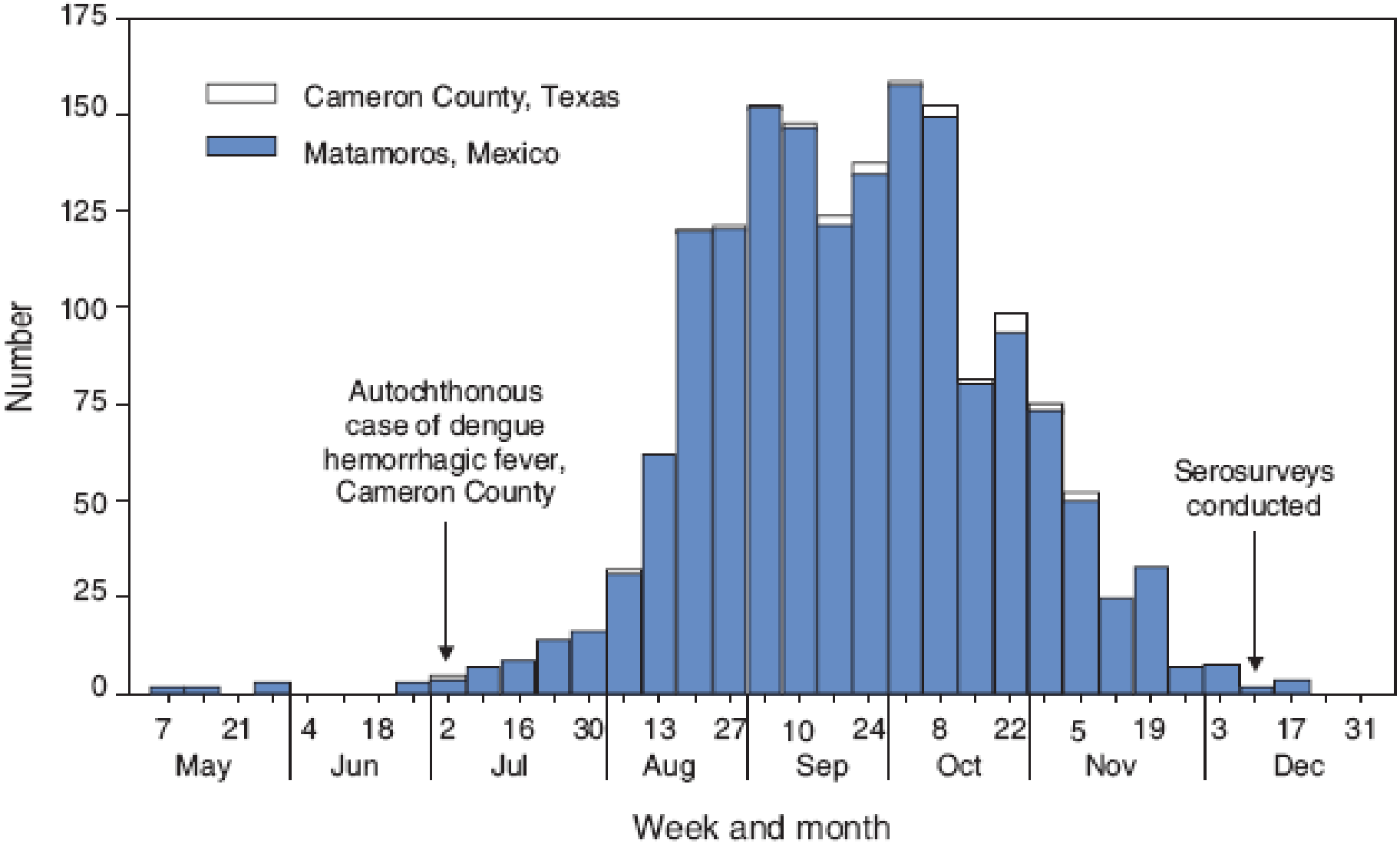
- Live attenuated tetravalent chimeric YF-DEN (Sanofi Pasteur) _ Pooled efficacy from phase III & IIb trials for symptomatic dengue during first 25 months:
  - 60.3% (95% CI, 55.7-64.5) for all participants
  - 65.6% (95% CI, 60.7-69.9) for ≥ 9 year olds
  - 44.6% (95% CI, 31.6-55.0) for < 9 year olds
- Pooled serotype-specific efficacy ranged from 47.1% for DENV-2 to 83.2% for DENV-4.

**Hadinegoro SR, et al. NEJM 2015*

Dengue in US

- Most U.S. cases were imported by infected travelers returning from Caribbean, Latin America, Asia, etc..
- Recent outbreaks with **local** transmission
  - **Florida**: (no locally acquired cases since 1934)
    - 2009-2010: 88 cases in Key West
    - 2013: 28 cases in Martin County outbreak
    - 2014: 7 cases
  - **Hawaii**: (no locally acquired cases since 1944)
    - 2001-2002: 122 cases
  - **Texas**: (no locally acquired cases since 1945)
    - 1980: 23 cases; 1980-1999: 64 cases
    - 2005: DEN-2 outbreak in Brownsville, Cameron Co
    - 2013: 33 cases in Cameron and Hidalgo counties: 12 locally acquired, 16 traveled to MX

FIGURE 2. Number of cases of dengue fever, by week of report — City of Matamoros, Mexico,* and Cameron County, Texas,† 2005



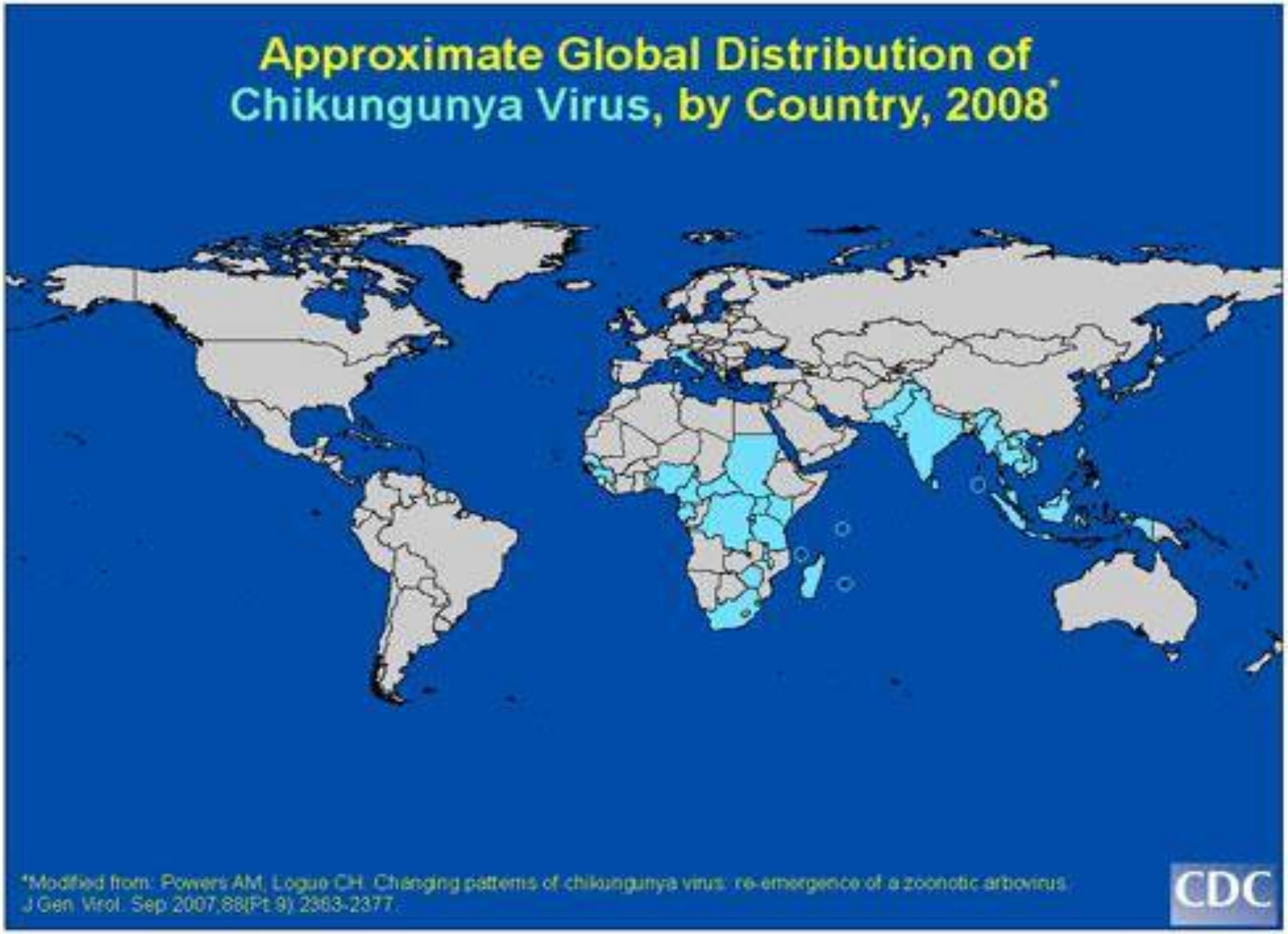
* n = 1,596.
† n = 25.

