

Emerging and Zoonotic Infections

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Objectives

1. Explore the growing threat of emerging/zoonotic pathogens to human health
2. Understand the recent outbreaks of emerging/zoonotic pathogens
3. Review past emerging pathogens

What is an zoonotic pathogen?

- An infection that naturally occurs in an insect or animal host that also can subsequently infect humans

(most newly identified pathogens...

...are zoonotic viruses)

Familiar zoonotic pathogens

- *Salmonella* (handling amphibians, reptiles, and birds)
- Shiga-like toxin producing *E. coli* (petting zoos and farm animal exposures)
- Rabies (bite of infected animal)
- Lyme disease – *Borrelia burgdorferi* (tick bite)
- Rocky Mountain Spotted Fever – *Rickettsia rickettsi* (tick bite)
- West Nile Virus (mosquito bite)



What is an emerging pathogen?

- A new infection, never before seen
or maybe
- An infection that is known, but newly emerging in new hosts or geographies
or maybe
- An infection that has always been there, but not tested for

Not so recent emerging pathogens

- HIV (sexual transmission, blood products)
- *Cryptosporidium* (contaminated water)
- Microsporidia (contaminated water, aerosolized spores)
- Hepatitis C Virus (blood, IV drug use)
- *Naegleria fowleri* (lake water exposure in nostrils)
- Lyme disease (tick bite)
- West Nile virus (mosquito bite)
- Ebola virus (infected human body fluids and animals)
- Severe Acute Respiratory Syndrome (SARS)
(human to human respiratory via animal exposure)
- Dengue virus (mosquito bite)

Emerging vs zoonotic

- Many emerging infections **ARE** zoonotic!
- Human activities at play?
 - Habitat disruption or restoration
 - “Exotic” foods
 - Global travel
 - Food globalization

Recent emerging infections

- Lets discuss:
 - Chikungunya virus (zoonotic)
 - Zika virus (zoonotic)
 - *Cyclospora cayetanensis*
 - Middle Eastern Respiratory Syndrome (zoonotic)

Chikungunya virus

A new epidemic for the Americas

Chikungunya virus

- +ve sense, ssRNA virus
 - Many strains, used to track outbreaks
- Family *Togaviridae*: Genus: *Alphavirus*
 - Other alphaviruses include:
 - *Eastern equine encephalitis*
 - *Western equine encephalitis*
 - *O'nyong'nyong* (closely related, serologically cross-reactive)

Signs and symptoms

- 3-7 day incubation
 - High fever ($>102^{\circ}\text{F}$)
 - Severe joint pain/stiffness
 - Rash
 - Fatigue
 - Nausea/vomiting
- **$\geq 50\%$ of cases result in long-lasting relapsing arthralgia (>6 mo.)**
- Fatality rate 1/1000



Origin

- First reported 1952, Makonde Plateau, Tanzania



- Derived from Makonde word kungunyala
“that which bends up”

Historical outbreaks

Similar disease in SE Asia as early as 1820s, not confirmed/defined as chikungunya

- 1952-53 original Makonde outbreak
- 1958-1980s Bangkok
- 1963 Cambodia, India
- 1967 Vietnam, Sri Lanka
- 1969 Philippines
- 1970 Myanmar
- 1982 Indonesia



Recent outbreaks

- **1999-2000:** Dem Rep Congo
- **2006:** R union (island east of Madagascar)
 - 266,000 cases (>33% of island population)
 - Cases imported to Europe
- **2006:** India
 - 1.25 million cases
- **2009:** Thailand
 - 24,000 cases

What is the common denominator

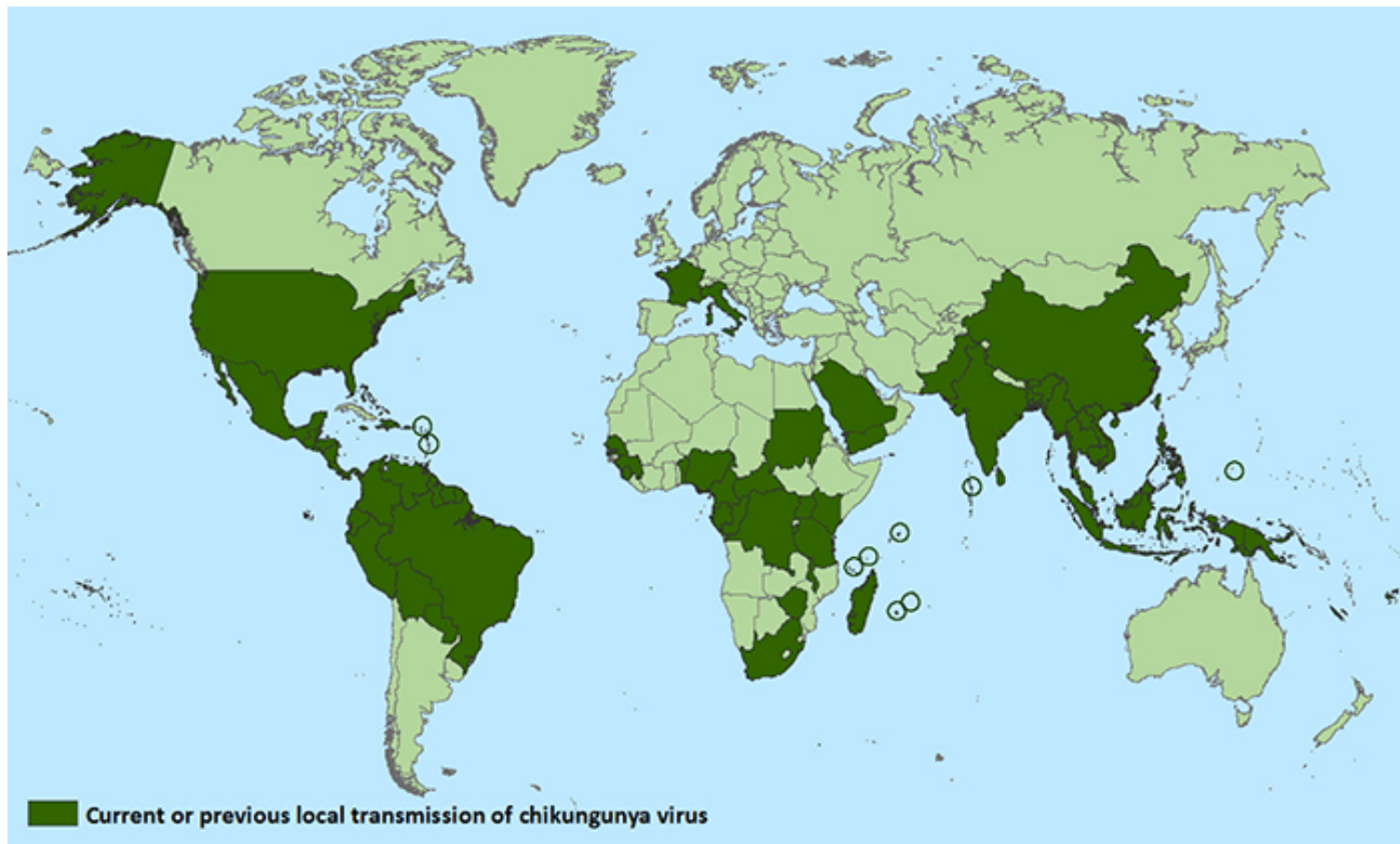


Aedes aegypti mosquito!

