




**Wisconsin State
Laboratory of Hygiene**
 UNIVERSITY OF WISCONSIN-MADISON




Chikungunya, MERS CoV, EV-D68---
They Keep on Comin'

Dave Warshauer, Ph.D., D(ABMM)
Deputy Director, CDD
Wisconsin State Laboratory of Hygiene

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Chikungunya Virus Disease




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Chikungunya

- Mosquito-born viral disease
- Acute onset febrile disease with severe polyarthralgias
- Often causes large outbreaks with high attack rates
- In Dec 2013, first locally-acquired cases reported in the Americas on St. Martin
 - Puerto Rico in May. Now >10,000 cases

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Countries with Reported Human Chikungunya Virus Infections As of November 2013



■ Reported human chikungunya virus infections
 □ No reported human infections
 Modified from: Powers AM, Logue CH. Changing patterns of chikungunya virus: re-emergence of a zoonotic arbovirus. J Gen Virol. Sep 2007;88(9):2163-2177.

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Chikungunya virus in the Americas May 2014



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Reported Cases in the Americas 2013- Dec 5, 2014

Country/Territory	Locally Acquired Suspected Cases	Imported Cases
USA	11	1,900
Mexico	74	13
Central America	137,186	
Caribbean	772,878	
Andes	65,614	
Total	975,678	

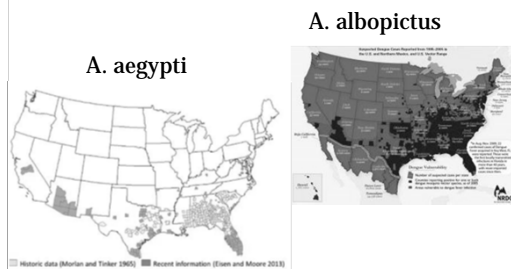
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Chikungunya in the USA

- Since 2006 averaged 28 imported cases/yr
 - No local outbreaks triggered
- Increase occurring in US travelers to the Caribbean
 - 243 traveler-associated cases in first half 2014
- First Chikungunya case acquired in the US reported in FL in June 2014
 - 7 months after first recognized in the Western Hemisphere
 - At least 11 more cases since then

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Aedes spp. Distribution



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Transmission

- Urban cycle
 - Human---Mosquito---Human---Mosquito
 - Aedes aegypti and Aedes albopictus
- Sylvatic cycle
 - Animal---Mosquito---Animal---Mosquito
 - Chimps, monkeys, baboons
 - Aedes fuscifer, Aedes africanus



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Other Rare Modes of Transmission

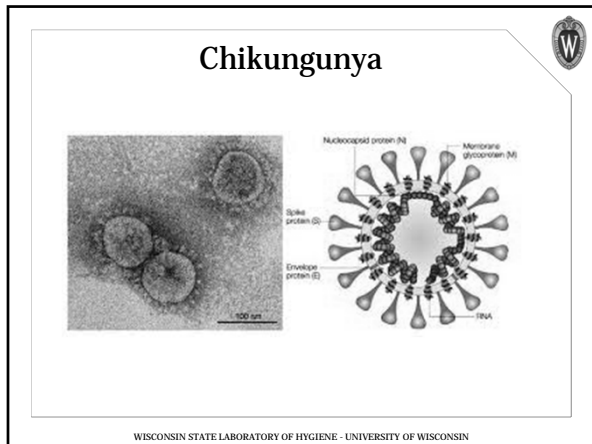
- In utero resulting in abortion
- Intrapartum from viremic mother-to-child
- Needlestick
- Lab exposures
- Possibility of transfusion or transplant transmission

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The Virus

- Family Togaviridae, genus Alphavirus
 - Enveloped, single-stranded RNA virus
 - Plus-sense, unsegmented genome of 11.5-11-8 kb
- First isolated from human serum during an outbreak in Tanganyika in 1953
- Asian and African strains
 - Distinct biological and transmission patterns

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Infection and Disease

- 72-97% of those infected develop clinical symptoms
- Incubation period usually 3-7 days (1-12)
- Primary symptoms of fever and polyarthralgia

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Clinical Manifestations

- Fever with abrupt onset
 - $\geq 102.2F$
- Joint pain
 - Severe
 - Most common in hands and feet
 - Multiple joints
 - Usually bilateral and symmetric
- Other manifestations
 - Headache, nausea/vomiting, rash, conjunctivitis, myalgia, arthritis

