

EMERGING INFECTIOUS DISEASE OUTBREAKS

Arizona, the United States, & the World

April 22, 2015

Arizona Department of Health Services

Outline

Vectorborne Transmission

- Chikungunya
- Dengue



Direct Transmission

- Ebola
- Measles





CHIKUNGUNYA

Chikungunya Background

- RNA virus spread via mosquitos
 - ▣ *Aedes spp.*
 - ▣ Mosquito-human-mosquito-human cycle
- All over the world
- First appeared in western hemisphere in December, 2013
 - ▣ Since then has caused a huge outbreak in the Caribbean and Latin America



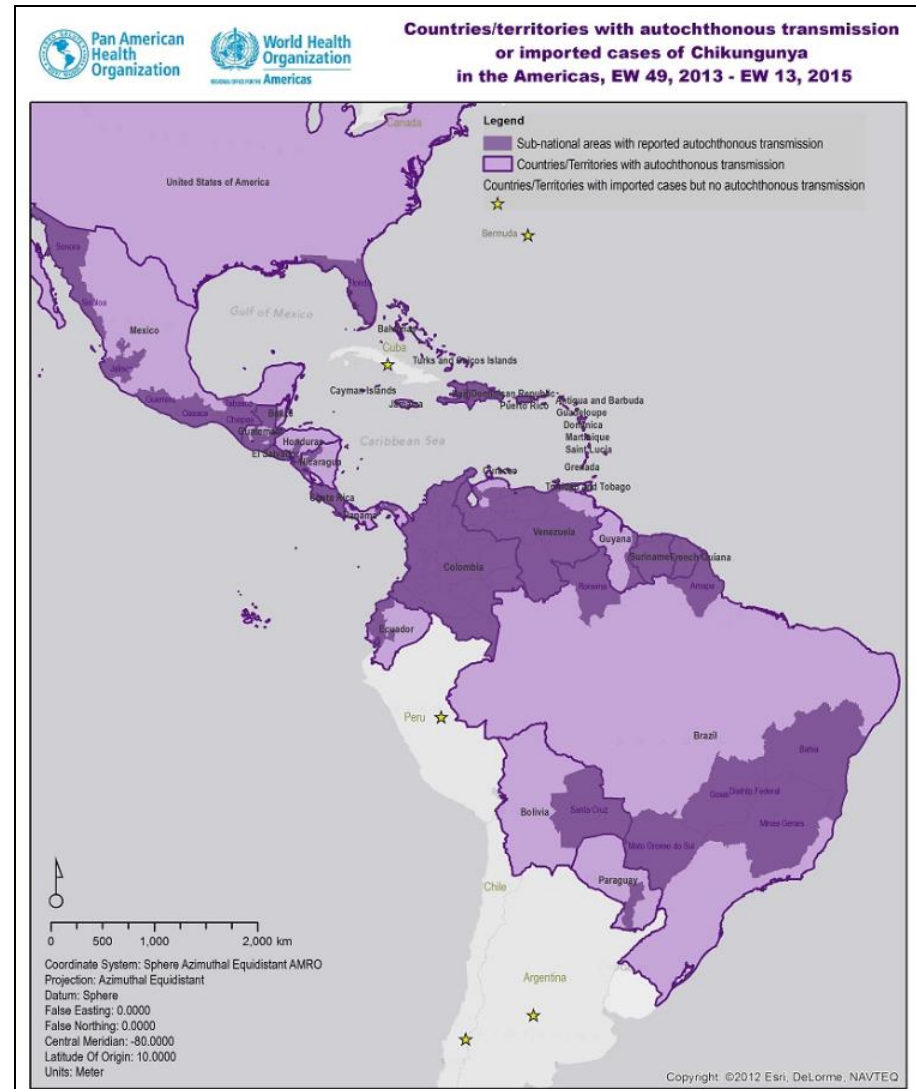
December 2013

- First chikungunya cases in Western hemisphere:
St. Martin

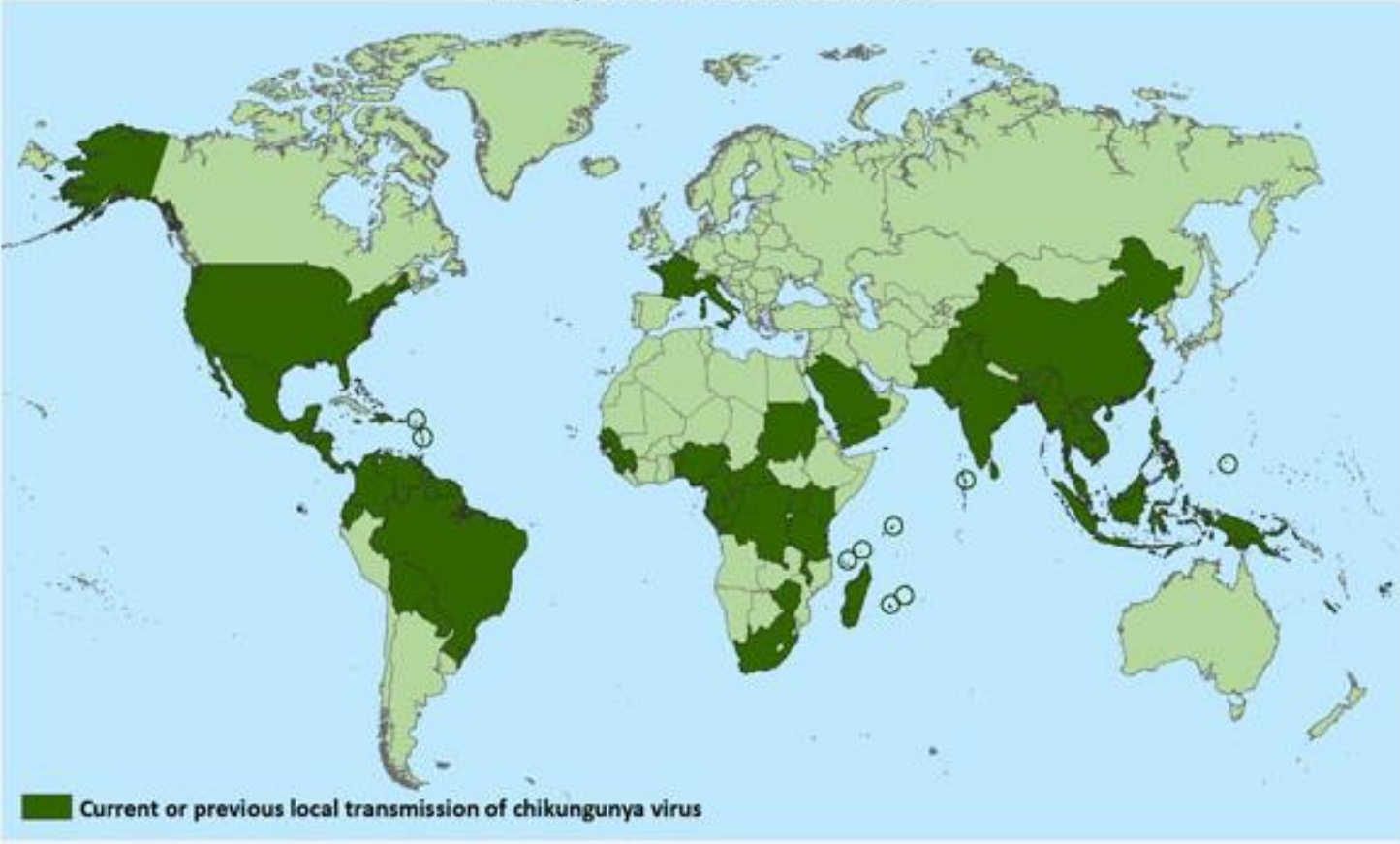


Chikungunya, the Outbreak

- Naïve population + *Aedes* vectors = large outbreak potential
- Moving northward through MX
- Since spread to 44 countries/territories
- Current outbreak:
 - As of 4/3/15
 - 1,356,611 cases
 - 184 deaths

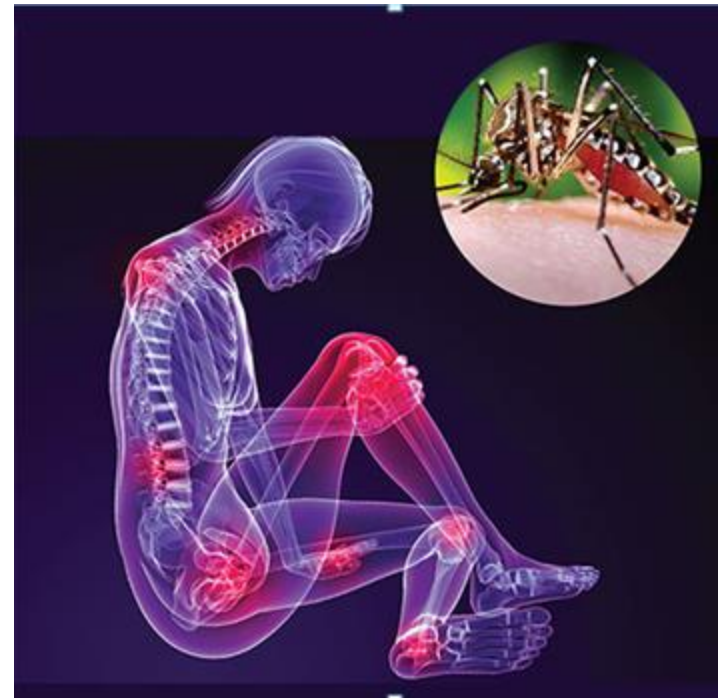


Countries and territories where chikungunya cases have been reported*
(as of March 10, 2015)