Vector for dengue, zika, and yellow fever viruses



Where is/was chikungunya?



2013 – Present outbreak

- **Dec 2013:** French Saint Martin
 - Initially just 2 cases reported, confirmed
- **Aug 2014:** 15 countries in & around Caribbean reporting local transmission
 - 500,000+ suspected cases
 - US 380 imported
- **Mar 2015:** 35 countries reporting local transmission
 - 1.2 million suspected cases
 - Dominican Republic (500,000), Colombia (200,000), El Salvador (144,000), Guadeloupe (81,000)
 - **US: 2500+ imported cases, local transmission (FL, PR, USVI)**

15 months

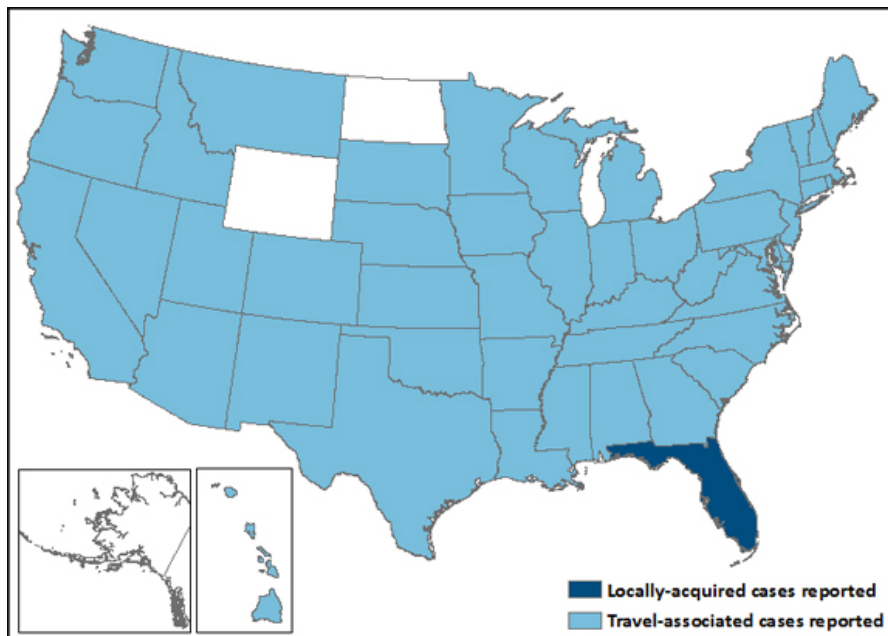
Multiple islands and countries

2 initial cases grew to...

>1.2 million!