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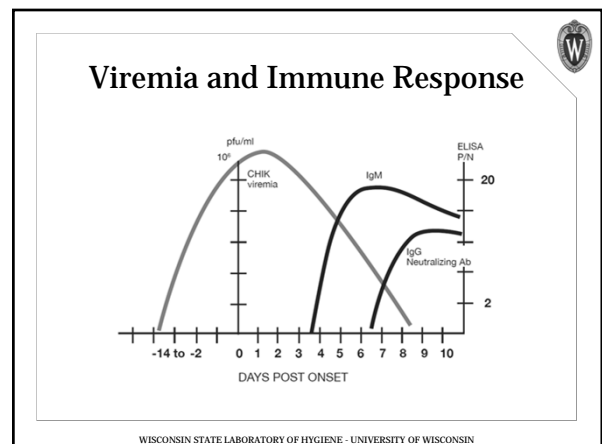
Maculopapular Rash

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Laboratory Diagnosis

- Virus culture
- RT-PCR
- IgM serology and confirmatory neutralizing antibody testing
- Serology for >4-fold antibody titer rise using PRNT or IFA

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Optimal Timing for Diagnosis

ASSAY	DAYS POST-ONSET
Viral Culture	<=3 days
RT-PCR	<=8 days
IgM Serology	>=4 days

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Test Availability

- CDC Arboviral Diseases Branch
- State Public Health Laboratories
 - California
 - New York
 - Florida
 - Others
- Commercial Laboratories
 - Focus Diagnostics
 - RT-PCR
 - IgG and IgM IFA

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Treatment

- No specific antiviral therapy
- Supportive care
 - Rest and fluids
- Non-steroidal anti-inflammatory drugs for fever and pain



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Surveillance and Reporting

- Consider chikungunya in travelers from areas where chikungunya is present who present with acute onset of fever and joint pain
- Be aware of possible local transmission where there are Aedes mosquitos
- Report suspect cases to local and state health departments


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State Vectorborne Disease Epidemiologist

Diep Hoang-Johnson
 Wisconsin Division of Public Health
 Bureau of Communicable Diseases
 608-267-0249

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MERS-Coronavirus



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MERS-CoV

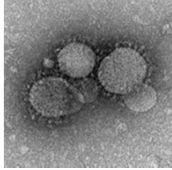
What we know!

- Initially referred to as "novel" coronavirus
- Virus is *different* from SARS-Coronavirus and seasonal coronaviruses OC43, HKU1, 229E & NL63
- First cases documented in spring 2012 (nurse & university student)-Jordan
- All cases linked to the Middle East
- Age range 1 to 94
- Severe morbidity and mortality
- Transmission mainly human-to-human
- Genetically stable

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Coronaviruses

- First identified in mid-1960s
- Single-stranded RNA
- Six infect humans
 - 229E, NL63, OC43, HKU1, SARS, MERS
- MERS
 - Clades A and B
 - Earliest cases Clade A
 - New cases Clade B
- Bat reservoir?




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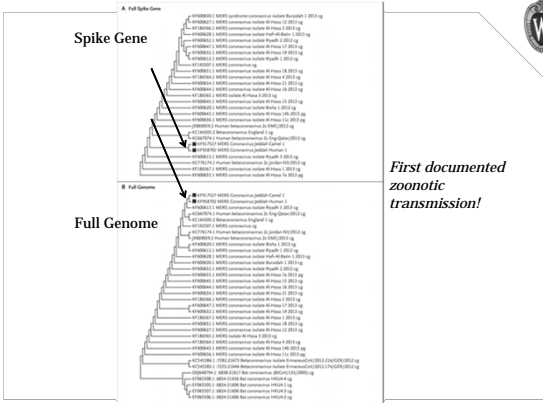
Transmission

Human ⇌ Human
Zoonotic

- Recent evidence of camel to human transmission (Azhar et al, 2014)
 - Index patient and 3 friends had contact with camels
 - Index patient, friends and camels tested for MERS-CoV by PCR



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Epidemiology

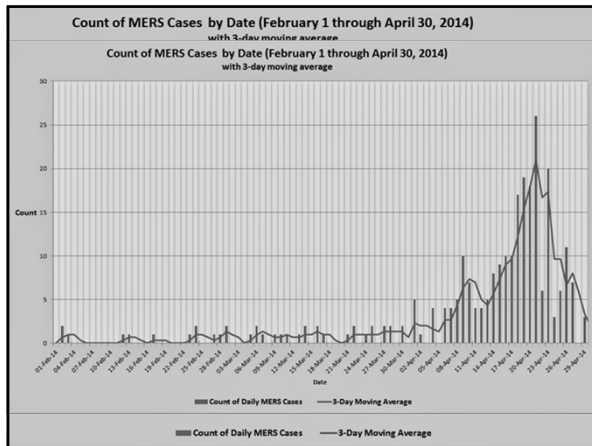
Human infections (MMWR, May 2014)