Chikungunya, Clinical

- Most common symptoms: severe joint pain, fever, rash, nausea, vomiting, diarrhea
 - ▣ Joint pain so severe can't leave bed
 - ▣ 80-90% of all infections lead to disease
- Mortality VERY LOW, <1%
- BUT morbidity may be very high
 - ▣ Chronic infection can cause months or years of rheumatic symptoms, fatigue and depression
 - ▣ More likely in elderly or sick



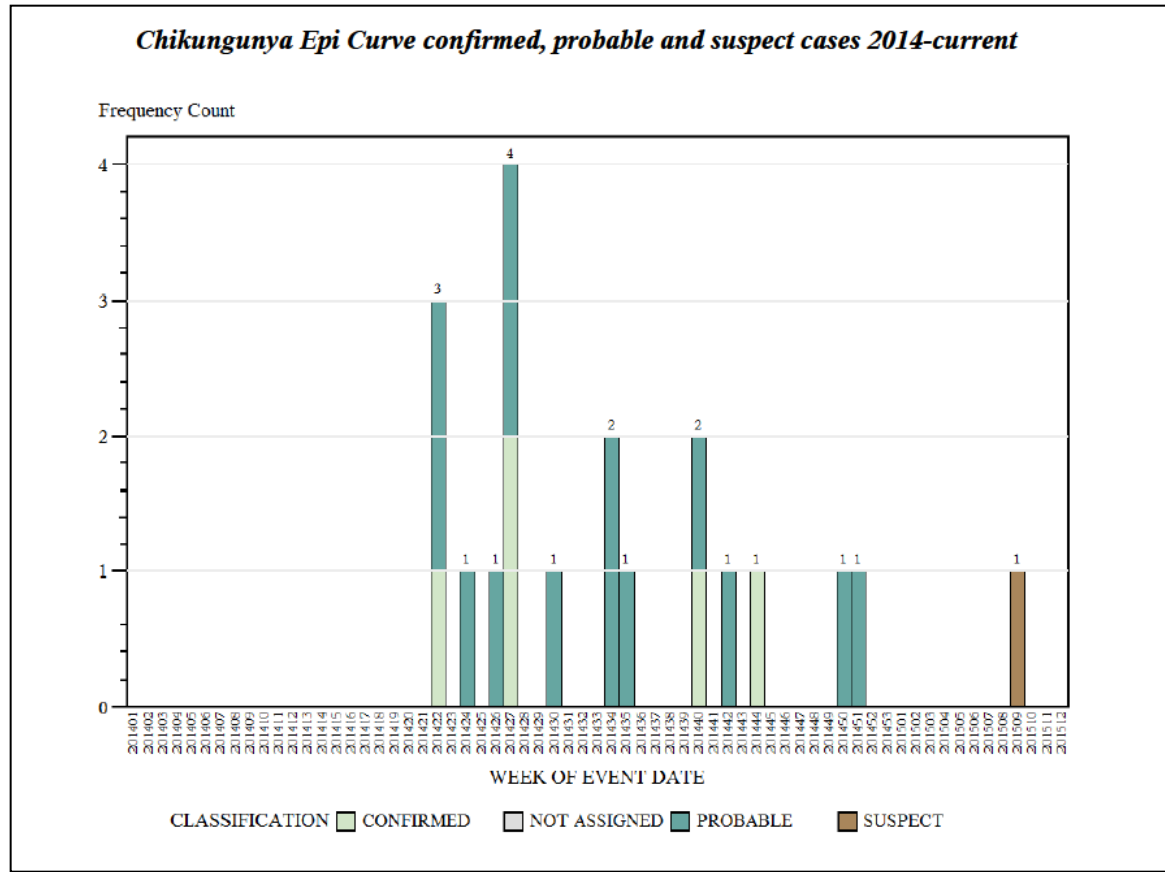
Chikungunya in Arizona

- U.S. has had 2,560 imported cases
 - ▣ Previous yearly average was 28

- Arizona has principal vector species, *Aedes aegypti*
 - ▣ Therefore, local establishment of virus is possible
 - None identified, to date
 - ▣ Locally acquired disease in FL (11)
 - ▣ CHIK + mosquito in Houston, TX

Chikungunya in Arizona

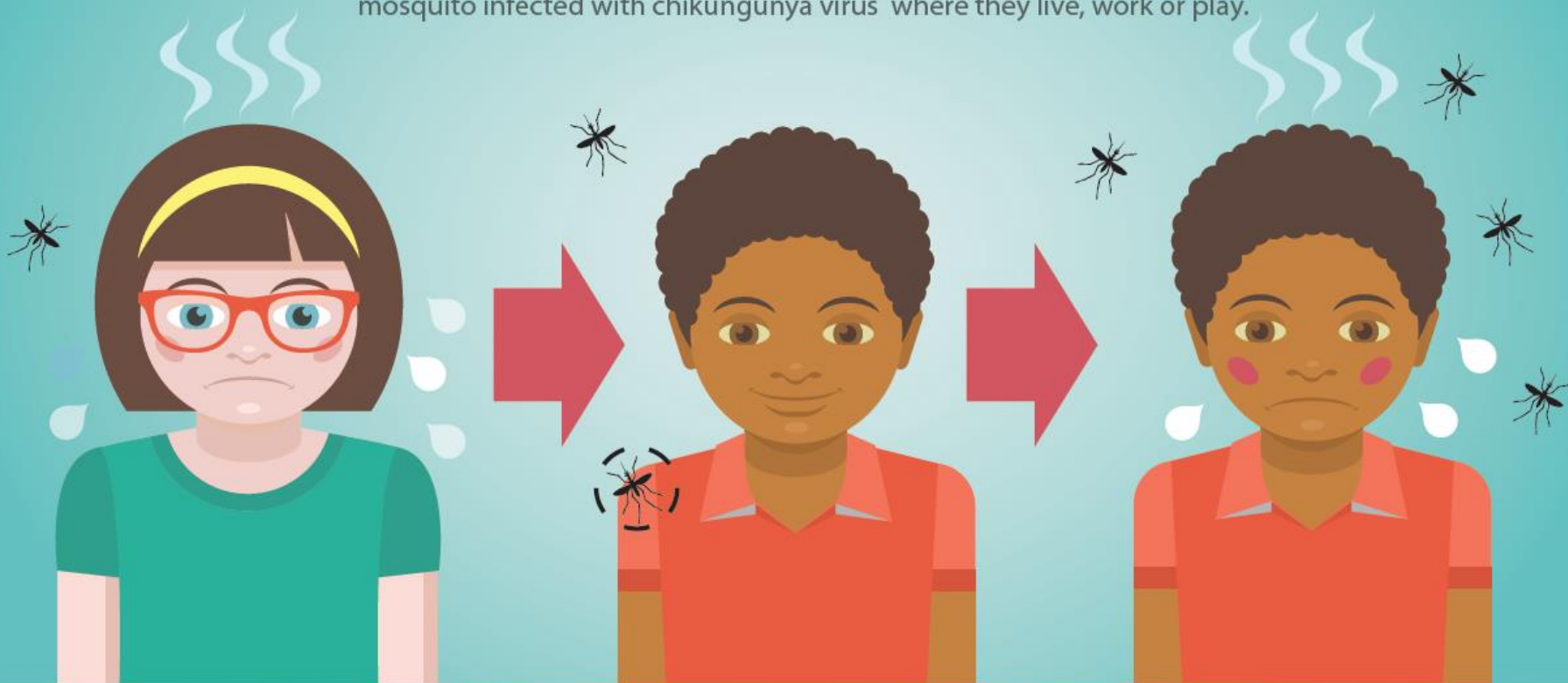
- 20 imported chikungunya cases in Arizona in 2014 - current
 - 15 in Maricopa County
 - 3 in Yavapai County
 - 1 in Mohave County
 - 1 in Yuma County
- First case in week 22
- Last case in week 09





CHIKUNGUNYA: What is local transmission?

A person with no recent history of travel to an area with the virus who gets bitten by a mosquito infected with chikungunya virus where they live, work or play.



A mosquito bites a person who is sick with chikungunya and picks up the virus from the infected person's blood.

Infected mosquitoes can then spread the virus to other people through bites.



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Treatment and Vaccines

- There is no treatment, only supportive therapy
- 2010: non-human primates protected from chikungunya following vaccine
- Aug. 2014: experimental vaccine in human trials. Shows promise; was safe, well-tolerated, and elicited an antibody response
- 2015: trials are ongoing



DENGUE

Dengue Background

- RNA virus transmitted by *Aedes* mosquito vectors, like CHIK
- Found throughout the tropics and subtropics
- First appeared in western hemisphere in 1981, has since spread throughout region
- Serotypes I, II, III, IV
 - No cross-immunity
 - Second infection (with different strain) much worse than first.
 - Antibody dependent enhancement

Laboratory-Confirmed DHF in the Americas
Prior to 1981 vs. 1981 - 2003



Figure 1.1 Countries/areas at risk of dengue transmission, 2008



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines or maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization Map
Production: Public Health Information and Geographic Information Systems (GIS) World Health Organization



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Global Dengue Burden

- Severe dengue is a leading cause of serious illness and death among children in some Asian and Latin American countries
- Global incidence has grown dramatically in the past decade
 - 390 million dengue infections each year
 - 96 million manifest disease, but others can still transmit