Source: CDC MMWR 56(31); 785-789

Chikungunya

- Pathogen: chikungunya virus (alphavirus)
- Diseases: asymptomatic infection (5-25%), chikungunya fever (75-95%)
- Mosquito vectors: *Aedes aegypti*, *Aedes albopictus*

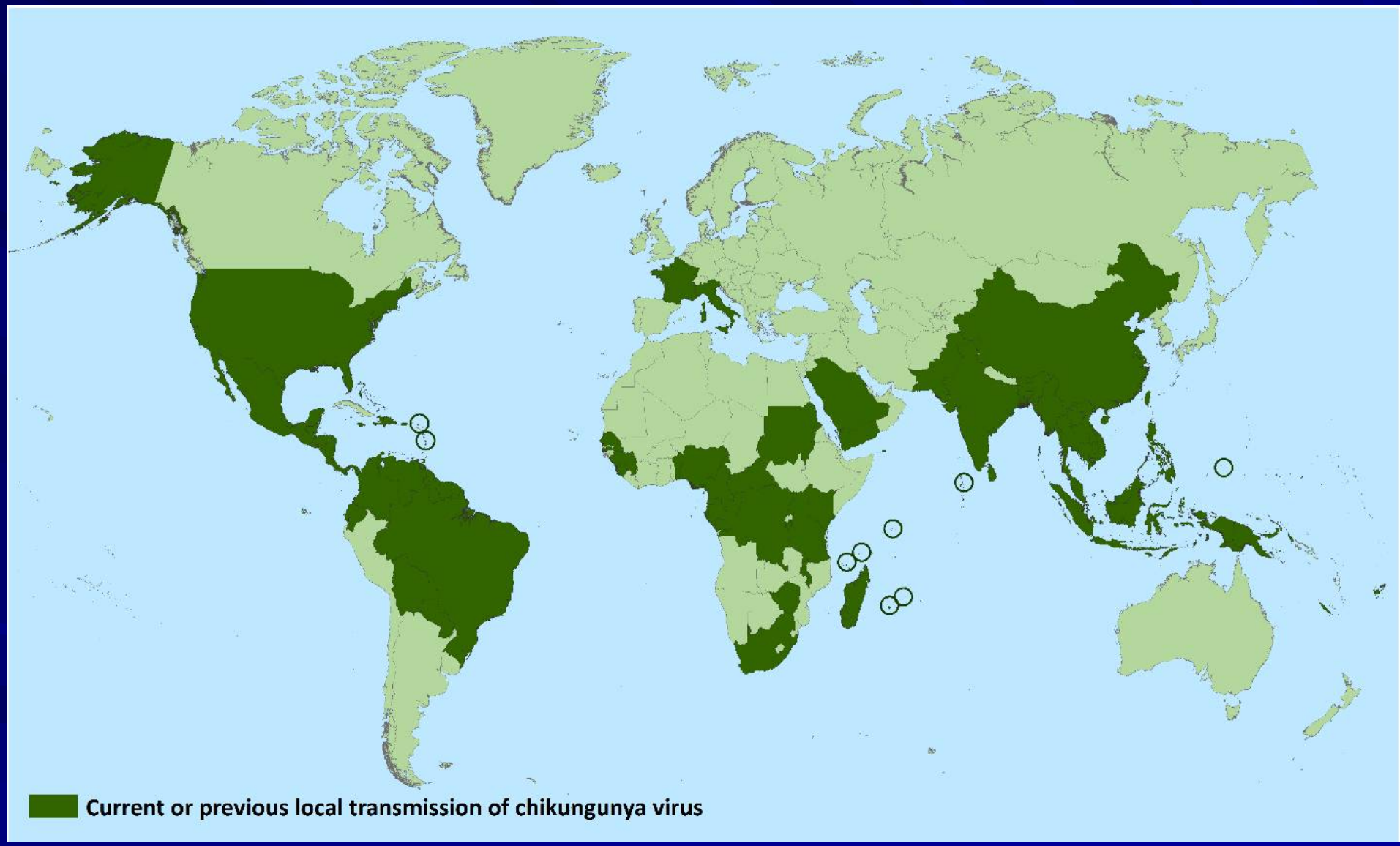
Approximate Global Distribution of Chikungunya Virus, by Country, 2008*



*Modified from: Powers AM, Logue CH. Changing patterns of chikungunya virus: re-emergence of a zoonotic arbovirus. J Gen Virol. Sep 2007;88(Pt 9):2363-2377.

CDC

Countries and territories where chikungunya cases have been reported*
(CDC, *as of March 10, 2015*)



Chikungunya Virus in the Americas, 2013-2014*

- ~1,110,034 suspected cases; 24,375 lab-confirmed.

*Pan American Health Organization 2015

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Chikungunya Fever

- Incubation period:
  - typically 3-7 days (range, 1-12 days)
- Disease:
  - High fever (>102 F/39 C), chills, headache, nausea, vomiting, multiple joint pain with or without swelling (finger joints, wrists, knees, ankles), lower back pain, rash.
  - Mortality rare, mostly in older adults

DIFERENCIAS ENTRE EL DENGUE Y LA CHIKUNGUNYA

50%
De los casos son indestinguibles

Dengue

* Dolor leve en articulaciones.
* Hemorragias, según el tipo de dengue.
* Alteraciones hematológicas.
* Dolor detrás de los globos oculares.
* Agrandamiento de ganglios linfáticos