- Median age 49 years
- 65% male
- 19% healthcare workers
- 62% severe disease (hospitalization)
- 5% mild illness
- 21% asymptomatic** (case investigations)
- June 4, 2014: 815 cases and 313 deaths (38% mortality)
- Role of co-morbidities

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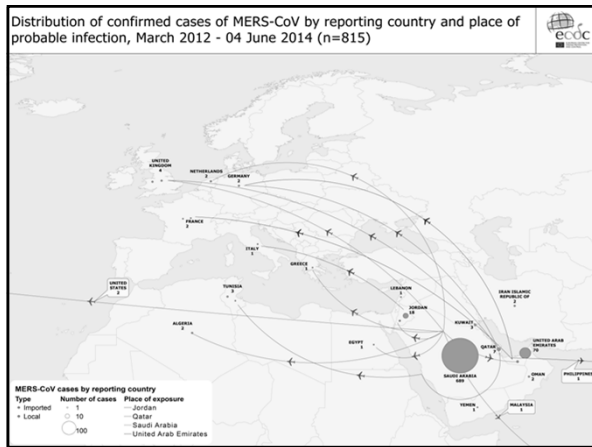
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Geographic Distribution

Confirmed cases, deaths and date of onset for the most recent case, by region as of 4 June 2014

Region/Country	Cases	Deaths	Date of onset for most recent case
Middle East			
Saudi Arabia	283	9	28/05/2014
United Arab Emirates	70	9	04/05/2014
Qatar	7	4	04/11/2013
Jordan	18	5	23/05/2014
Oman	2	2	20/12/2013
Kuwait	3	1	02/11/2013
Egypt	1	0	22/04/2014
Yemen	1	1	17/03/2014
Libanon	1	0	22/04/2012
Iran	2	1	27/05/2014
Europe			
UK	4	3	06/02/2013
Germany	2	1	08/05/2013
France	2	1	08/05/2013
Italy	1	0	31/05/2013
Greece	1	0	08/04/2014
Netherlands	2	0	05/05/2014
Africa			
Tunisia	1	1	01/05/2013
Algeria	2	0	24/05/2014
Asia			
Malaysia	1	1	08/04/2014
Philippines	1	0	11/04/2014
Americas			
USA	2	0	01/05/2014
Total	653	33	



MERS-CoV in the US

- Two cases identified in the US
- Travel related (SA → UK → US)
- **Case 1: Indiana (Reported 5/1/2014)**
 - HCW w/onset 4/24/14
 - Flew to Chicago 4/24/14
 - Travelled to Indianapolis via bus 4/24/14
 - Hospitalized 4/28/14
 - Recovered and discharged 5/9/14
 - Symptom monitoring for 14 days
 - A small number of exposed WI residents were tested for antibody

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MERS-CoV in the US

- **Case 2: Florida (Reported 5/11/2014)**
- Travel related (SA → UK → Boston → Atlanta → Orlando)

 - HCW NOT linked to Indiana case
 - Began travel 5/1/14
 - Hospitalized 5/8/14
 - MERS-CoV testing 5/10/14
 - Patient recovered & discharged 5/19/14
 - A small number of exposed WI residents were tested for antibody

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What testing is available?

- FDA issued an EUA in 2013 authorizing qualified PHL to perform **MERS-CoV PCR**
- WSLH Test Code: **VR01738**
- CPT Code: **87798**
- Fee exempt
- Serology available only at CDC

If you have a suspect case of MERS-CoV, please contact your local public health agency, or Tom Haupt (608-266-5326) at the WDPH.

All requests for MERS-CoV testing must be approved by public health before the WSLH will perform any testing.

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MERS Enhanced Surveillance

- Criteria for testing
 - History of travel from the Arabian Peninsula or a neighboring country
 - OR close contact with a person with the above risk factor
 - Exposure timeline
 - Within 14 days prior to illness onset
 - Signs and symptoms (must have all 3)
 - Fever ≥ 100.4
 - Cough
 - Suspicion of pulmonary parenchymal disease
 - Pneumonia, ARDS, consolidation

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Specimens for Testing

- PCR
 - Lower respiratory tract specimen preferred
 - Sputum
 - Bronchoalveolar lavage
 - Bronchial wash
 - Tracheal aspirate
 - Nasopharyngeal swab
 - Stool

Additional specimen collection information is available from CDC at <http://www.cdc.gov/coronavirus/mers/guidelines-clinical-specimens.html>

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Knowledge Gap

What we don't know, but wish we did!