Dengue, the Outbreak

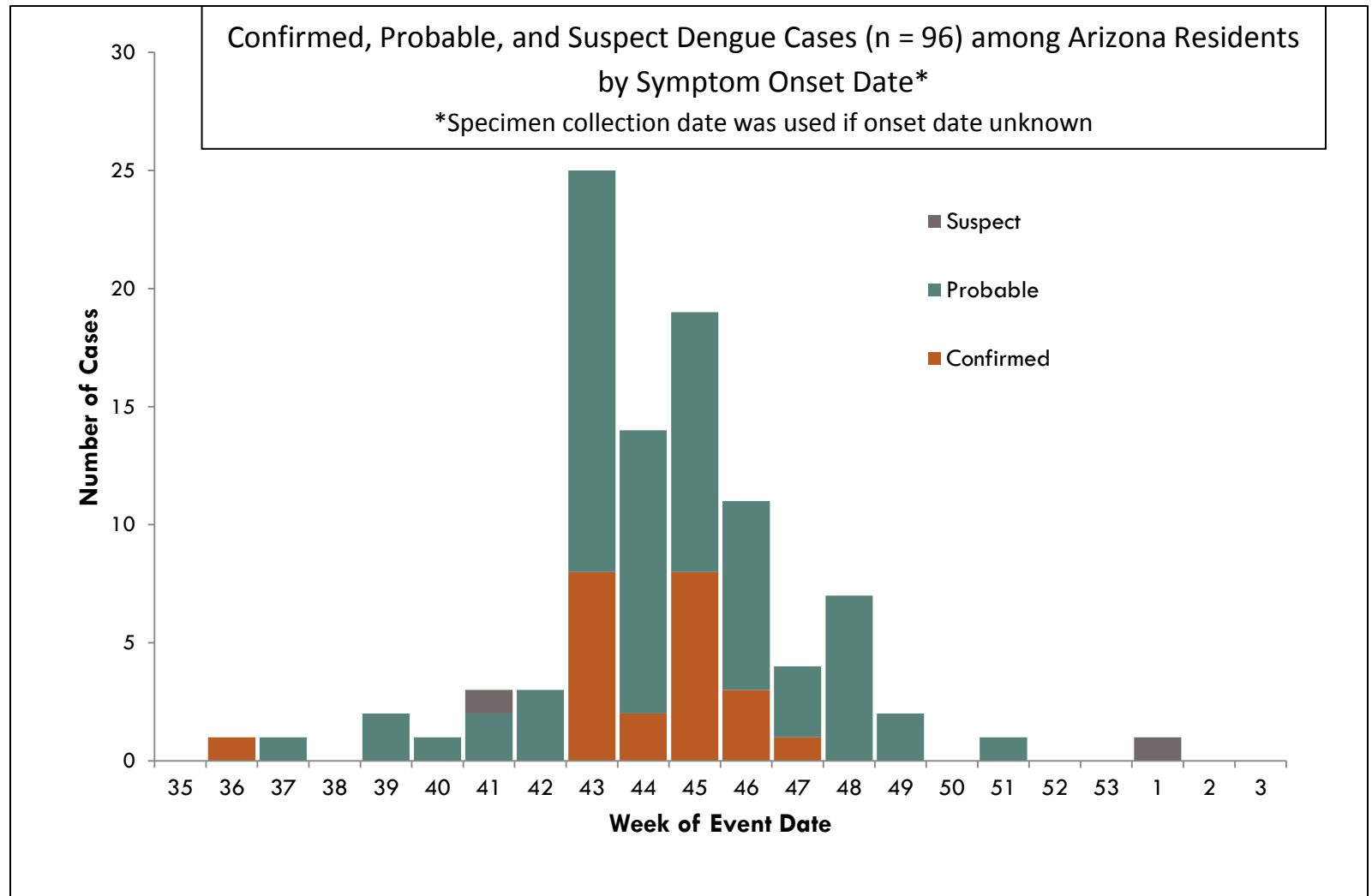
- Increasing incidence of dengue cases in Mexico
- Cases further north and closer to AZ/MX border than ever before (& CA/MX border)
- The virus spreads along with its mosquito vector



Dengue, the Outbreak

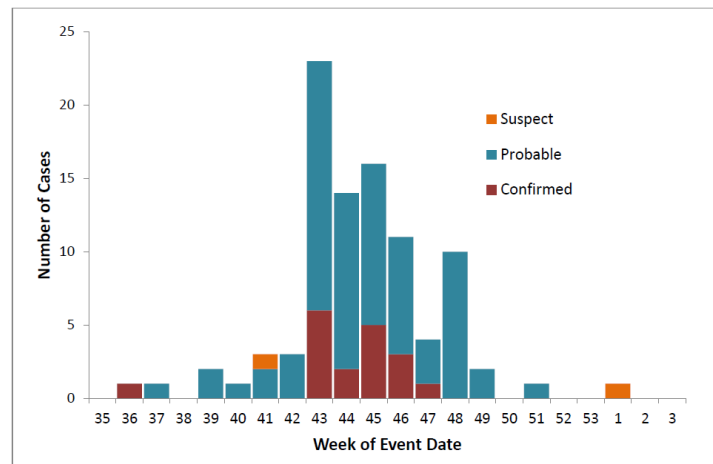
- 96 dengue cases identified among Arizona residents September 1, 2014–March 26, 2015
 - ▣ 7 additional out-of-state cases identified (not included in analyses)
- No locally-acquired cases have been identified as of April 6, 2015
- Most cases (n = 71) reported from Yuma County
- Most cases (n = 72) identified as Hispanic or Latino
- Many cases (n = 72) reported travel history to Sonora, Mexico

2014-2015 Dengue outbreak: Epidemic curve

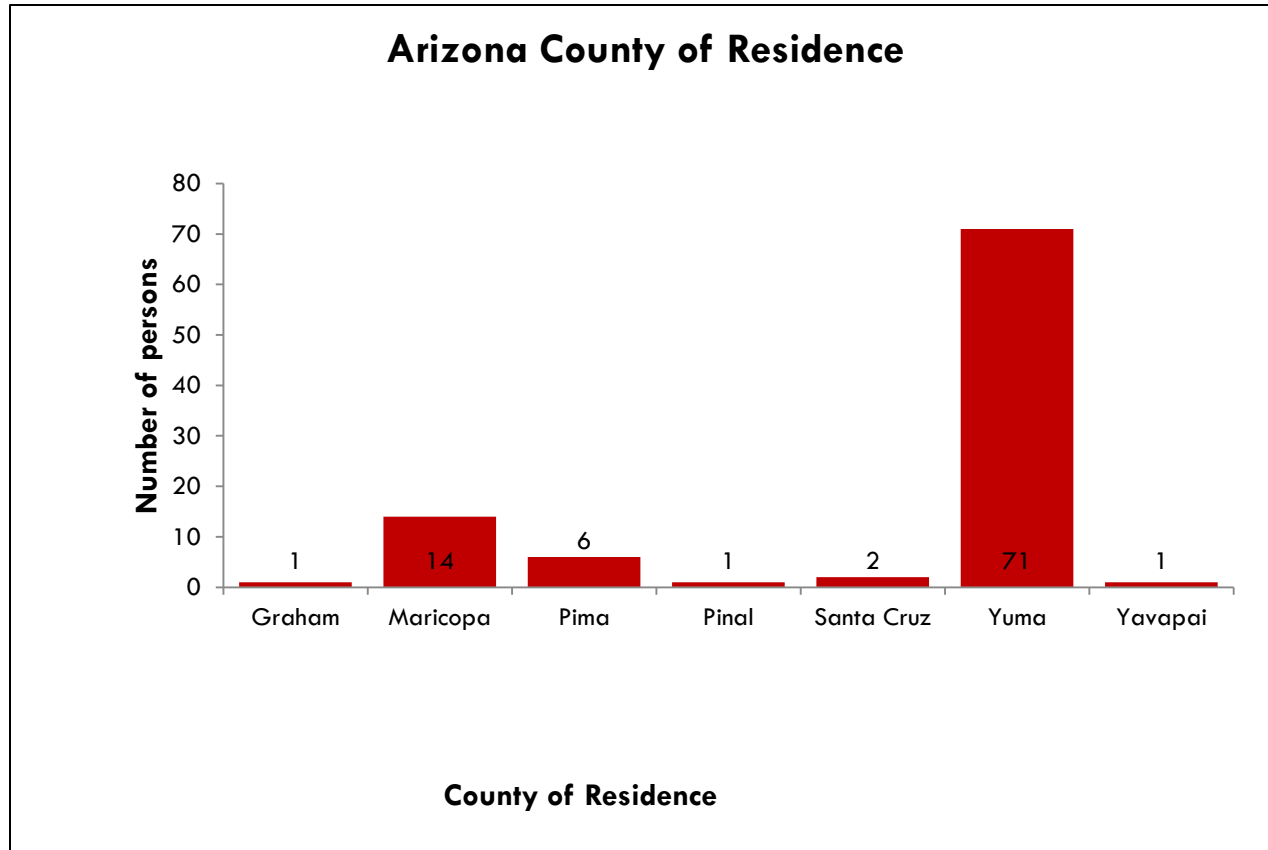


Epidemic curve

- An epidemic curve is a graph that plots the number of new cases by time of disease onset
- Different disease outbreaks have different curve types
 - Propagated source epidemic → an epidemic in which the first wave of infection serves as the source of the next wave of infections
 - There are also point source and continuous point source