Sintomas

Duración de la fiebre: Entre 2 y 7 dias

Duración de la fiebre: Entre 4 y 10 dias

Chikungunya

* Dolor severo en las articulaciones que obliga a encorvarse
* Mayor picazón de manos y pies.
* No hay alteraciones importantes hematológicas
* En algunos casos los dolores articulares pueden durar meses o incluso un año

noticia AL DIA

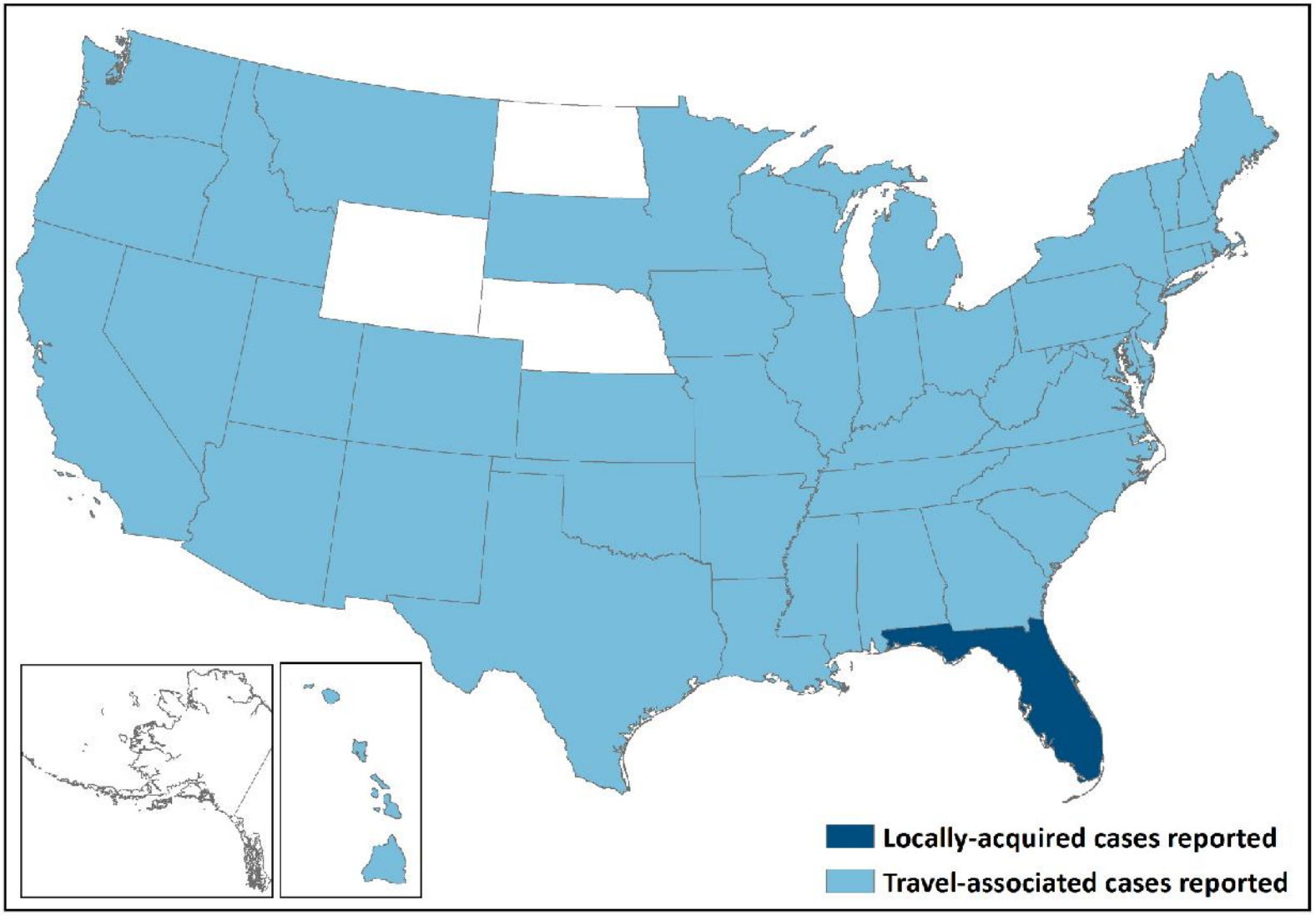
Chikungunya Treatment & Prevention

- Treatment:
  - Rest, fluids, acetominophen for fever and joint pain (avoid aspirin and NSAIDs until dengue ruled out).
  - usually recover in 7-10 days; in some, joint pain may persist months-over a year.
- Prevention:
  - Avoid mosquito bites in risk areas
- Vaccine:
  - None

Chikungunya: Laboratory

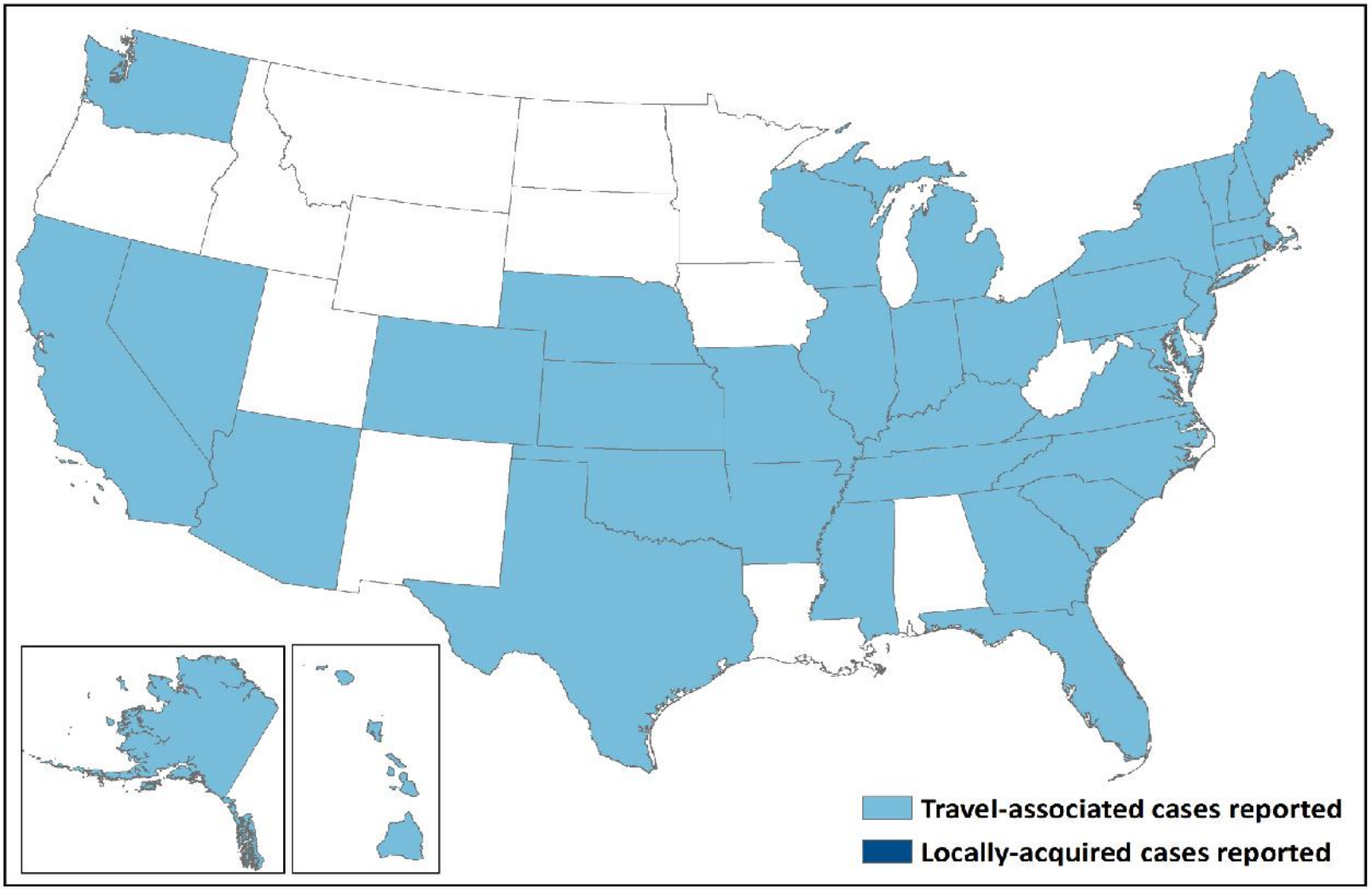
- Tests:
  - RT-PCR
  - Serology: IgM & IgG IFA, IgM-capture ELISA, IgG ELISA
  - Neutralizing antibody for confirmation
- Availability:
  - CDPH VRLD
  - CDC