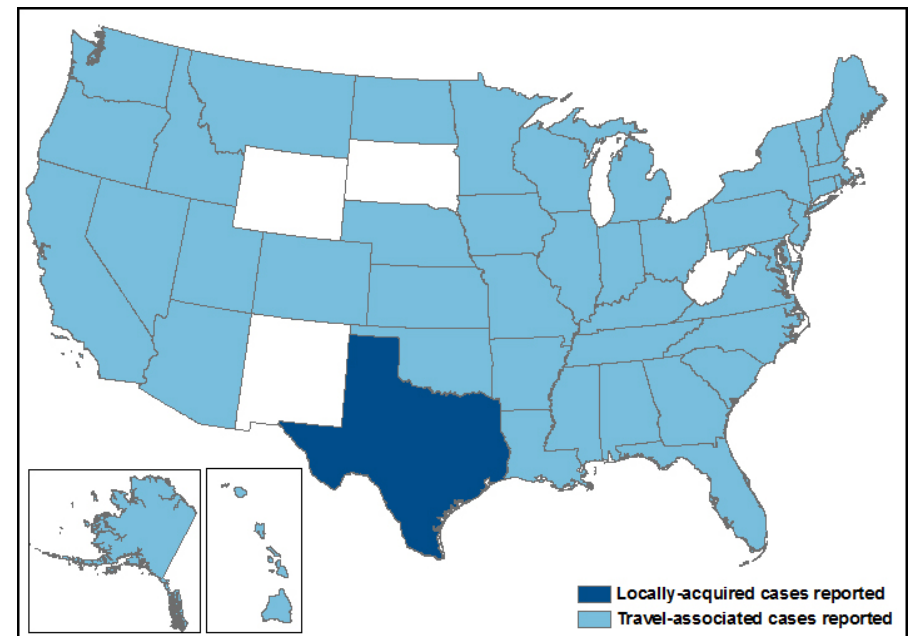
US case distribution

2014



2799 imported cases
12 Local Cases in FL

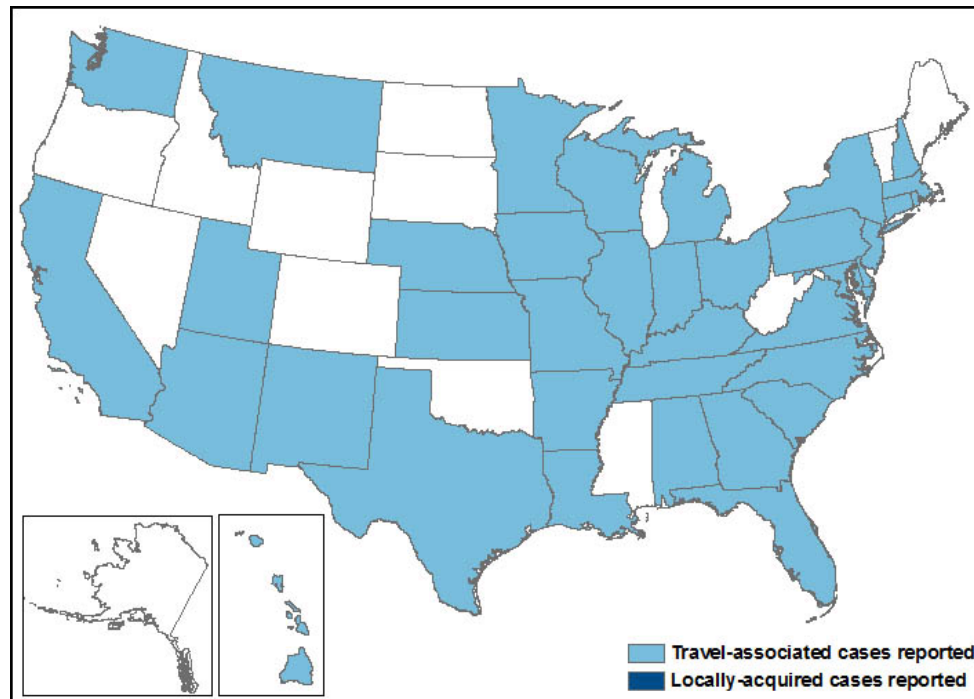
2015



895 imported cases
1 Local Case in TX

US case distribution

2016



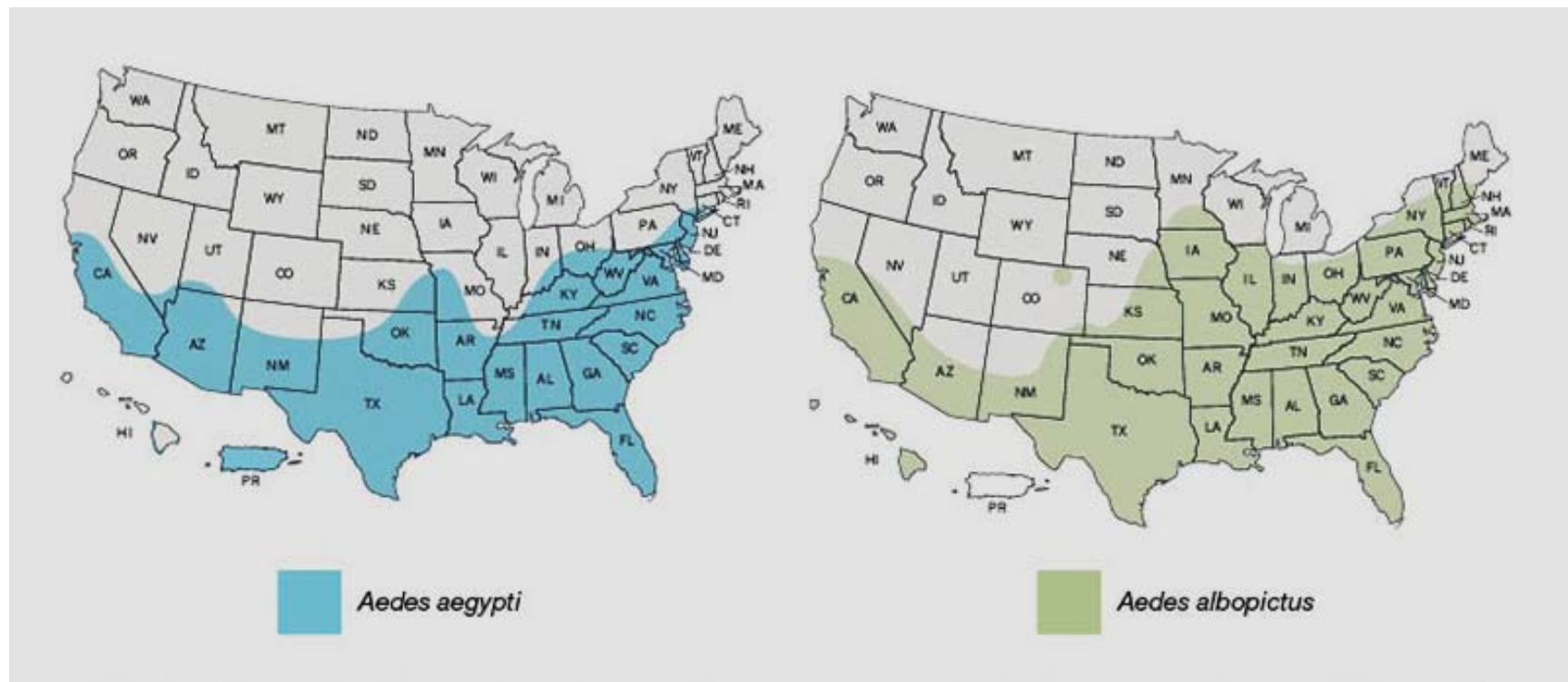
175 imported cases

Potential for spread

- Asian strain (*A. aegypti* only)
 - Current American outbreak
- East/Central/South African strain
 - *A. aegypti*
 - 2 mutations = *Aedes albopictus* (Asian tiger Mosquito)
 - *A. albopictus* = more aggressive, becoming more adapted to temperate regions
 - 32 endemic states (vs 14 for *A. aegypti*)