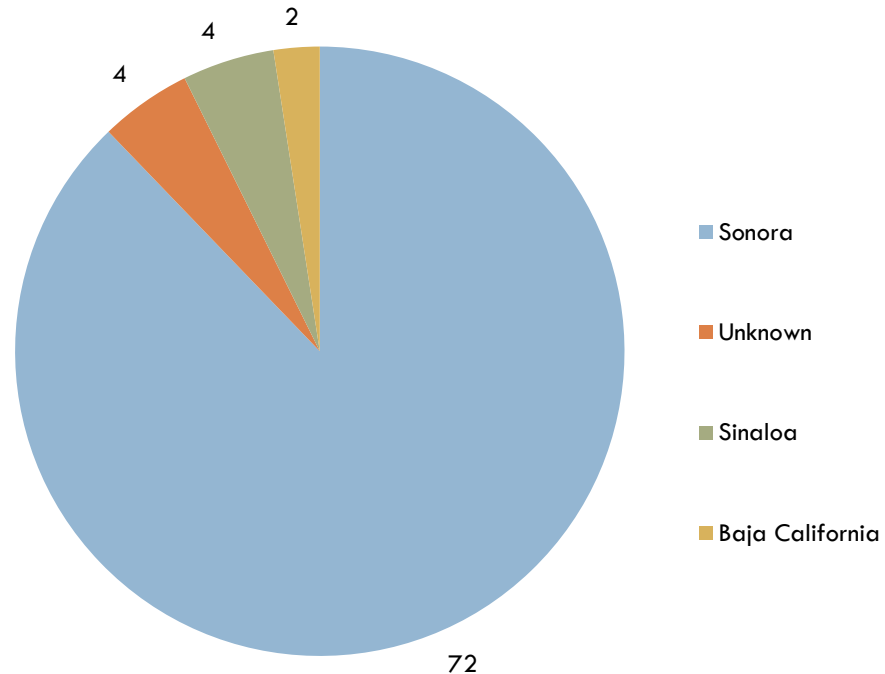
2014-2015 Dengue outbreak: cases counts by county



Imported dengue cases from Mexico, by Mexican state

- As of 3/26/15
- Of 96 total dengue cases in Arizona:
 - 85 have information about travel history
 - 82 of these 85 traveled to Mexico during the incubation period
 - Remaining 3 traveled to Central America or Africa

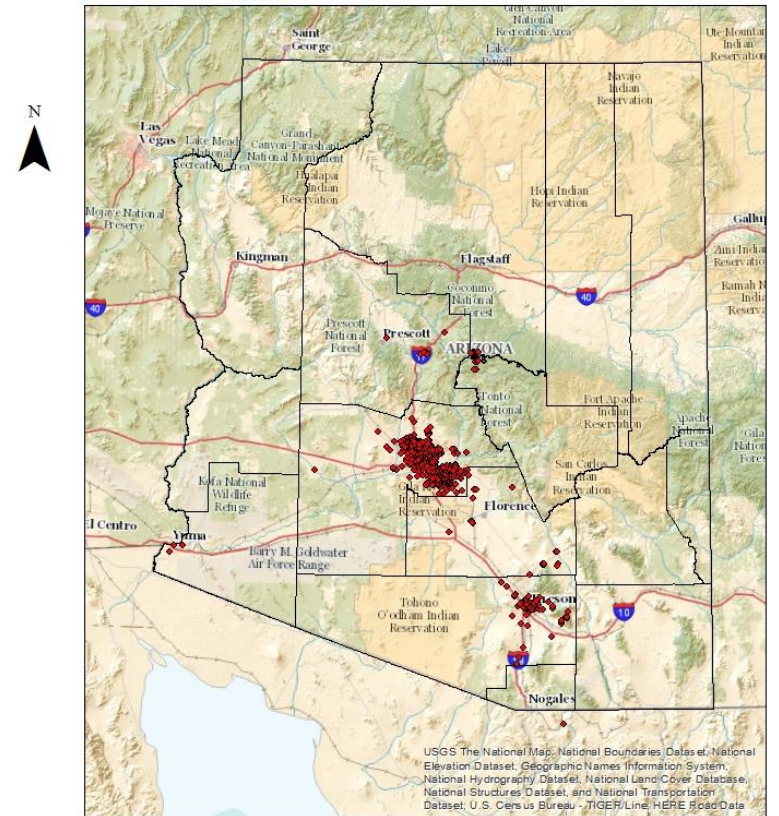
Reported Travel History to State in Mexico (n=82)*



Dengue in Arizona

- Imported cases
 - ▣ Increase from 4 to 96
- Vectors present in AZ
- Could lead to local viral establishment
- Border counties especially at risk
- Enhanced vector and disease surveillance is ongoing

Confirmed Presence of *Aedes aegypti* in Arizona, 2004-2013

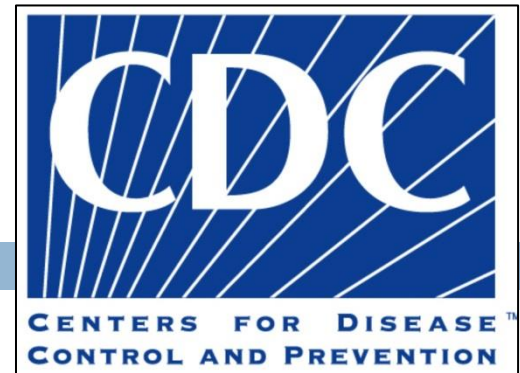


0 20 40 80 120 160 Miles

Legend

- ◆ *Aedes aegypti* Presence Confirmed
- Counties

Dengue Epi-aid



- ▣ **Partners:** CDC Dengue Branch, CDC Division of Global Migration and Quarantine, ADHS (OIDS and OBH), University of Arizona, and Yuma County Public Health

- ▣ Four new cases were identified. All had travel history. No locally acquired cases were found.

- ▣ **Cluster investigations performed with case's household members and homes within a 50meter radius – household forms and individual forms**
 - Performed as part of active case finding
 - Completed for Yuma cases only
 - Entered and stored in EpiInfo database
 - Electronic version shared with Yuma, ADHS, and CDC

Enhanced laboratory surveillance

- Most private laboratories only perform IgM testing, additional testing is being conducted at CDC Dengue Branch to:
 - ▣ Confirm IgM test results
 - ▣ Perform PCR testing to identify false negative results
 - ▣ Identify the dengue serotypes of interest
- Specimens forwarded by ASPHL, Sonora Quest Labs, Focus Diagnostics, and ARUP between 11/17/14 – 2/3/15
- 16% (11/69) of the specimens tested at AZ labs were false negatives
- 23% (11/47) of the negative results were false negatives

Multiple Clinical Manifestations

- Dengue-like illness
 - ▣ Fever and travel to dengue-endemic area

- Dengue
 - ▣ Fever and at least one of the following:
 - Nausea/vomiting, rash, aches/pains, tourniquet test positive, leukopenia, abdominal pain/tenderness, extravascular fluid accumulation, mucosal bleeding, liver enlargement, increasing hematocrit with platelet count decrease

- Severe dengue
 - ▣ Dengue with any of the following:
 - ▣ Severe plasma leakage, severe bleeding, severe organ involvement



PHYSICIAN POCKET CARD

PUT DENGUE IN YOUR DIFFERENTIAL

Has your patient **recently traveled** to any of the following affected areas?

Africa, Asia, Pacific Islands, South America, Central America, the Caribbean, or **Mexico**

In addition to **high fever**, does your patient have any of the following signs and symptoms?

Severe aches and pains (headache, eye pain, joint, muscle or bone pain), rash, nausea, vomiting, mild bleeding, thrombocytopenia or elevated hematocrit

If YES to both, test and treat for dengue!

TEST AND TREAT

Order RT-PCR **if ≤ 5 days** after illness onset

Order ELISA (serology) **if ≥ 5 days** after illness onset

Also consider testing for chikungunya or West Nile Virus

For more information, visit www.cdc.gov/dengue

No specific treatment is available for dengue.

DO—manage fever, early signs of shock and hemorrhage, fluid balance

DON'T—administer corticosteroids or NSAIDs, excessive fluid therapy, or platelet transfusions


Treatment

- There is no treatment
- BUT early diagnosis and supportive therapies save lives
 - ▣ For severe dengue mortality decreases from 20% to <1%
 - ▣ Maintenance of body fluid volume is paramount

Vaccine Research and development

- Challenging due to multiple serotypes and antibody dependent enhancement.
 - Vaccine must impart immunity to all serotypes

- Global study in Phase III trials, for CYD-TDV
 - 40,000 volunteers in Asia, Latin America, and the Caribbean
 - 60% efficacy for all 4 serotypes
 - Reduced hospitalization rates due to severe dengue by 80% among children 2-14 years old
 - Likely, each vaccine roll out would have to be tailed to each regions
 - Least effective against dengue-2, which is the most common serotype in Asia, but not elsewhere



EBOLA

Ebola Background

- A zoonotic RNA virus found around Africa
- In past has caused sporadic outbreaks
- Likely carried by fruit bats
 - ▣ *Rousettus spp.*
- Transmitted by infected body fluids of bush meat or humans
- Previous outbreaks across Africa, but were small and contained



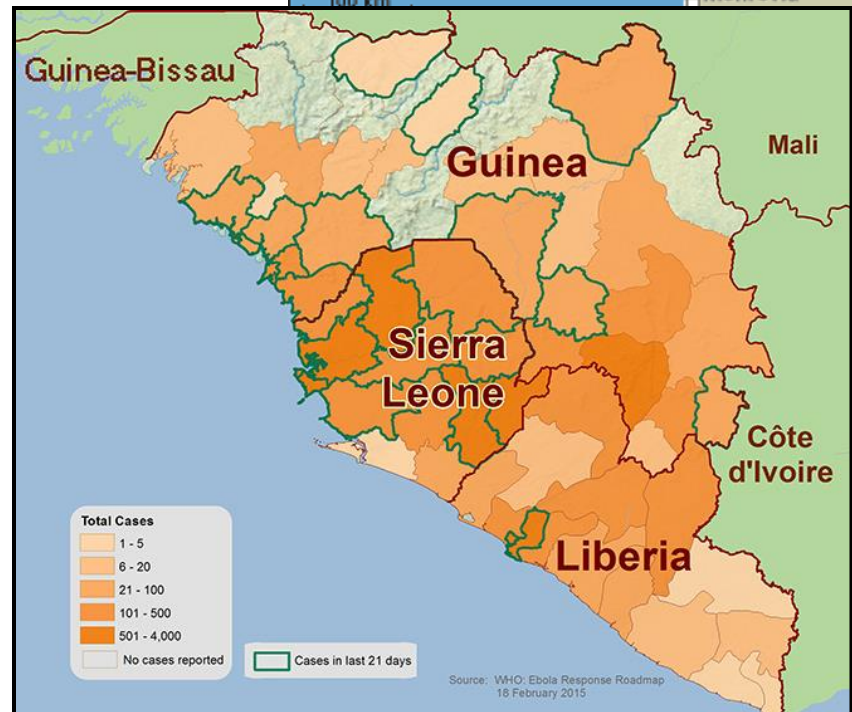
Ebola, Clinical



- ❑ Very severe disease
- ❑ Fever, nausea, vomiting, diarrhea, body aches, unexplained hemorrhaging
- ❑ No specific treatment → supportive therapies
- ❑ Case fatality rate may be very high
 - ▣ Between 30-70%
 - ▣ Death typically due to shock or organ failure

Ebola, the Outbreak

- Largest Ebola outbreak in history
- Opportunistic outbreak following years of civil conflict
- As of 3/31/15:
 - 25,263 cases
 - 10,477 deaths
 - CFR: 41%
 - Often changing



Outbreak geography

CURRENTLY AFFECTED

- Guinea
- Liberia
- Sierra Leone

DECLARED EBOLA FREE

- United Kingdom
- Mali
- Nigeria
- Spain
- United States
- Senegal



Ebola in the U.S.