States reporting chikungunya cases – United States, 2014 *
N = 2,792 cases



***CDC**

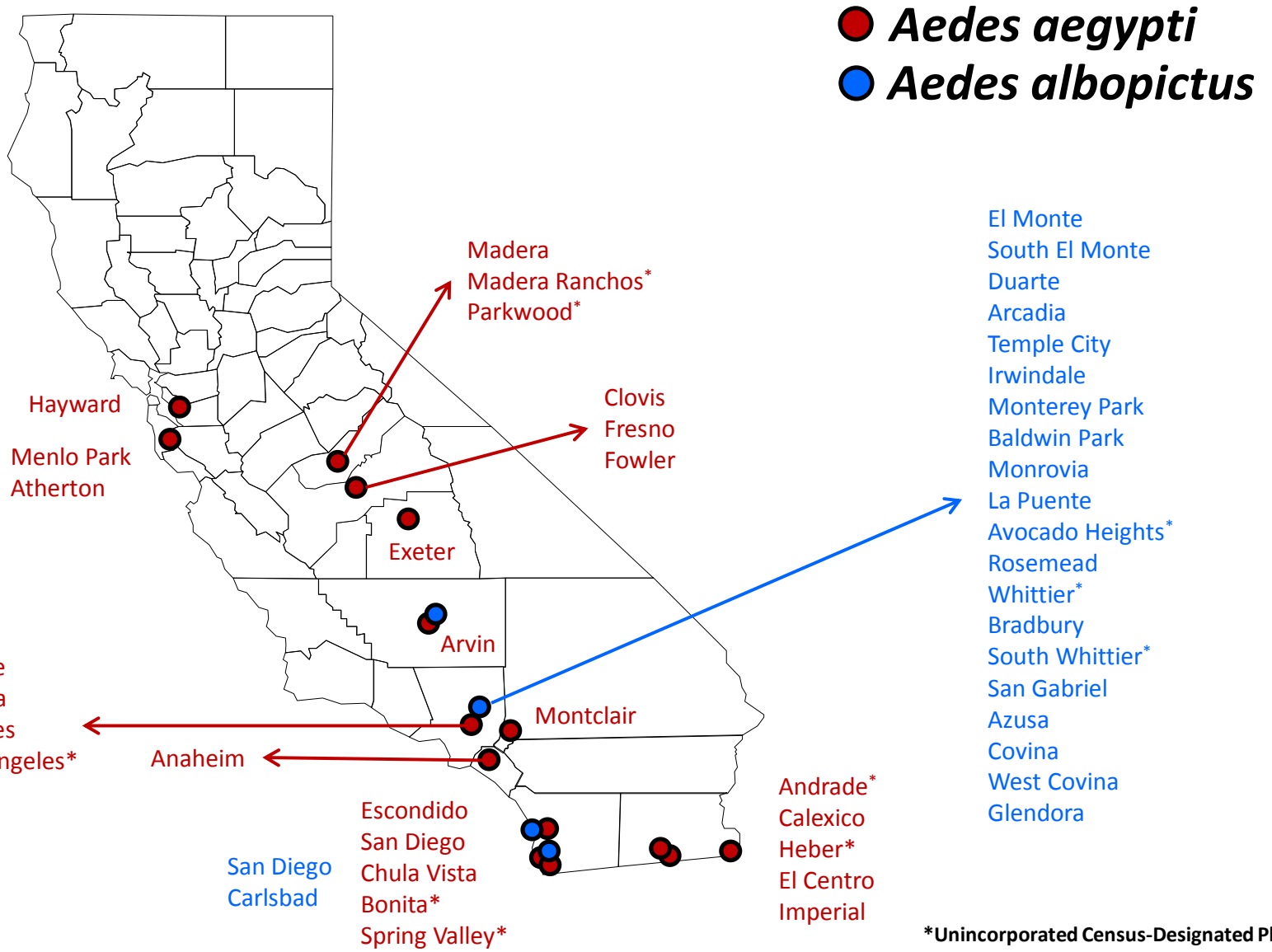
States reporting chikungunya cases – US, 2015 (as of August 11, 2015)* _ N = 273 cases from 36 states



***CDC**

Aedes aegypti and *Aedes albopictus* Mosquitoes Detection Sites in California, 2011-2015

Updated October 5, 2015



*Unincorporated Census-Designated Places

Critical Factors Needed for Local Transmission of Dengue or Chikungunya in California

- Presence of a competent vector
  Aedes aegypti or *Aedes albopictus*
- Presence of an infected person who is viremic (up to 7 days after illness onset) in an infested area during periods when vectors are active and abundant
- Mosquito vector biting infected person and then living long enough (approx. 10-11 days) to bite another person

➢ **Risk of local transmission is currently low in California**

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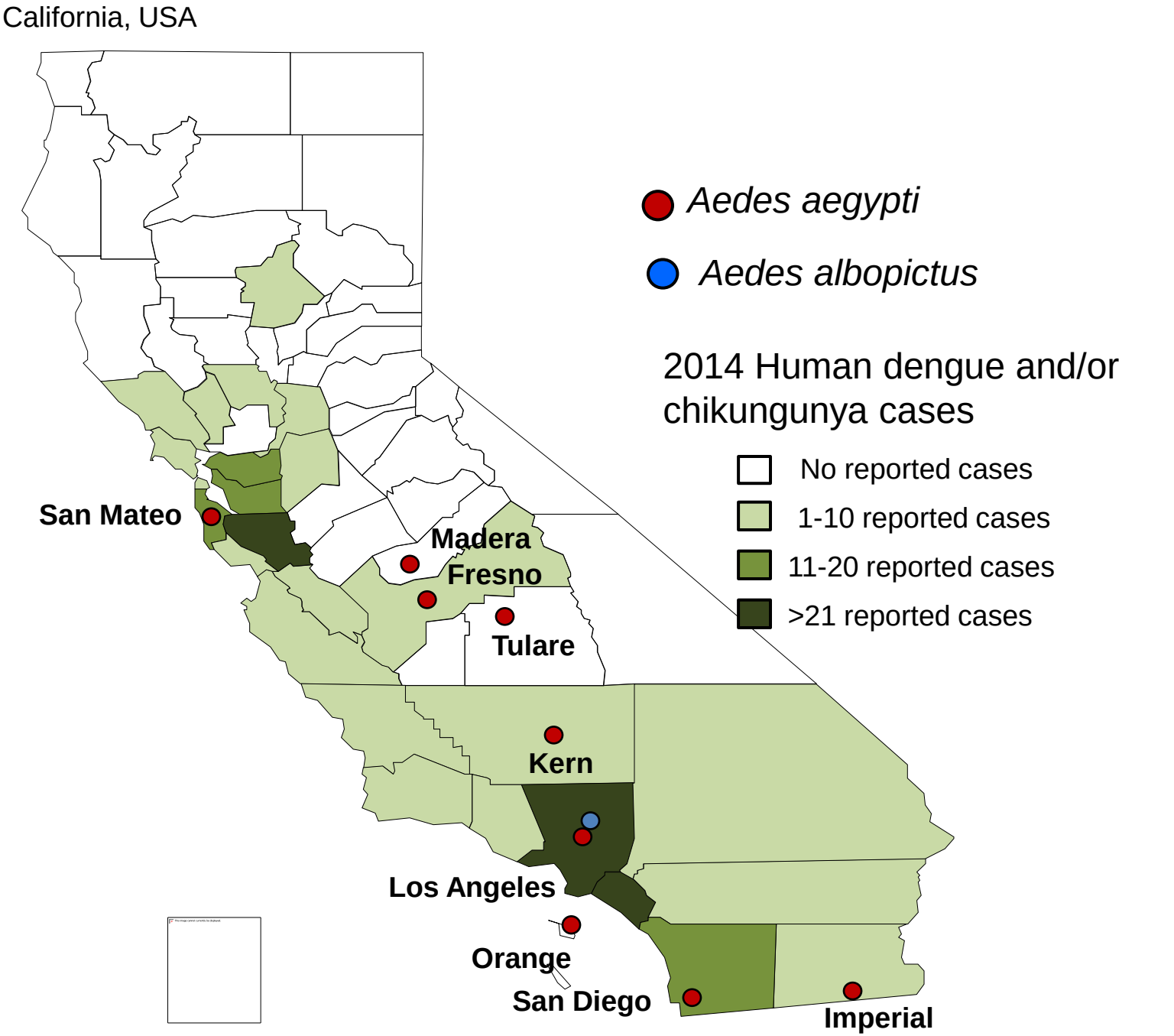