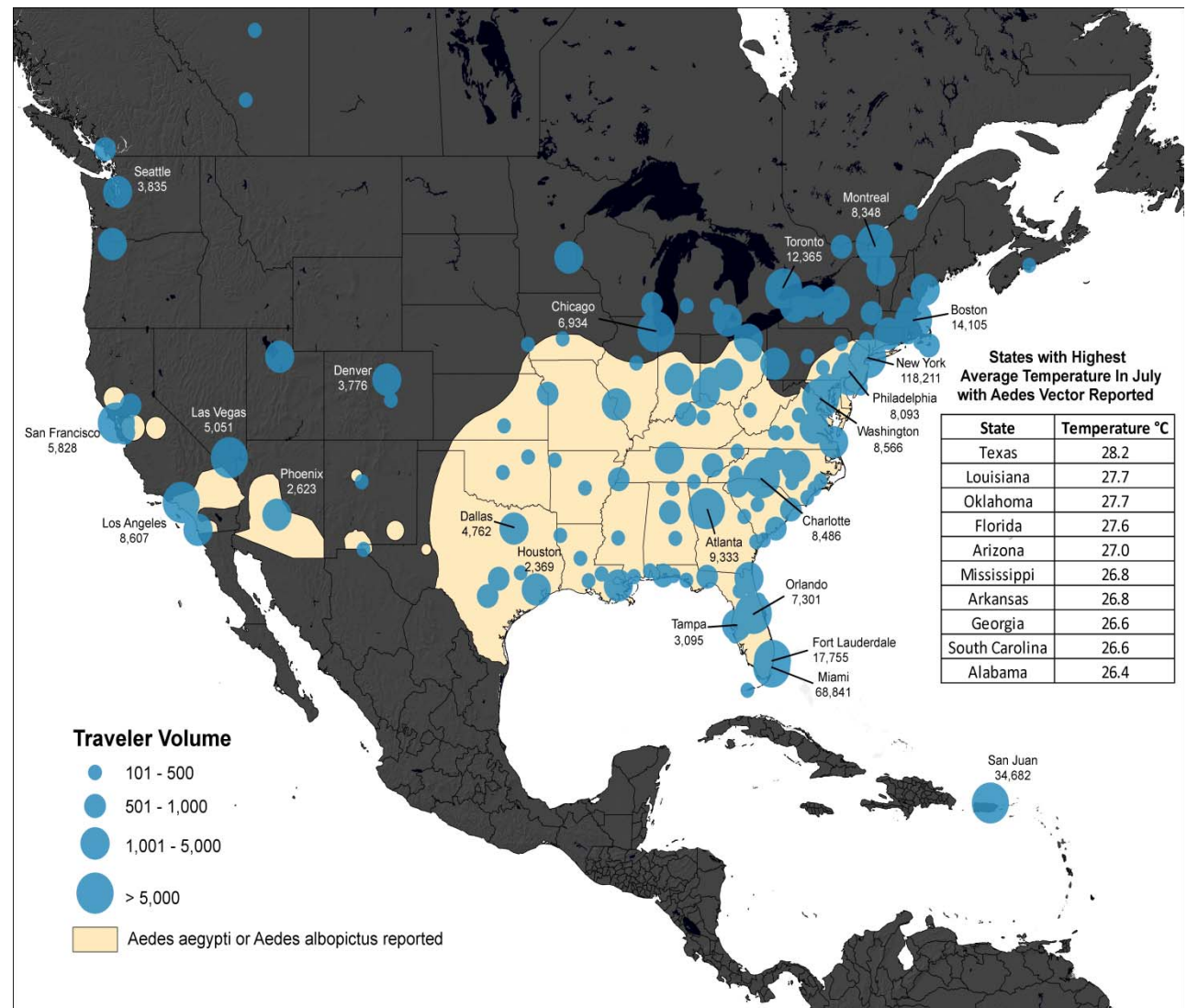


Estimates ranges of *Aedes* in the USA

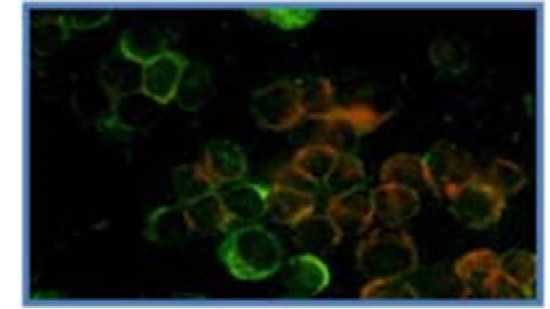


Potential for seeding

- Travel records for patients from chikungunya endemic nations to *Aedes* endemic regions



Diagnosis



- IgM antibody detection
 - Cross-reactive with other alphaviruses (*O'nyong'nyong*)
 - IgM most sensitive 3-5 weeks post-symptoms (often detectable at 10-14 days)
 - Wane at 2 months
- RT-PCR
 - Most sensitive first week of symptoms

Chikungunya in summary

- Now endemic in the Americas
 - Puerto Rico for now
 - Sparsely in Florida & Texas
- Infections were reported exponentially
 - Slowing to carrying capacity
- High quality testing is available
- Coming to America?

Zika Virus

Another epidemic for the
Americas

Zika virus

- *Flaviviridae*, +ve sense ssRNA
 - See also: dengue virus, West Nile virus, yellow fever virus, Japanese encephalitis virus, tick-borne encephalitis virus
- Discovered in 1947, Zika forest of Uganda
- First human case 1952
- Vectored by *Aedes* spp. of mosquito
 - See also: chikungunya virus, dengue virus, yellow fever virus, Japanese encephalitis virus



Disease symptoms

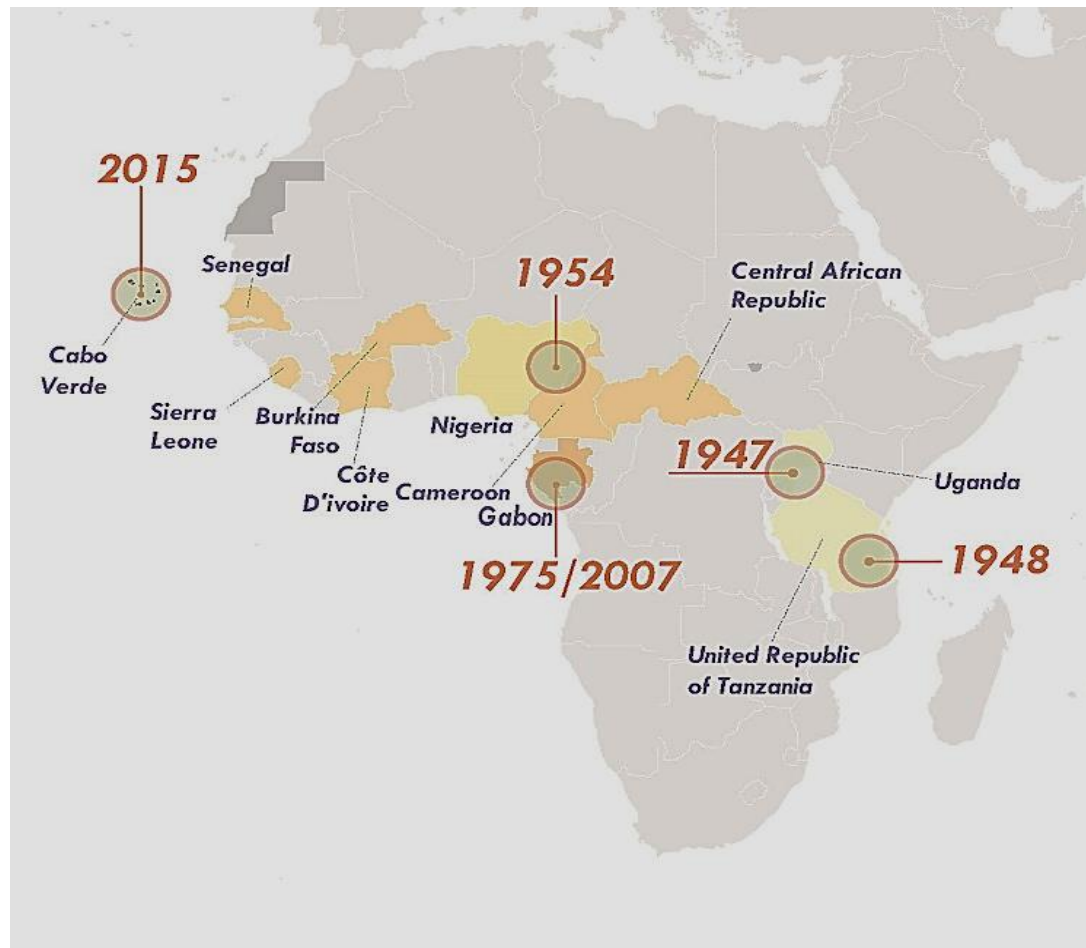
- Common symptoms include:
 - Fever
 - Rash
 - Joint pain
 - **Conjunctivitis**
- Duration: days to weeks
 - Typically mild, non emergency
 - Many asymptomatic cases suspected
 - Death is rare