- What is the real risk?
- As long as the outbreak continues in West Africa there is the risk of travel associated cases in the U.S.
- Hospitals must prepare for this possibility
 - ▣ HCWs are at greatest risk
- The general public is **NOT** at risk

Ebola and Arizona

- ADHS
 - Education to HCWs and the public
 - Preparedness plans for an Ebola case in AZ

- County health departments
 - Tracking travelers who are doing self-monitored temperature and symptom checks
 - Typically have around 10 travelers under monitoring, statewide

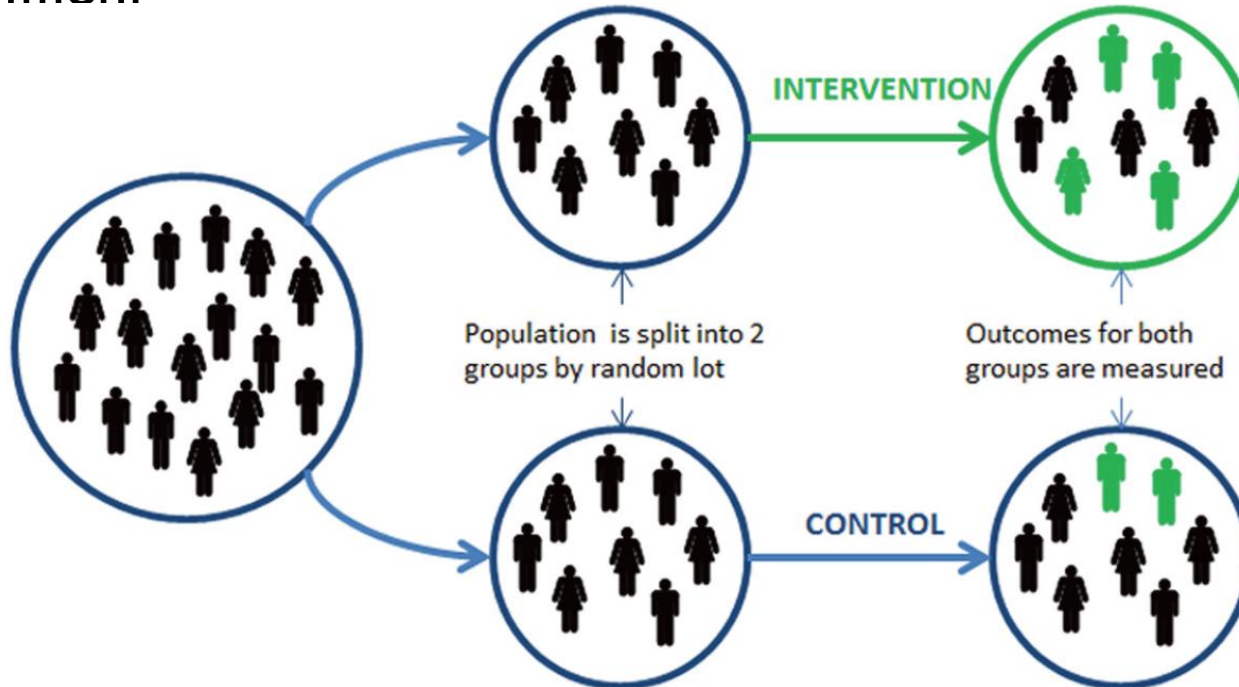
- There have been no suspect cases of Ebola in AZ
 - Overall, less likely in AZ (when compared to other states)

Treatment and vaccines

- Large clinical trial now open to volunteers in Liberia, testing two vaccine candidates
- cAd3-EBOZ, uses a chimpanzee-derived cold virus to deliver Ebola virus genetic material from the Zaire strain
- VSV-ZEBOV, employs vesicular stomatitis virus, an animal virus that primarily affects cattle, to carry an Ebola virus gene segment.
- Cases are increasing in Guinea and decreasing in Liberia and Sierra Leone, this will effect vaccine trials
 - Different vaccine trial in Liberia was canceled earlier this year

Randomized controlled trials

- Why so long for a vaccine?
 - ▣ There were ethical concerns regarding randomized controlled trials
- Now, decreasing transmission threatens future prevention investment





MEASLES

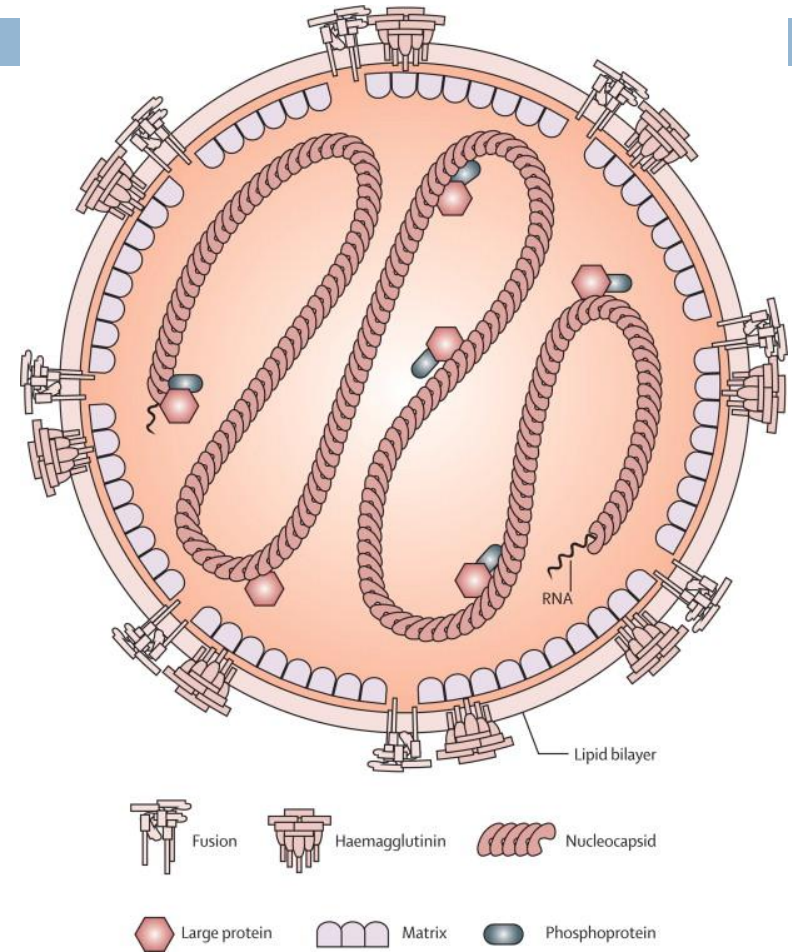
Disease Overview

- Respiratory disease caused by measles virus
- Replicates in cells of throat and lungs
- Symptoms include:
 - Fever
 - Coryza (runny nose)
 - Cough
 - Rash
- Rubeola → From Latin, red



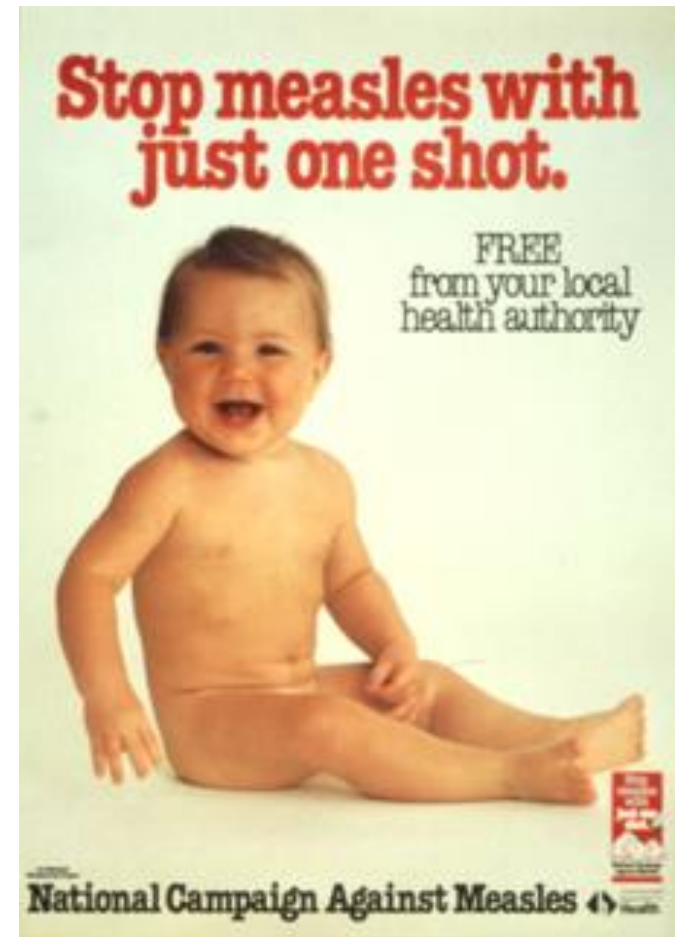
Virus Overview

- Family: Paramyxoviridae
- Genus: *Morbillivirus*
- Enveloped RNA
- 1 serotype
- Only spread by humans
 - ▣ Asymptomatic carrier state has not been seen