California, USA
Aedes aegypti
Aedes albopictus
2014 Human dengue and/or chikungunya cases
No reported cases
1-10 reported cases
11-20 reported cases
>21 reported cases
San Mateo
Madera
Fresno
Tulare
Kern
Los Angeles
Orange
San Diego
Imperial

Chikungunya in California*

- Chikungunya is not yet reportable in CA, but LHDs are notified of laboratory-confirmed cases and can report to CDPH via CalREDIE.
- Between 2009 and 2013, CDPH was notified of 3 confirmed cases among returned travelers.
- In 2014, 137 cases were documented, all with travel history to chikungunya-affected areas in Latin America and Caribbean.
- Of 2014 case-patients, 67% likely viremic while in CA, 42% with illness onset after arrival and 26% with illness onset within 7 days before arrival.
- Of these likely viremic patients, 59% arrived in a county with a known invasive *Aedes* infestation.

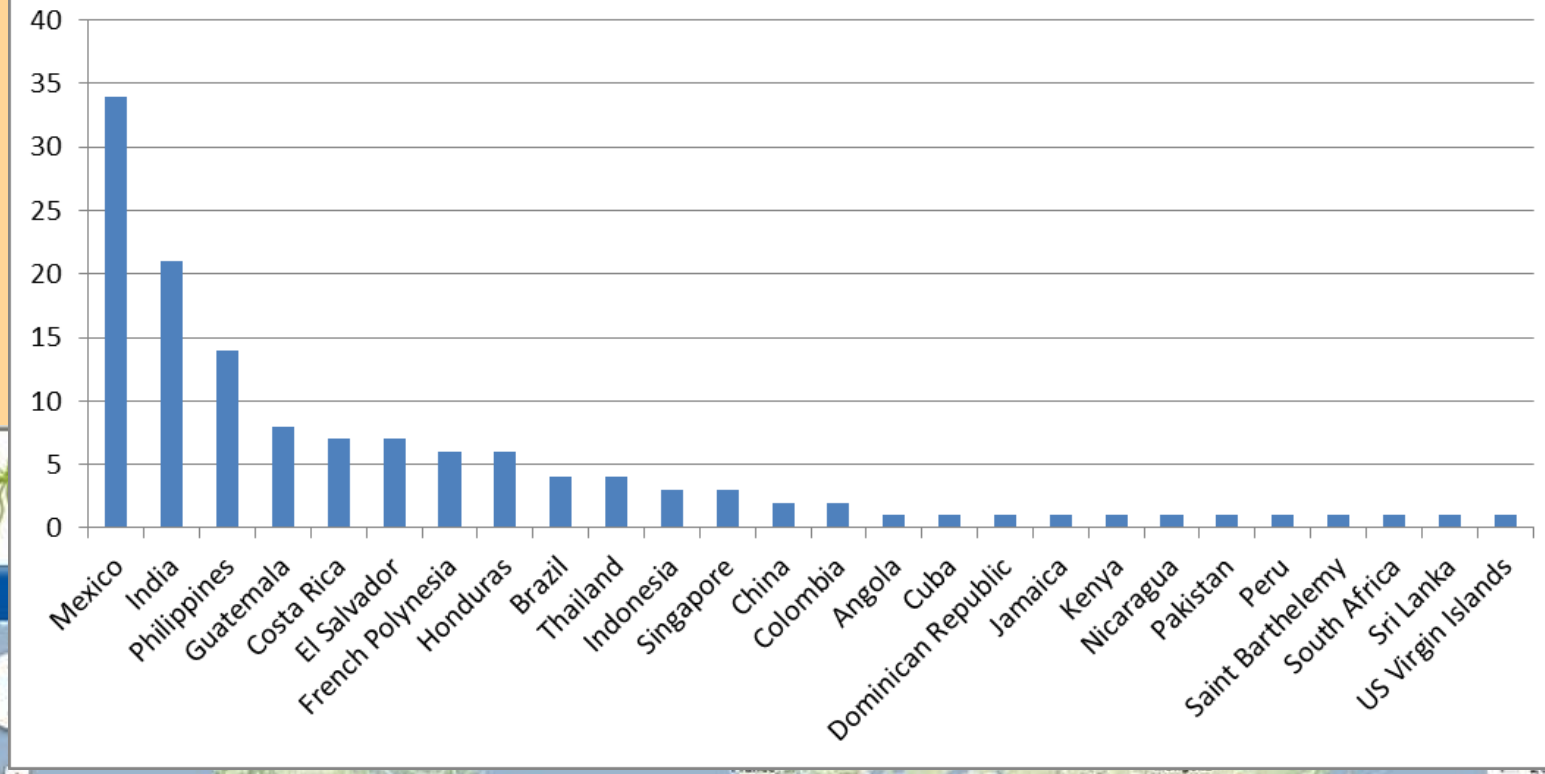
**Porse CC et al. Emerg Infect Dis 2015*