Zika virus outbreaks

- Likely under-reported
 - Lack of awareness
 - Lack of testing capabilities
 - Overlapping symptoms
- Outbreaks in:
 - Africa
 - SE Asia
 - Pacific Islands
 - Americas

Zika: African outbreaks



Zika: SE Asia/Pacific outbreaks



Zika: Americas outbreak

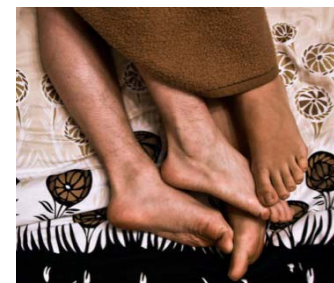


2015-2016 Americas outbreak

- May 2015 – Pan American Health Organization reports “alert” due to confirmed Zika cases in Brazil
- Summer/Fall – 2015 perceived increase in children born with microcephaly in Brazil
 - Link to Zika infection/congenital transmission suspected
 - Link to Guillain-Barré syndrome (GBS) suspected
- February 2016 – World Health organization declares Zika a Public Health Emergency of international concern

Mechanisms of transmission

- Infected mosquito bite
- **Blood transfusions**
- Sexual transmission
 - ♂ → ♀ & ♀ → ♂
- Congenital infection
 - Maternal blood → placenta → fetus



Congenital transmission

- Previously unreported
 - Microcephaly
 - Brain malformation
 - Ocular/auditory defects
 - Growth retardation
- Virus from maternal bloodstream, subsequently found in:
 - Fetal brain samples (post mortem)
 - Cord blood
 - Placental tissue



Microcephaly and Zika



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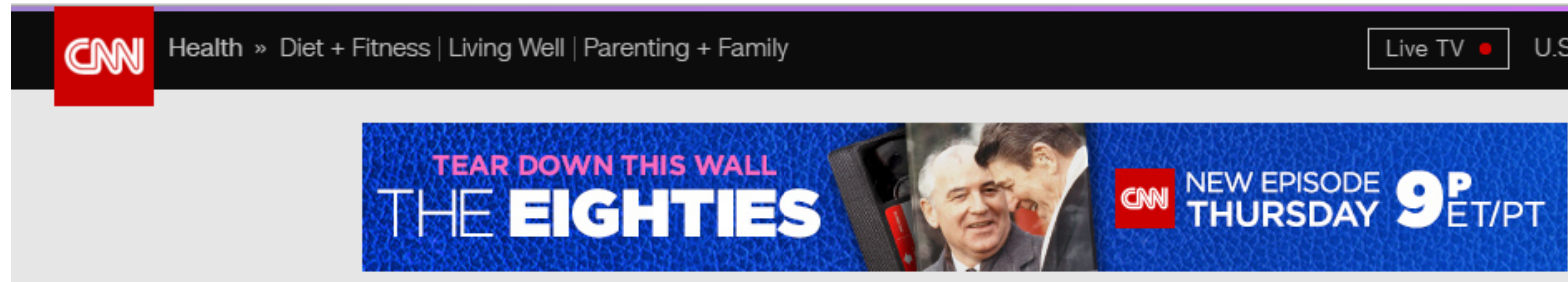
ORIGINAL ARTICLE
BRIEF REPORT

Zika Virus Associated with Microcephaly

Jernej Mlakar, M.D., Misa Korva, Ph.D., Nataša Tul, M.D., Ph.D., Mara Popović, M.D., Ph.D., Mateja Poljšak-Prijatelj, Ph.D., Jerica Mraz, M.Sc., Marko Kolenc, M.Sc., Katarina Resman Rus, M.Sc., Tina Vesnaver Vipotnik, M.D., Vesna Fabjan Vodusek, M.D., Alenka Vizjak, Ph.D., Jože Pižem, M.D., Ph.D., Miroslav Petrovec, M.D., Ph.D., and Tatjana Avšič Županc, Ph.D.