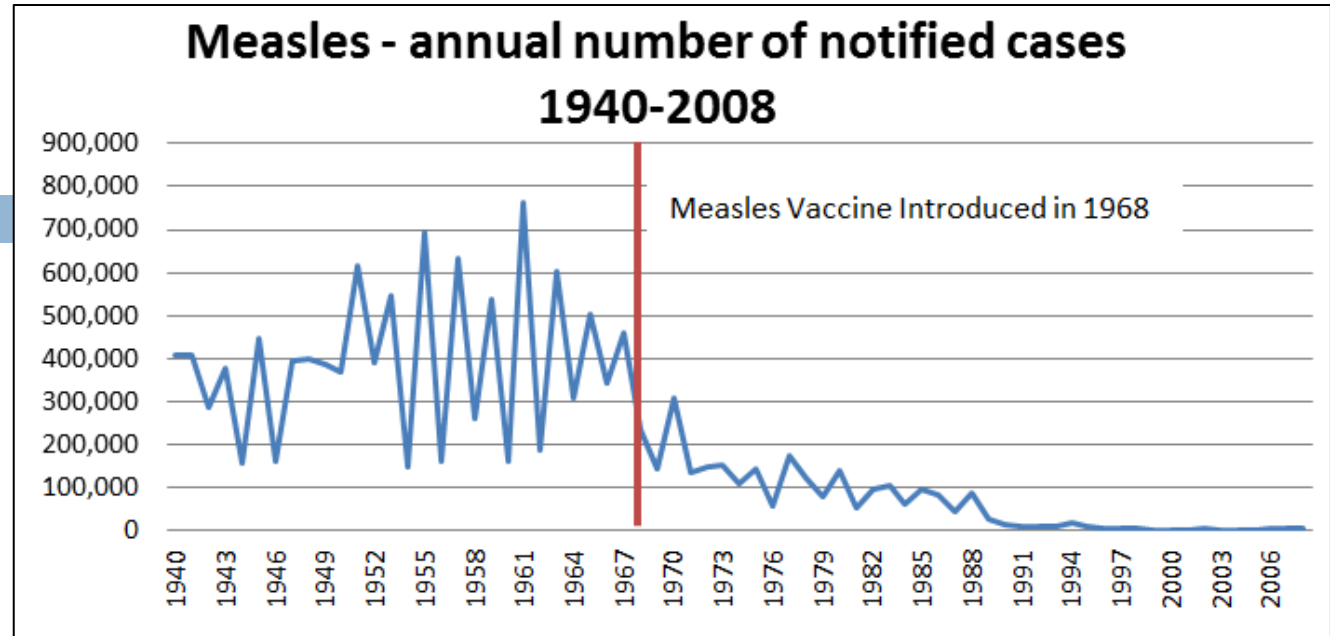
History

- 1958 – First measles vaccine tested
- 1962 – Killed – virus vaccine created
- 1963 – Vaccine for measles licensed
- 1968 – Safer vaccine created with fewer side effects
- 1971 – MMR vaccine becomes available
- 1978 – CDC targets measles for eradication in US
- 1998 – MMR *allegedly* linked to autism
- 2000 – Endemic measles eliminated from US



Vaccine

- Lifelong immunity
- Currently a live attenuated vaccine
- MMR or MMRV
- First dose at 12 - 15 months
- Second dose at 4 - 6 years
- Prior to 1963 in US average of 549,000 measles cases and 495 deaths reported annually
- AZ has medical, religious, and personal belief exemptions



Transmission

- Highly communicable
- Spread via droplets in the air
 - ▣ Airborne transmission via aerosolized droplet nuclei has been documented in closed areas
- Transmission can occur 4 days before appearance of rash to 4 days after appearance of rash
 - Potentially spread via fomite
 - Can remain viable for 2 hours on a surface
- Inactivated by heat, light, low pH, ether, and trypsin



Rash

- Occurs 2 – 4 days after prodrome
 - ▣ 14 days after exposure
- Lasts 5 – 6 days
- Maculopapular rash
- Areas on the skin become red with small bumps
- Starts on the face and head
- Eventually appears on the extremities
- Can cause the skin to peel off

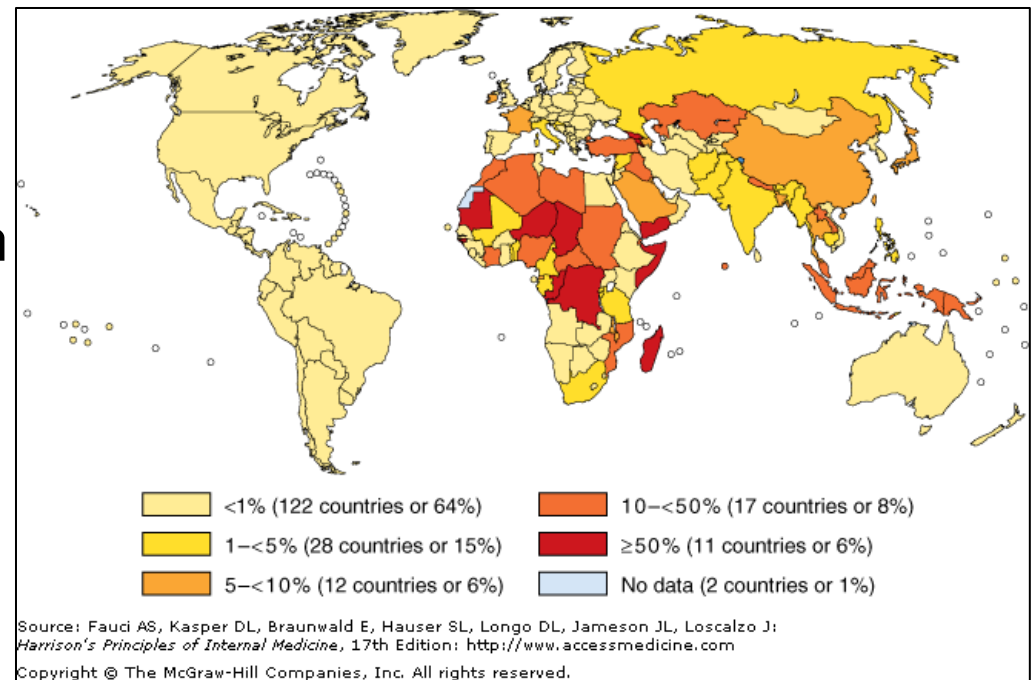


Treatment

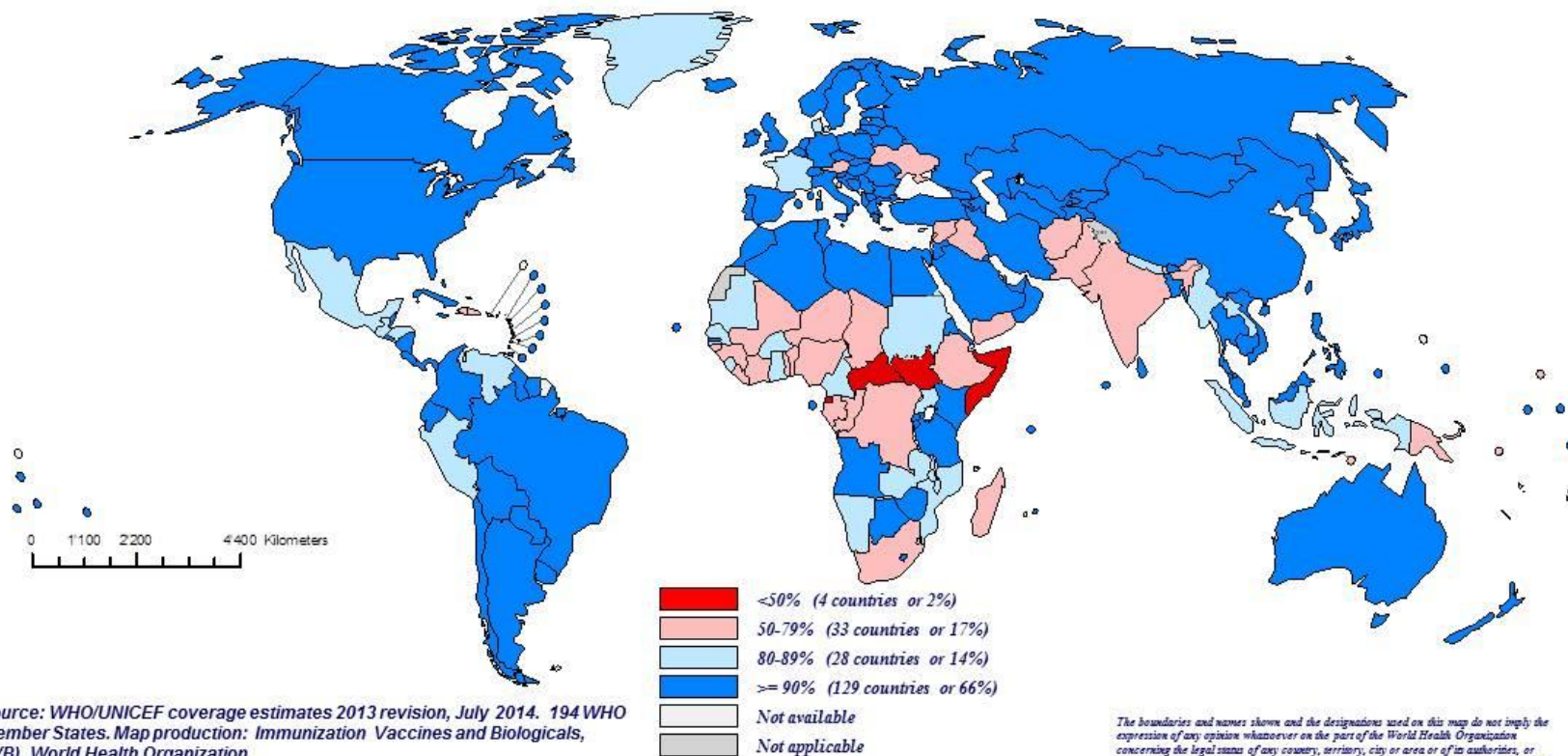
- There is no specific antiviral therapy for measles
- Post exposure vaccination or antibodies
- Treat symptoms
 - ▣ Reducing fever, pain meds, fluids
- Two doses of vitamin A over two days
 - ▣ Associated with reduction in mortality of children <2 years of age

Measles Burden

- The majority of people who get measles are unvaccinated
- Measles is still common in many parts of the world
 - ▣ Europe, Asia, the Pacific, and Africa
- Travelers may bring measles into the U.S.