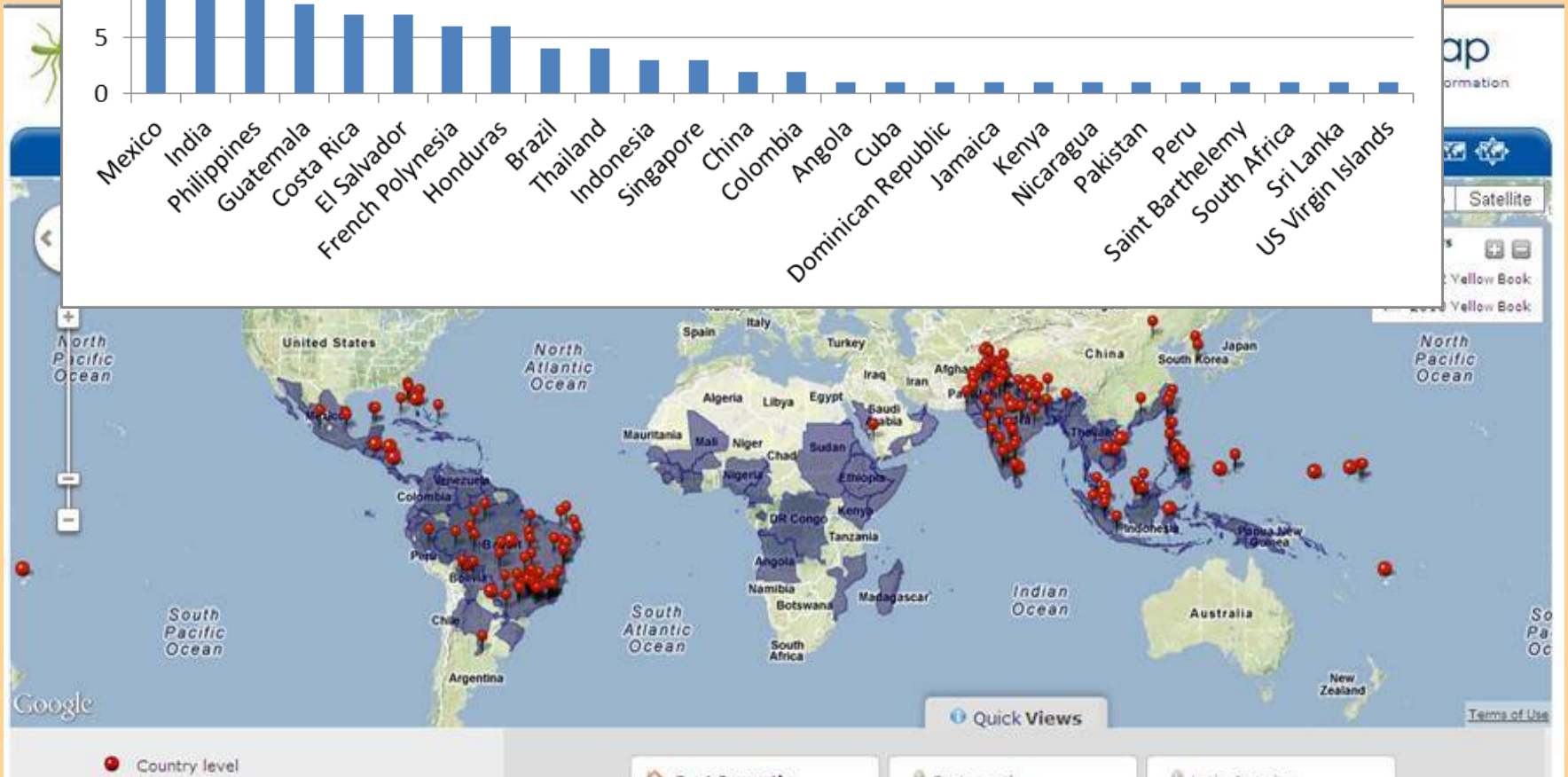
Dengue in California*

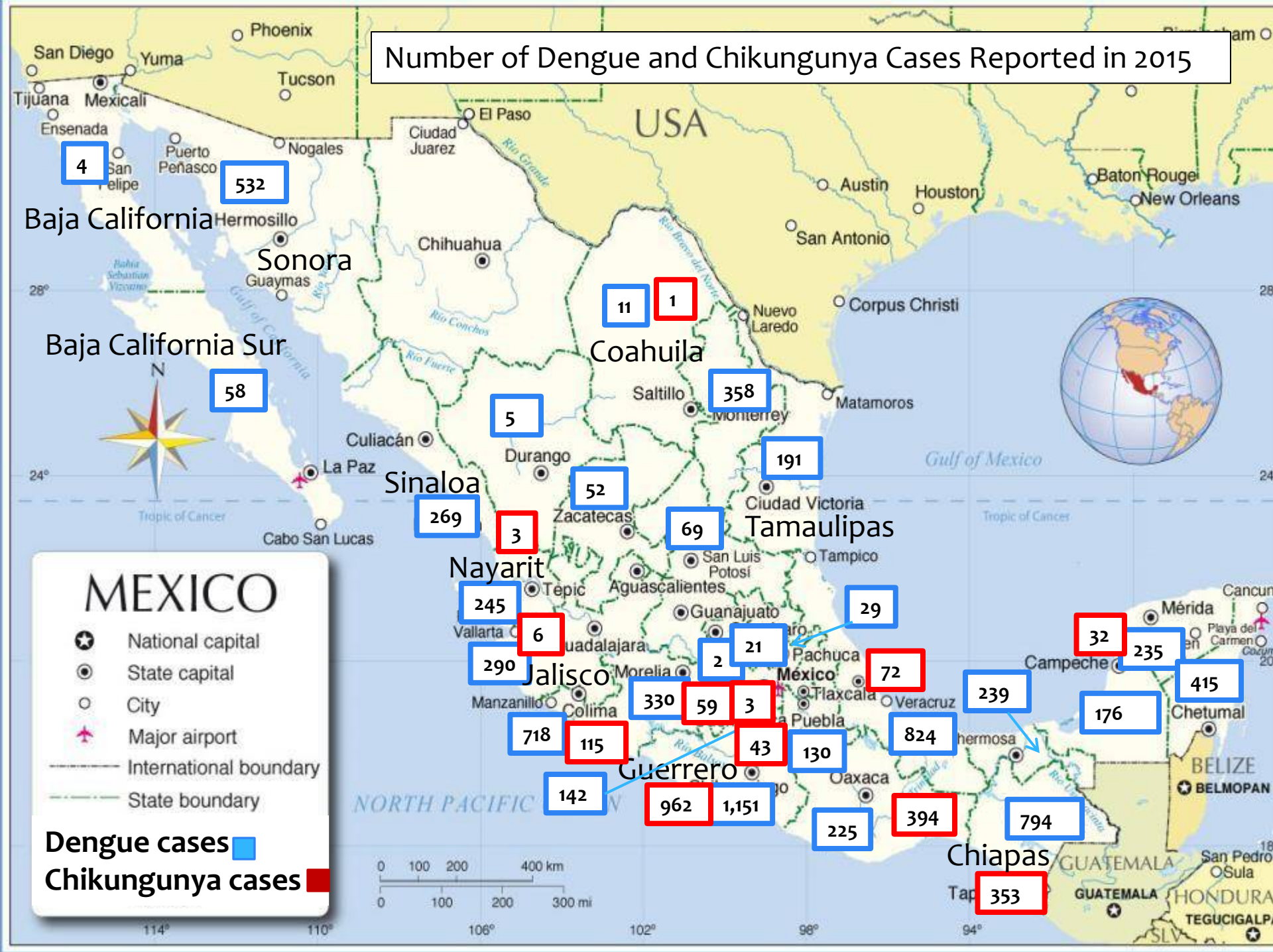
- To date, all CA cases were in travelers returning from dengue-affected areas.
- The annual number of dengue cases increased from 41 in 2011 to 132 in 2014.
- Of the 2014 dengue case-patients, 74% were likely viremic while in CA, 54% with illness onset after arrival and 20% with illness onset within 5 days before arrival.
- Of likely viremic patients, 43% arrived in a county with a known invasive *Aedes* infestation.