N Engl J Med 2016; 374:951-958 | March 10, 2016 | DOI: 10.1056/NEJMoa1600651

Microcephaly and Zika

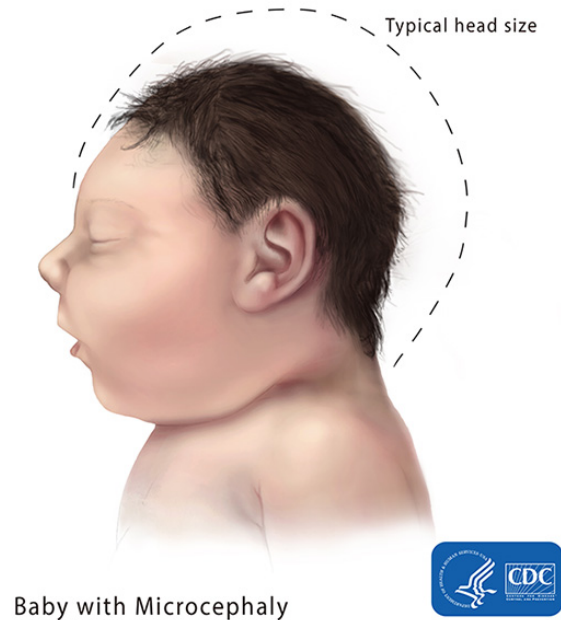


Zika virus definitely causes birth defects, CDC says

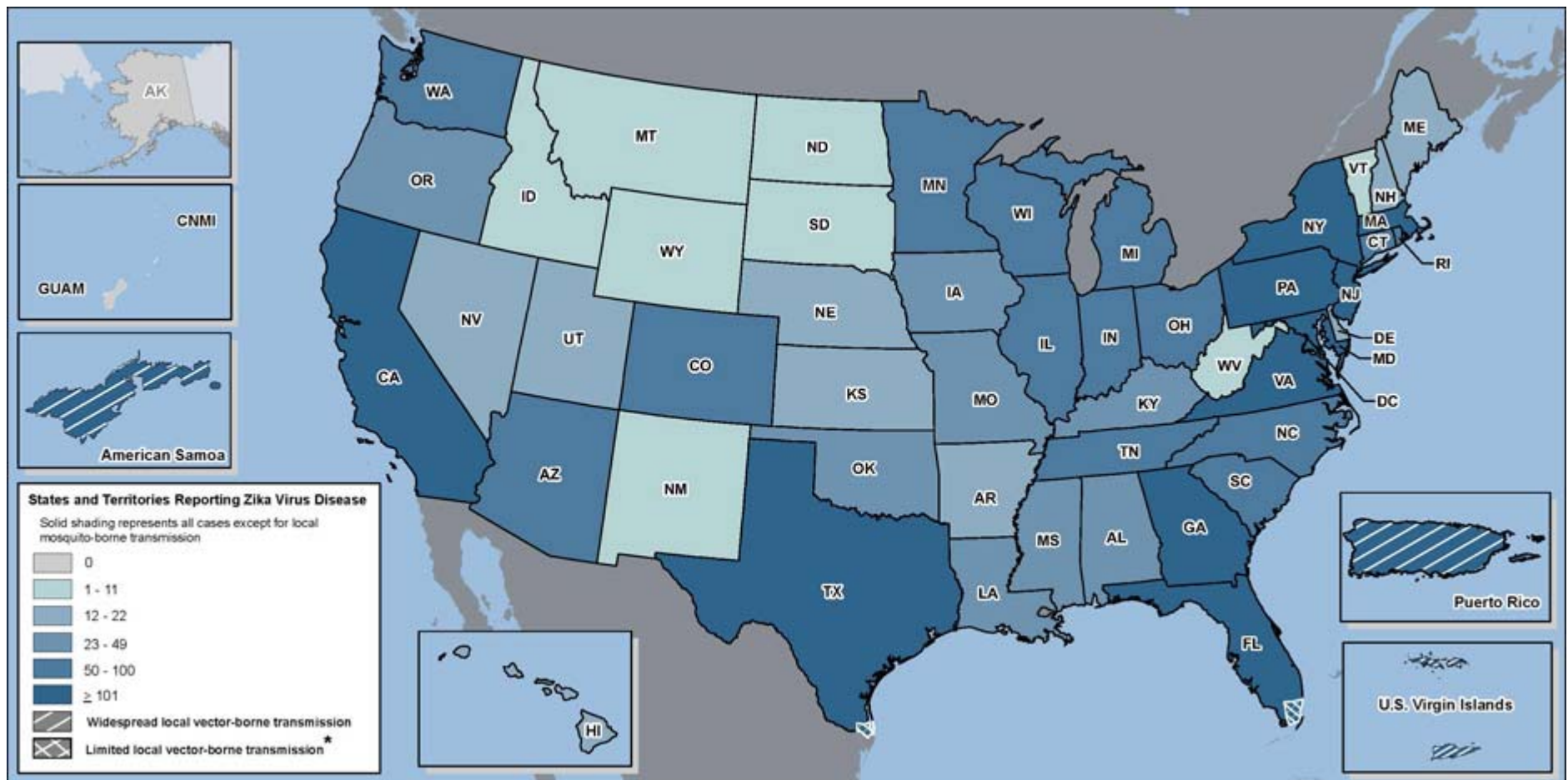
By Debra Goldschmidt, CNN

🕒 Updated 9:45 PM ET, Wed April 13, 2016

Microcephaly



US Zika cases



US Zika cases

US States

- 222 locally acquired
- 4861 travel associated
- 75 “other”
 - 45 Sexual
 - 28 congenital
 - 1 Laboratory
 - **1 person-to-person non-sexual**

US territories

- 147 travel associated
- 38212 locally acquired

CORRESPONDENCE

Fatal Zika Virus Infection with Secondary Nonsexual Transmission

N Engl J Med 2016; 375:1907-1909 | November 10, 2016 | DOI: 10.1056/NEJMc1610613

Sankar Swaminathan, M.D.
Robert Schlaberg, M.D., M.P.H.
Julia Lewis, D.O.
Kimberly E. Hanson, M.D., M.H.S.
Marc R. Couturier, Ph.D.
University of Utah School of Medicine, Salt Lake City, UT

What we don't know...

- Transmission through oral or anal sex?
- Transmission through breast milk (no evidence)
- Duration of persistence in semen?
 - At least 62 days (vs days-weeks for blood)
- Presence in vaginal secretions and risk to baby during delivery?
- Does stage of pregnancy matter?
- If infected, what is likelihood risk for baby?
- Why is this only happening now?
 - Other environmental factors?

Diagnostic testing

- IgM Antibody Capture ELISA (MAC-ELISA)
 - >5-7 days after symptom onset
- RT-PCR
 - Best for first 7 days of illness in serum but can be detected up to 14 days
 - Urine also detectable for up to 14 days, likely longer.

Guidelines are continuously updated

See the CDC website for recent guidelines for testing:

<https://www.cdc.gov/zika/laboratories/lab-guidance.html>

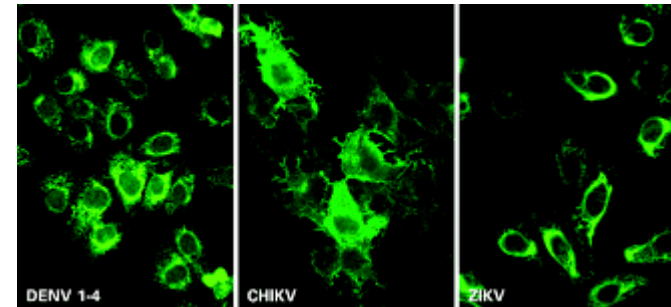
Antibody detection challenges

- IgM antibodies are cross-reactive among *Flaviviridae*
- Commercial MAC-ELISAs (CDC, Diasorin, & InBios) require PRNT confirmation testing (CDC)
- PRNT cannot always resolve reactivity
 - Dengue vs Zika vs both
- Patient pre-screening needed to optimize test performance

Antibody detection challenges

- Testing for other endemic viruses required by package insert

- Dengue
- Chikungunya
- NOT West Nile virus! (problem)



- Chikungunya does not cross-react but may cause similar syndrome
- Dengue cross-reacts heavily and can cause false positives
- WNV shows limited cross-reactivity but data is not publicly available for independent review

Zika virus in summary

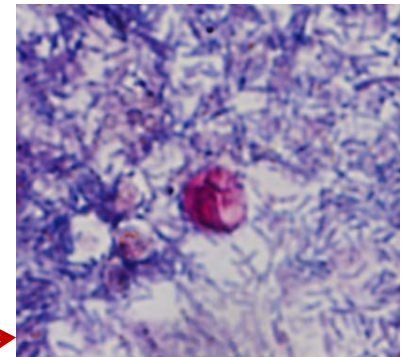
- Major global concern, particularly in the Americas
- Could become endemic in the United States
 - TX & FLA
- Associated with microcephaly
- There is a lot we still don't know
- Testing is still in flux
- November 2016: WHO declares “No Longer a Public Health Emergency of International Concern”