Immunization coverage with measles containing vaccines in infants, 2013



Source: WHO/UNICEF coverage estimates 2013 revision, July 2014. 194 WHO Member States. Map production: Immunization Vaccines and Biologicals, (IVB). World Health Organization

Date of slide: 16 July 2014

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Measles Cases and Outbreaks

January 1 to April 3, 2015*

159

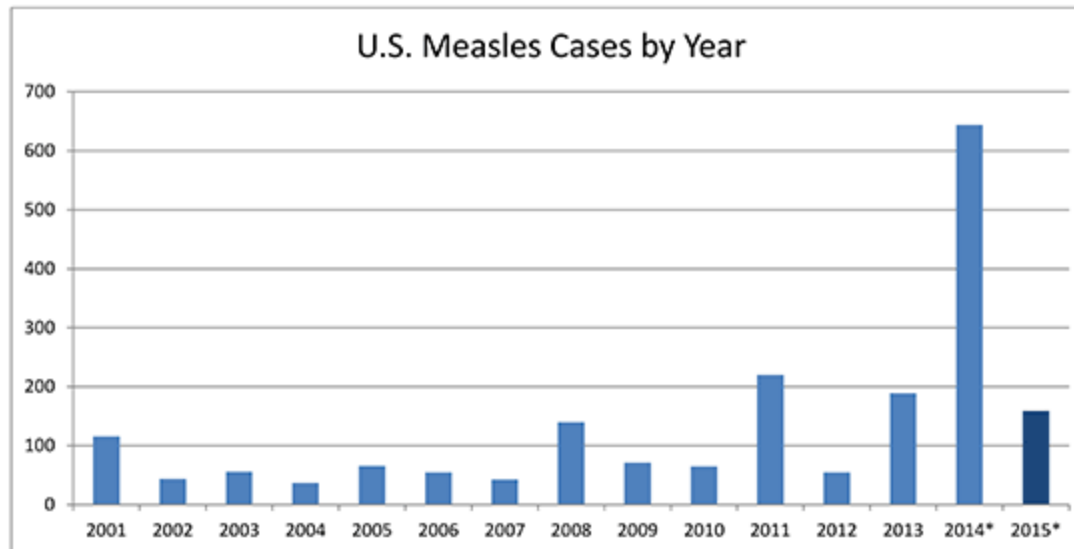
Cases

reported in 18 states and the District of Columbia: Arizona, California, Colorado, Delaware, Georgia, Illinois, Michigan, Minnesota, Nebraska, New Jersey, New York, Nevada, Oklahoma, Pennsylvania, South Dakota, Texas, Utah, Washington

4

Outbreaks

representing 91% of reported cases this year

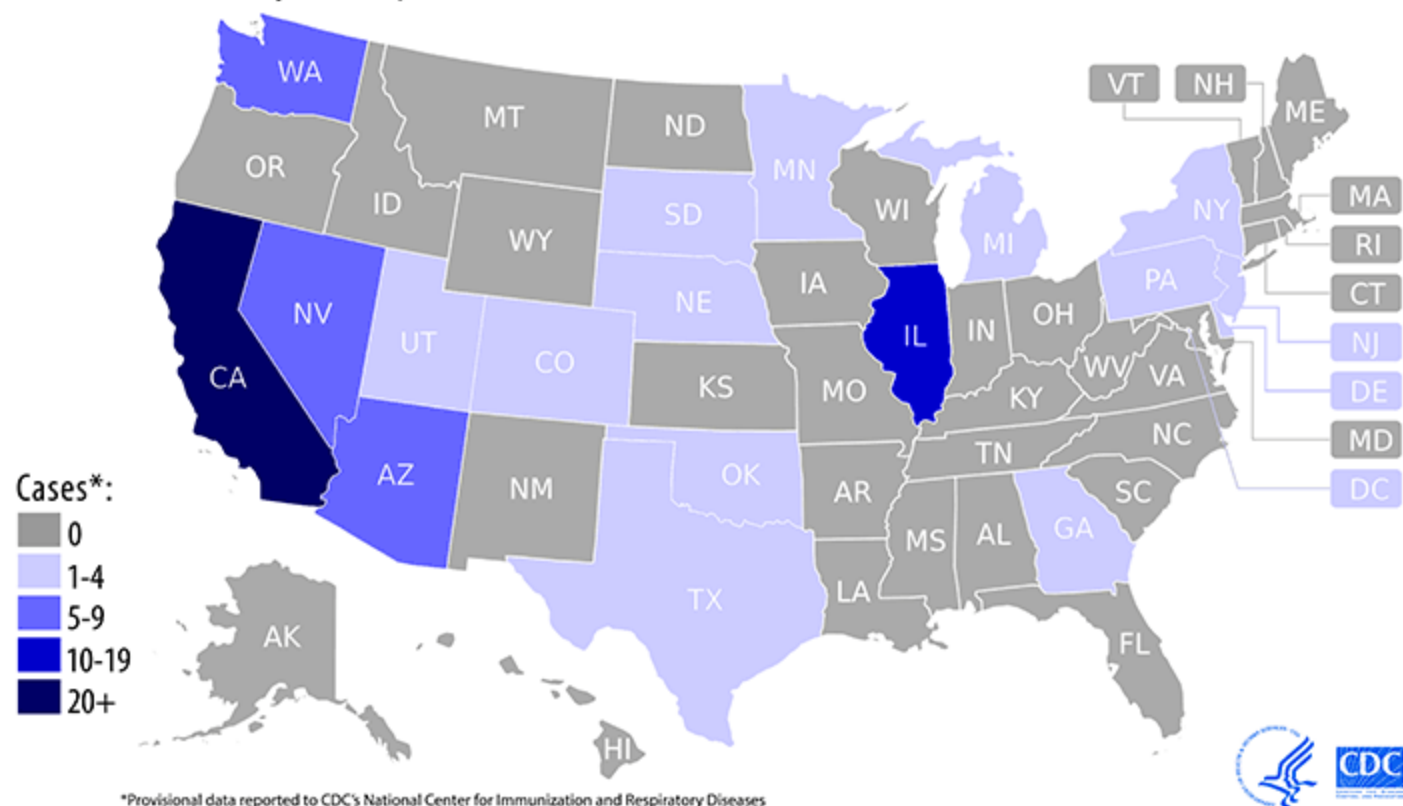


*Provisional data reported to CDC's National Center for Immunization and Respiratory Diseases