- Limited person-to-person so why the spike in cases recently?
- Camels intermediate host or natural reservoirs?
- Natural reservoir that maintains the virus?
- Community prevalence?
- Route of transmission? Food, water, vector??
- Treatment options?
- Testing & surveillance capacity in other countries?

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EV-D68

- More than 70 types of HEVs
- Less common than other Evs
- First identified 1962 in CA
- August 2014 increase in severe resp illness
 - Kansas City, MO
 - Chicago, IL
 - >65% asthmatic or history of wheezing
- As of 9/15---104 confirmed cases in 10 states
 - No deaths documented

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Symptoms

- Low grade fever—many afebrile
- Cough
- Runny nose
- Sneezing
- Body/muscle aches
- No specific treatment
 - Supportive therapy



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Association with Neurologic Disease

- Colorado
 - 9 children ages 1-18 with suddene onset of neurologic illness from Aug 9 - Sept 15-2014
 - Muscle weakness in one or more arms or legs
 - Double vision, difficulty swallowing,difficulty speaking (dysarthria)
 - All had fever, most with respiratory illness about one week prior to onset of muscle weakness
 - No altered mental status or seizures

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Association with Neurologic Disease

- MRI scans ---abnormalities in the gray matter in the spinal cord
- CSF negative for viruses, including WNV and enteroviruses
- 8 tested with RVP
 - 6 Rh/Ent; 4 of those were EV-D68
- Evs known to cause aseptic meningitis, less commonly encephalitis, and rarely, acute myelitis and paralysis

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Association with Neurologic Disease

- Sept 26---CDC issued request for states to report similar neurologic illnesses
- As of Oct 23
 - 51 cases reported in 23 states
 - Investigating another half-dozen
- Other possible causes
 - Guillain-Barre, other Enteroviruses, Adenovirus, WNV and similar viruses, HSV

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Enhanced EV-D68 Surveillance

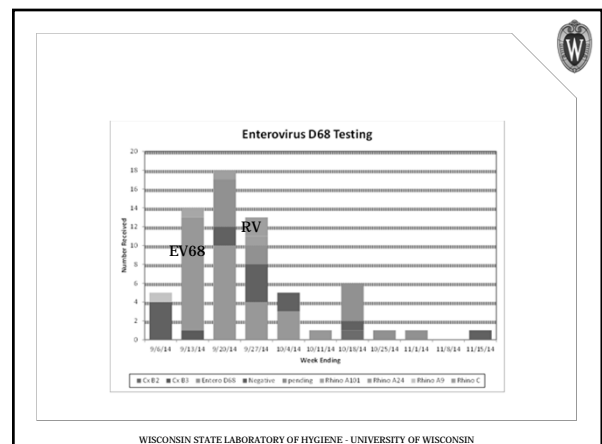
- Population for surveillance
 - Inpatient pediatric** clusters with severe respiratory illness (w/wo fever)
 - Individual ICU-admitted **pediatric** cases of severe respiratory illness
- Specimens
 - Combined NP/OP swabs placed in viral transport medium

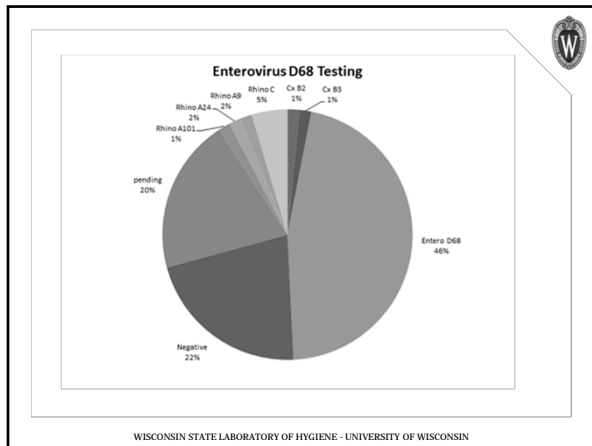
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Diagnostic/Surveillance Testing

- Clinical laboratory testing**
 - Perform normal diagnostic testing for RV/ENT
 - If patient meets surveillance criteria:
 - Set aside a 1 ml aliquot and store at 2-8C
 - If specimen positive for RV/ENT
 - Send aliquot to WSLH
- WSLH**
 - Test for RV/ENT with single-plex PCR assay
 - Submit specimens to CDC for typing

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