Cyclospora cayetanensis

An unwelcomed traveler from the
Americas

Cyclospora cayetanensis

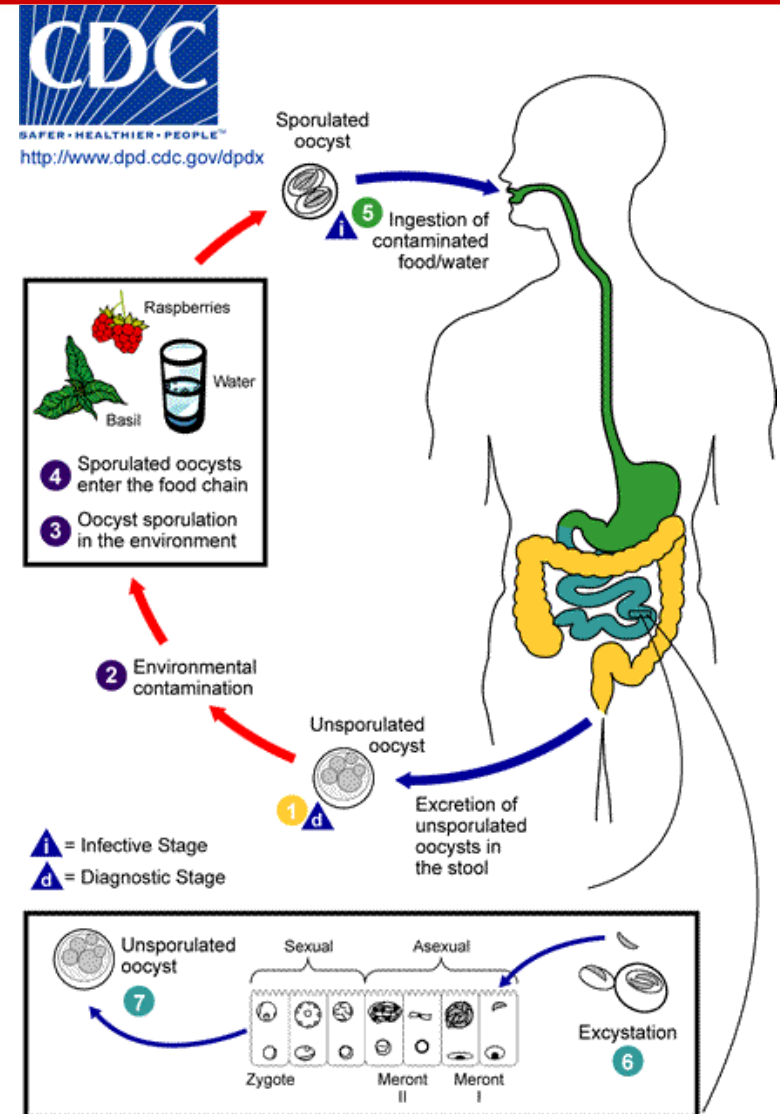
- Emerging gastrointestinal pathogen
- Infected humans are vector
- Distribution: tropical/subtropical regions
- Coccidian protozoa, diagnosed in stool
 - Stained with modified acid fast or safranin
 - Autofluorescence by UV light
 - More sensitive
 - Rarely used



8-10 μ m



C. cayetanensis life cycle



Cyclospora clinical symptoms

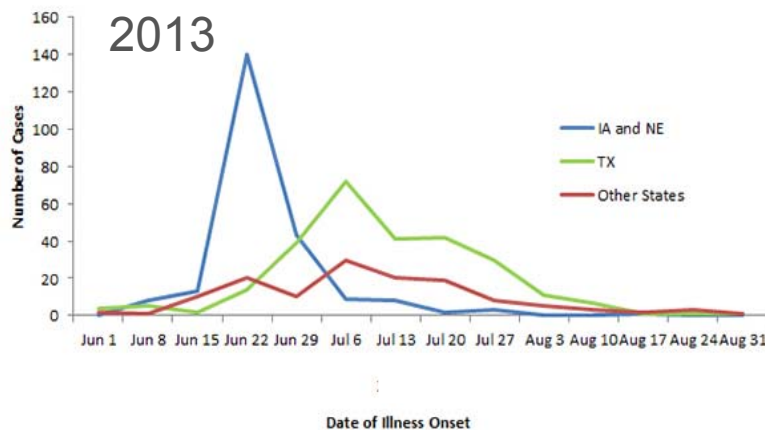
- Watery diarrhea
(can last months if untreated)
 - Cramping
 - Nausea
 - Weight loss
 - Loss of appetite
 - Gas/bloating
 - Fatigue
 - **OR** asymptomatic
- Vomiting & low fever (rarely)
- **Oocysts not infective when shed** (no direct human-to-human)

Why do we care about this bug?

- Sporadic cases in USA each year
- Travel or imported food related
- 4 major recent outbreaks
 - Iowa & Nebraska - July/August 2013
 - Bagged salad mix from Mexico
 - Texas - August 2013
 - Cilantro from Mexico
 - Texas - August 2014
 - Cilantro from Mexico
 - Multistate - May - August 2015
 - Cilantro from Mexico



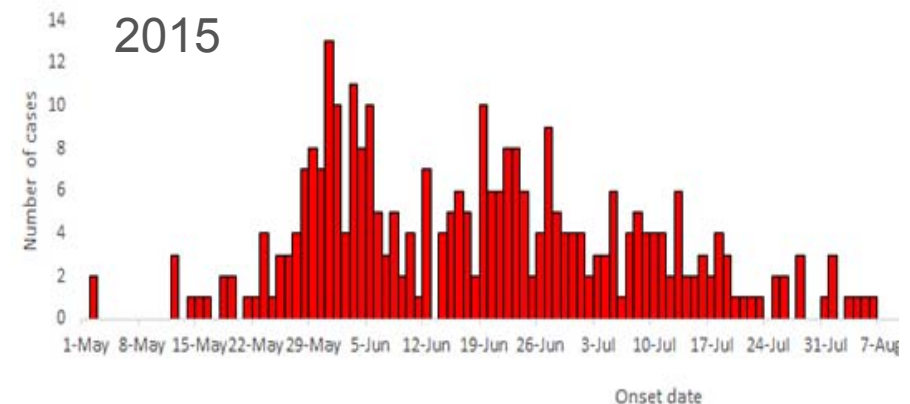
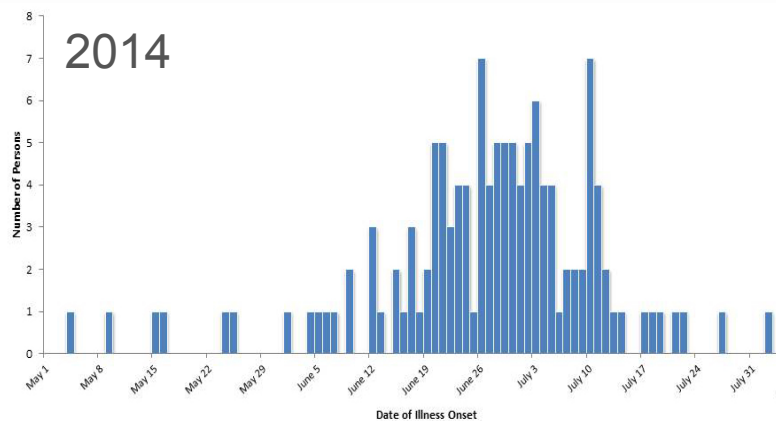
Cyclospora recent outbreaks