2015 Measles Cases in the U.S.

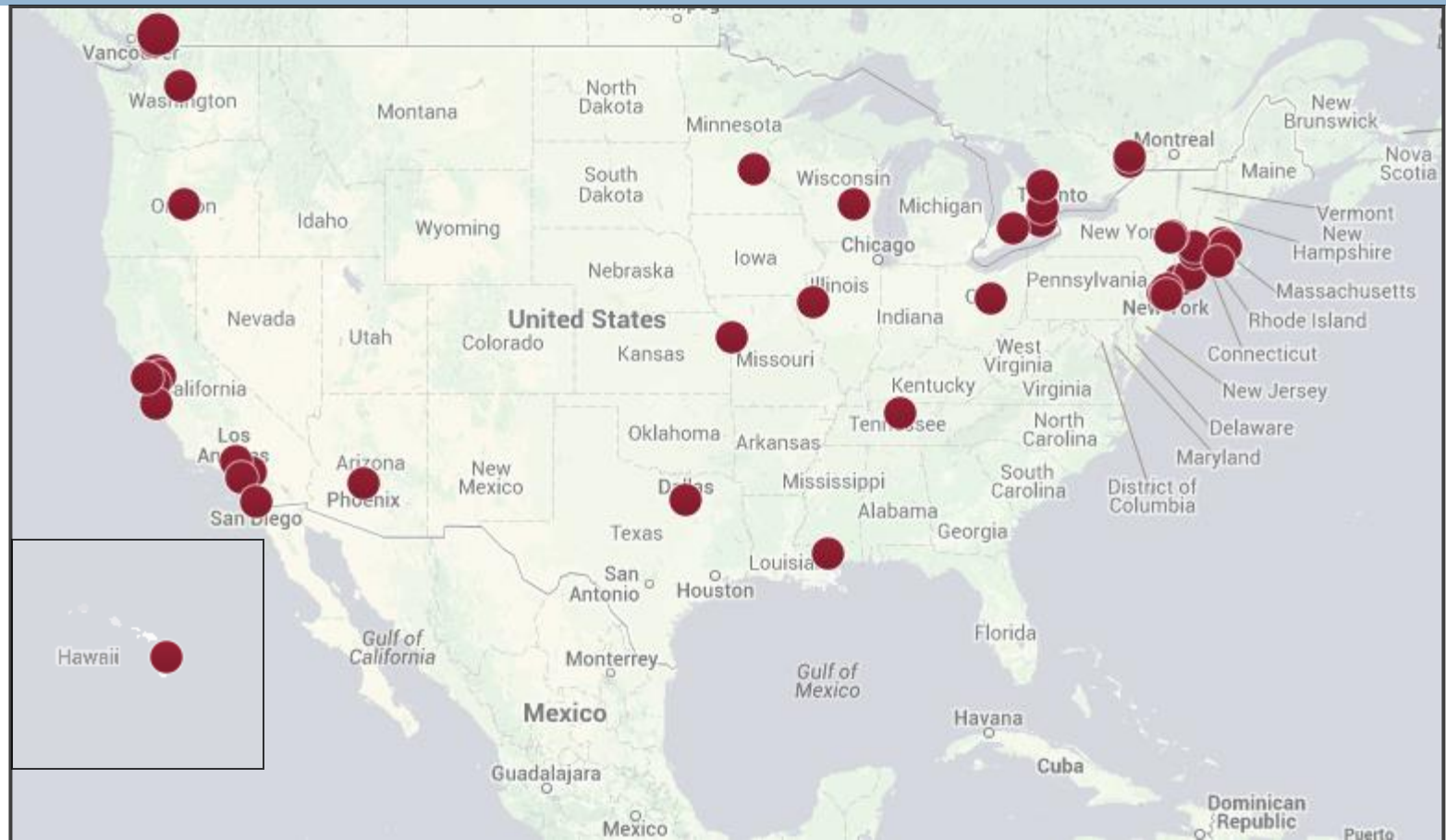
January 1 to April 3, 2015



† CDC will update these data weekly on Mondays.

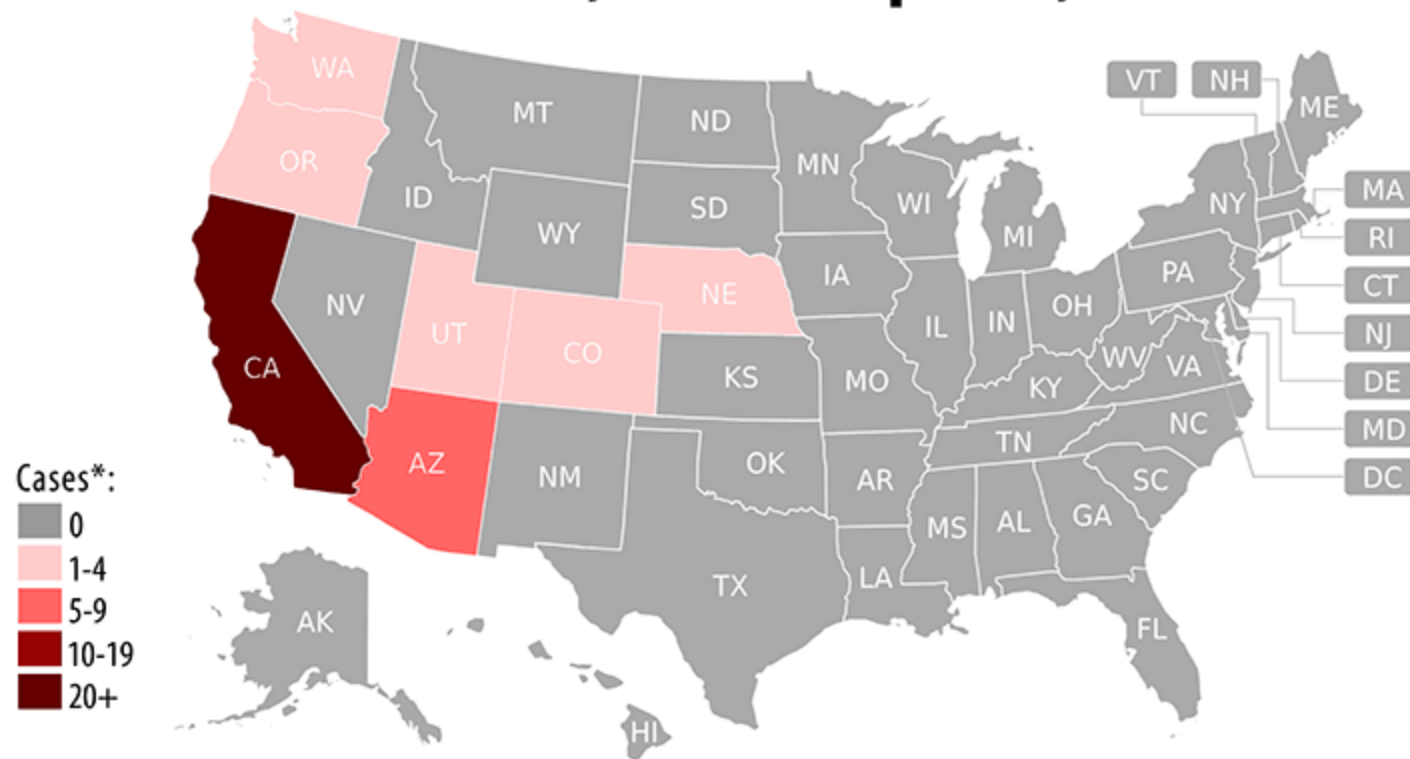
The United States experienced a record number of measles cases during 2014, with 668 cases from 27 states reported to CDC's National Center for Immunization and Respiratory Diseases (NCIRD). This is the greatest number of cases since [measles elimination](#) was documented in the U.S. in 2000.

Measles Outbreaks in the US: 2014



The United States is currently experiencing a large, multi-state outbreak of measles linked to an amusement park in California.

U.S. Multi-state Measles Outbreak December 28, 2014 - April 3, 2015



From December 28 to April 3, 2015, 147 people from 7 states [AZ (7), CA (131), CO (1), NE (2), OR (1), UT (3), WA (2)] were reported to have measles and are considered to be part of a large outbreak linked to an amusement park in California*.

*Provisional data reported to CDC's National Center for Immunization and Respiratory Diseases



Measles in Arizona

- 2013- 1 confirmed case
- 2014- 1 confirmed case
- 2015- 7 confirmed cases
 - Over 1500 potential exposures
 - Using contact tracing
 - Pinal, Maricopa, and Gila County

Contact tracing

- A fundamental activity in epidemiology
- Used for all directly transmitted infectious diseases
- Helps control outbreaks and prevent further spread



Measles Control Measures

- Ig given within 6 days
- All household members should be vaccinated
- Vaccinating individuals within 72 hours of exposure can provide protection
- Ensure that all workers and volunteers in health care facilities are immunized
 - ▣ Keep immunization documentation on hand
- Patient hospitalized for measles should be isolated

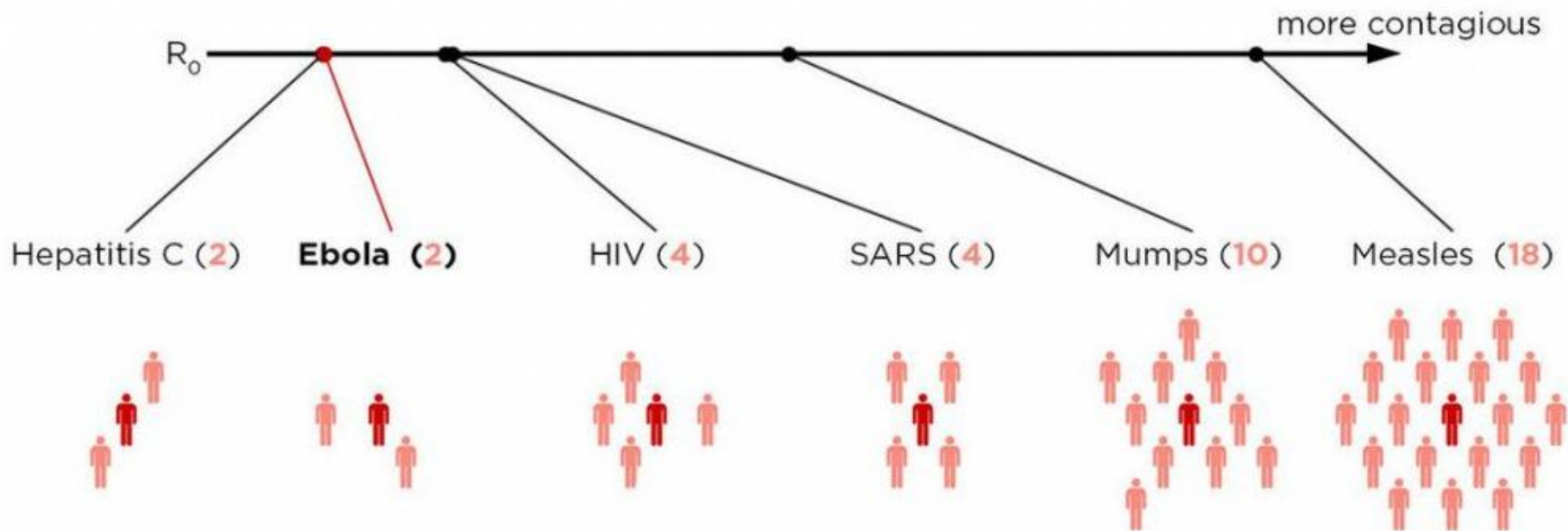


**NO
TOUCHING**



R_0 = basic reproduction number

The number of **people** that **one sick person** will infect (on average) is called R_0 . Here are the maximum R_0 values for a few viruses.



Common Threads

- All are emerging or reemerging diseases
- Viruses!
- No specific treatments
 - But one has a vaccine!
 - Vaccines are in development for the other 3

QUESTIONS?



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