**Porse CC et al. Emerg Infect Dis 2015*

Imported Dengue Cases to California, 2014






Number of Dengue and Chikungunya Cases Reported in 2015
USA
Baja California
4
532
Sonora
Hermosillo
Baja California Sur
58
Chihuahua
Coahuila
11
1
Nuevo Laredo
Corpus Christi
Saltillo
358
Monterrey
Matamoros
5
Culiacán
Durango
191
Ciudad Victoria
Tamaulipas
Sinaloa
269
52
3
Zacatecas
69
Nayarit
Tepic
San Luis Potosí
Tampico
Aguascalientes
245
Guanajuato
29
6
21
2
290
Jalisco
Morelia
Pachuca
México
72
Manzanillo
Colima
330
59
3
Tlaxcala
Veracruz
239
718
115
43
130
Puebla
824
142
Guerrero
Oaxaca
962
1,151
225
394
794
Chiapas
353
Mérida
32
235
Campeche
415
176
Chetumal
BELIZE
BELMOPAN
GUATEMALA
HONDURAS
Gulf of Mexico
NORTH PACIFIC
Tropic of Cancer
MEXICO
National capital
State capital
City
Major airport
International boundary
State boundary
Dengue cases
Chikungunya cases
0 100 200 400 km
0 100 200 300 mi

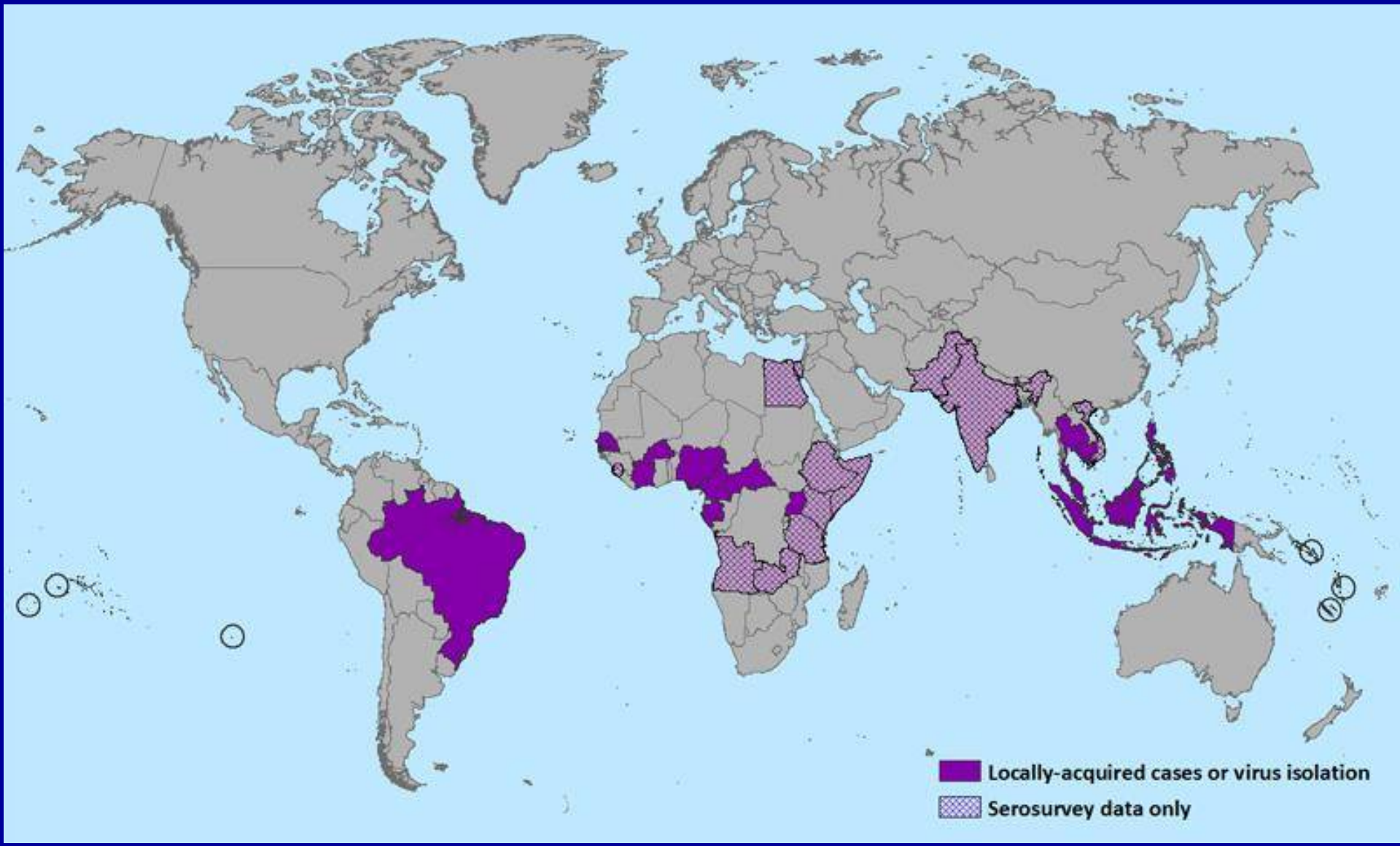
Mosquito Vectors of Infectious Disease Risks to Travelers

- Chikungunya: ***Aedes aegypti*, *Ae. albopictus***
- Dengue: ***Aedes aegypti* > *Ae. albopictus***
- Malaria: ***Anopheles* species**
- Zika virus disease: ***Aedes* species**
- Japanese encephalitis: ***Culex* species**
- Yellow fever: ***Ae. aegypti*, other *Aedes* spp.**
- WNV disease: ***Culex pipiens, Cx. tarsalis, Cx. quinquefasciatis*, other mosquito species**
- Filariasis: ***Anopheles, Culex, Mansonia* spp.**

Zika Virus

- Another Flavivirus transmitted by *Aedes* mosquitoes.
- About 80% asymptomatic, 20% symptomatic: fever, arthralgia, maculopapular rash, or conjunctivitis.
- Illness usually mild for several days; reports of Guillain-Barre syndrome (also seen with dengue).
- Test may cross-react with related flaviviruses (e.g., dengue and West Nile viruses).
- Treatment is supportive for symptoms; no specific antiviral available.

Countries with past/current Zika virus transmission (as of May 2015) *



** CDC*

Mosquito Precautions for Travelers

- Protect yourself outside
  - Cover exposed skin (long pants, long-sleeved shirts, hats)
  - Use mosquito repellent (DEET, picaridin, oil of lemon eucalyptus, IR3535)
  - Use permethrin-treated clothing and gear
- Protect yourself inside
  - Stay in screened or air-conditioned rooms
  - Use bed nets

Guidance for Surveillance of and Response to Invasive *Aedes* Mosquitoes and Locally Acquired Exotic Infections Transmitted by These Mosquitoes in California _ 2014

Recommended surveillance, coordination, and response actions for local vector control agencies and local health departments under four scenarios:

- Pre-detection of *Aedes aegypti/albopictus*
- Post-detection of *Aedes aegypti/albopictus*
- Detection of *Aedes aegypti/albopictus* positive for dengue, chikungunya, or another exotic mosquito-borne virus before local human infection documented
- Detection of locally acquired human infection with dengue, chikungunya, or another exotic mosquito-borne virus

CDPH California Department of PublicHealth

Recommended Actions for Local Agencies

All actions emphasize coordination and collaboration between local vector control and public health agencies

Pre-detection of *Aedes* (Vector and/or LHD)

- Identify agencies and resources that can be consulted regarding identification, surveillance, and control of invasive *Aedes* and exotic arboviral infections in humans
- Develop and implement an early detection plan for invasive mosquitoes
  - Include mosquito identification, a public outreach program, and appropriate mosquito surveillance tools
- Develop a response plan that can be implemented at the first detection of invasive mosquitoes
- Continue to report any cases of dengue, chikungunya, and other exotic mosquito-borne viruses via CalREDIE
  - Ensure report includes travel history