2013 – 631 cases (49 hospitalized)
25 states
(two outbreaks)

2014 – 304 cases (7 hospitalized)
19 states

2015 – 546 cases (21 hospitalized)
31 states



Advancements in *Cyclospora* diagnostics

- Molecular multiplex panel testing
 - Commercial assay: BioFire FilmArray
 - ARUP LDT
- Oct 2014 – March 2016
 - 771 tests, 59 positives (7.7%)
 - 16 (27%) *Cyclospora cayetanensis* detected
 - More than detected in 10 years using microscopy!
 - 10/16 from Utah

Cyclospora cayetanensis take home points

- Treatment is very specific
 - Trimethoprim sulfamethoxazole (conventionally an antibacterial)
- Treatment is critical in immunocompromised patients
- Healthy patients may require treatment
- Physicians:
 - May not recognize the pathogen
 - May not think about the pathogen
 - May not order the correct tests
- Globalization of food will allow ongoing US outbreaks

Middle East Respiratory Syndrome (MERS) Corona Virus

A zoonotic NOT from the
Americas

MERS CoV

- *Coronaviridae*, +ve sense ssRNA virus
- First widely reported in Saudi Arabia, September 2012
- All cases located on or transmitted from the Arabian peninsula
 - Larger 2015 outbreak in S. Korea linked to traveler returning from Arabian peninsula
 - Cases found in Europe through returned travelers w/contact cases
- 30-40% case based fatality rate

MERS Corona map

Updated 3 months ago

1625	585	36%
Infected	Died	Case fatality rate

[Countries](#)
[Top cities](#)
[Latest cities](#)

All data are by WHO and Health Ministries
Colored circles indicate current active cases

82 Riyadh Saudi Arabia
Total 526 | 262 recovered | 182 died

63 **Jeddah** Saudi Arabia
Total 216 | 90 recovered | 63 died
1st case was diagnosed on 17th of April, 2013

50 Abu Dhabi United Arab Emirates
Total 71 | 14 recovered | 7 died

21 Unknown city Saudi Arabia
Total 113 | 92 died
The Saudi Ministry of Health announced +113 cases (+92 deaths) which were previously unreported without any more details.




MERS CoV symptoms & spread

- Respiratory pathogen
- Severe acute respiratory illness
 - Fever
 - Cough
 - Shortness of breath
- Likely spread through respiratory secretions
 - Caregivers and household contacts can become infected
- Patient age range 1-99 years of age

Where does MERS CoV come from?

- Possible bat origin?
- Likely maintained by dromedaries



EMERGING INFECTIOUS DISEASES®

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Volume 20, Number 7—July 2014

Dispatch

MERS Coronavirus in Dromedary Camel Herd, Saudi Arabia

Maged G. Hemida¹, Daniel K.W. Chu¹, Leo L.M. Poon, Ranawaka A.P.M. Perera, Mohammad A. Alhammadi, Hoi-ye Ng, Lewis Y. Siu, Yi Guan, Abdelmohsen Alnaeem✉, and Malik Peiris✉

Author affiliations: King Faisal University, Al Hofuf, Saudi Arabia (M.G. Hemida, M.A. Alhammadi, A. Alnaeem); Kafrelsheikh University, Kafr Elsheikh, Egypt (M.G. Hemida); The University of Hong Kong, Hong Kong, China (D.K.W. Chu, L.L.M. Poon, R.A.P.M. Perera, H.-y. Ng, L.Y. Siu, Y. Guan, M. Peiris)

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MERS Coronavirus in Dromedary Camel Herd, Saudi Arabia

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Avoiding MERS CoV

- Avoid contact with ill travelers from the Arabian Peninsula
- Avoid camel contact:
 - Avoid urine
 - Avoid camel milk
 - Do not eat undercooked camel
- Exercise excess hygiene practices such as handwashing when visiting markets, farms, or areas where camels may be present

MERS CoV testing & laboratories

- CDC and select public health labs: RT-PCR only
- Specimens originating from suspect MERS CoV patients must be handled with extreme caution
- Respiratory viral cultures can grow MERS CoV
 - High concentrations of virus are potentially dangerous
 - Perform PCR testing for other viruses only

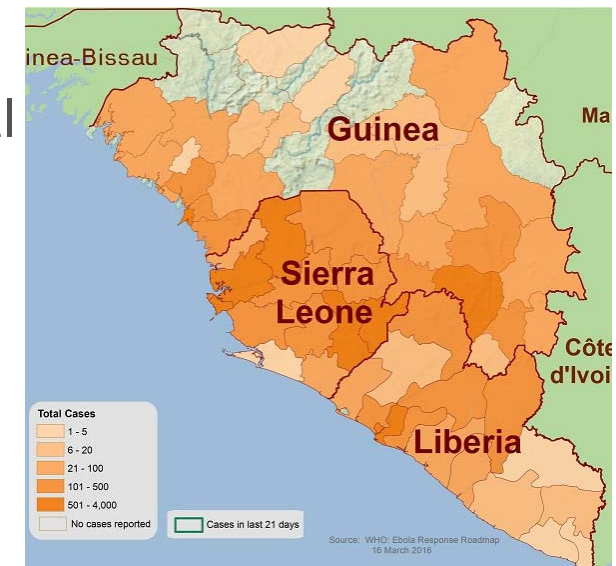
These guidelines are changing in real-time

MERS CoV Summary

- Highly pathogenic respiratory virus
 - High case fatality rate
- May originate in bats, camels provide source for human exposure
- Travel to, or contact with travelers from ,the Arabian Peninsula is major risk factor
- Burned out?
 - SARS in 2000 followed this same path

A final, well publicized example

- Ebola virus
 - Filovirus, highly publicized, recently discovered (1976)
 - Sporadic small outbreaks typically
 - Associated w/ infected fruit bats or primates (blood or “bushmeat”)
 - Before person-to-person occurs
 - **Patient body fluids also highly infectious**
 - 2014-2015 West African outbreak was atypical
 - Zaire strain: most deadly
 - Total cases suspected: 28,652
 - Lab confirmed: 15,325
 - Deaths: 11,325



General Considerations

Many emerging infections are not directly transmissible between humans, others are:

- Chikungunya and *Cyclospora* are not a risk
- Zika may require precautions for body fluids (blood, saliva, tears)
- MERS can be transmitted by respiratory secretions
 - Requires caution
- Ebola is transmittable by body fluids, including saliva and blood

Summary

- Most emerging pathogens are zoonoses
 - Most are viral
- Globalization can explain many of these recent examples in America
 - Movement of insects
 - Movement of people
 - Movement of food
- Some emerging pathogens are too virulent and “kill” themselves off
 - SARS, MERS, Ebola