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Locally acquired human infection identified

- Issue joint media release and intensify all public outreach and education efforts
- Enhance mosquito surveillance and control in vicinity of case-patient's residence, neighborhood, and other locations patient visited if *Aedes* present
- Enhance surveillance for additional locally acquired human cases by notifying the local medical community to look for and encourage testing of all suspected infections, regardless of travel history, and to report ASAP
- Follow-up promptly on all suspect cases and notify CDPH via CalREDIE or by phone
- Enhance mosquito surveillance and control in neighborhoods of suspect cases

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CDPH VRDL

- Tests for dengue, chikungunya, WNV, other mosquito-borne viruses (e.g., WEE, SLE, Zika) in suspect patients
- For dengue:
  - RT-PCR
  - Serology: IgM & IgG IFA, IgM-capture ELISA, IgG ELISA
  - For confirmation, PRNT for neutralizing antibody
- For chikungunya:
  - RT-PCR
  - Serology: IgM & IgG IFA
  - For confirmation, PRNT for neutralizing antibody
- For WNV:
  - RT-PCR
  - Serology: IgM & IgG IFA, IgM-capture ELISA, IgG ELISA
  - For confirmation, PRNT for neutralizing antibody

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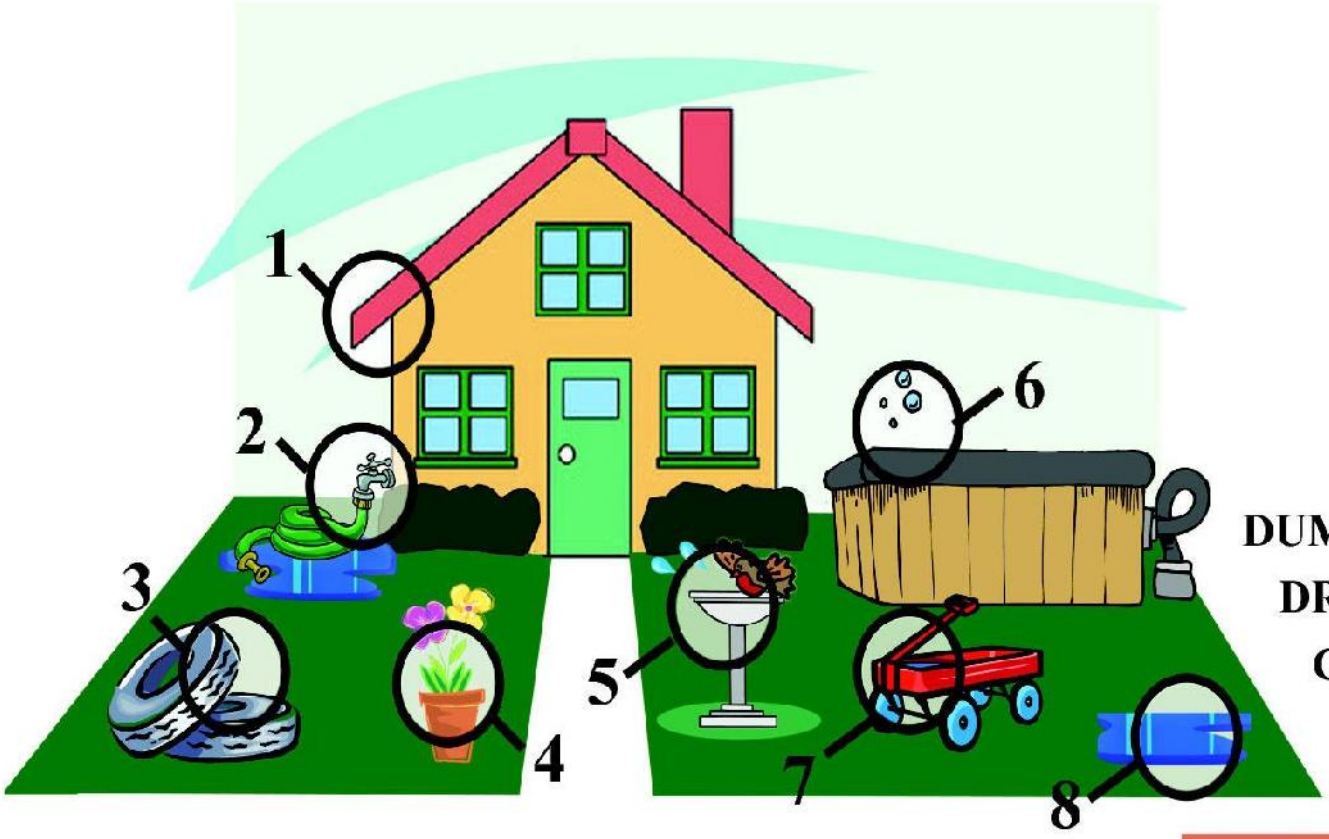
Mosquito Breeding Sites for Dengue and Chikungunya



DUMP IT
DRAIN IT
CLEAN IT UP

1. Keep gutters clean
2. Repair leaky faucets
3. Eliminate debris that holds water
4. Drain excess water from plant pots and saucers
5. Change birdbaths twice a week
6. Maintain pools and spas; keep water from pooling on covers
7. Turn toys and equipment upside down to prevent water from collecting inside
8. Avoid overwatering

Help your community reduce mosquito-borne diseases like West Nile Virus by keeping your property free from mosquito breeding sites

California Traveler #1

- In May 2015, a 55 y.o. male California resident presented to medical attention complaining of a week of fever, chills, night sweats, and joint pain. No headache, no eye pain, no muscle aches, no rash. Had some bleeding gums.
- He just returned from El Salvador where he had stayed over 2 weeks. He recalled having had mosquito bites while there.
- Diagnosis: acute and convalescent IgM for dengue positive; chikungunya negative.

California Traveler #2

- In April 2015, a 44 y.o. male California resident was hospitalized for fever, headache, muscle aches, malaise, and rash. Blood tests show low WBC and low PLT.
- A week before illness onset, he had returned from Honduras where he had stayed for a week. Did not recall mosquito bites.
- Diagnosis: Acute IgM dengue 0.74 negative, chikungunya 1:10 positive; Convalescent IgM dengue 4.33 positive, chikungunya 1:640 positive => coinfection !

Summary

- Dengue and chikungunya are mosquito-borne infections threatening California.
- Dengue and chikungunya human cases have recently increased, all among travelers returning from affected areas/countries.
- Recent transmissions documented in US states where *Ae. aegypti* and/or *albopictus* abundant.
- *Ae. aegypti* or *Ae. albopictus* are present and spreading in some counties in California.
- Local public health and vector control should have a plan for surveillance, coordination, and response, and continue monitoring of *Aedes* mosquitoes and human cases of dengue and chikungunya.

Resources

- Report suspect cases of dengue and chikungunya to the CDPH Vector-Borne Disease Section,

  Charsey Porse, PhD, MPH, (916) 552-9730

  Charsey.porse@cdph.ca.gov

- For information on testing for arboviruses:

  CDPH Viral and Rickettsial Disease Lab (VRDL), (510) 307-8585

  CDPH VRDL Guidelines for Laboratory Services: http://www.cdph.ca.gov/programs/vrdl/Pages/default.aspx

- CDPH website (type *Aedes* in search box)
- CDC website (*Aedes*, dengue, chikungunya)

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Questions?