Updated CDC Zika Laboratory Testing Guidance

Clinician Outreach and Communication Activity (COCA) Call

December 1, 2016

Office of Public Health Preparedness and Response
Division of Emergency Operations

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Planners have reviewed content to ensure there is no bias.

This presentation will include discussion of the unlabeled use of a product or products under investigational use.

Objectives

At the conclusion of this session, the participant will be able to:

- **Describe all available Food and Drug Administration Emergency Use Authorizations for Zika virus assays.**
- **Discuss Zika virus testing methods, including molecular and antibody detection.**
- **Explain the role of public health laboratories, clinicians, and health departments in Zika testing and diagnosis.**
- **Identify Zika virus laboratory testing algorithms and resources.**

TODAY'S PRESENTER

Christy Ottendorfer, Ph.D.
Microbiologist
Team Lead, Zika Lab Team Task Force
Emergency Operations Center
Centers for Disease Control and Prevention

TODAY'S PRESENTER

Matthew J. Binnicker, Ph.D., D(ABMM)

Director of Clinical Virology

Associate Professor of Laboratory Medicine and Pathology

Mayo Clinic

American Society for Microbiology

TODAY'S PRESENTER

Grace Kubin, Ph.D.
Laboratory Director
Texas Department of State Health Services
Association of Public Health Laboratories

ZIKA VIRUS: INFORMATION FOR CLINICIANS

December 1, 2016

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

Guidance for US Laboratories Testing for Zika Virus Infection

Christy Ottendorfer, PhD
Microbiologist

December 1, 2016

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

What is new?

CDC updated its laboratory guidance to support improved detection of Zika virus infection

Questions:

- *Why has whole blood been added as an approved specimen type for detection of Zika virus?*

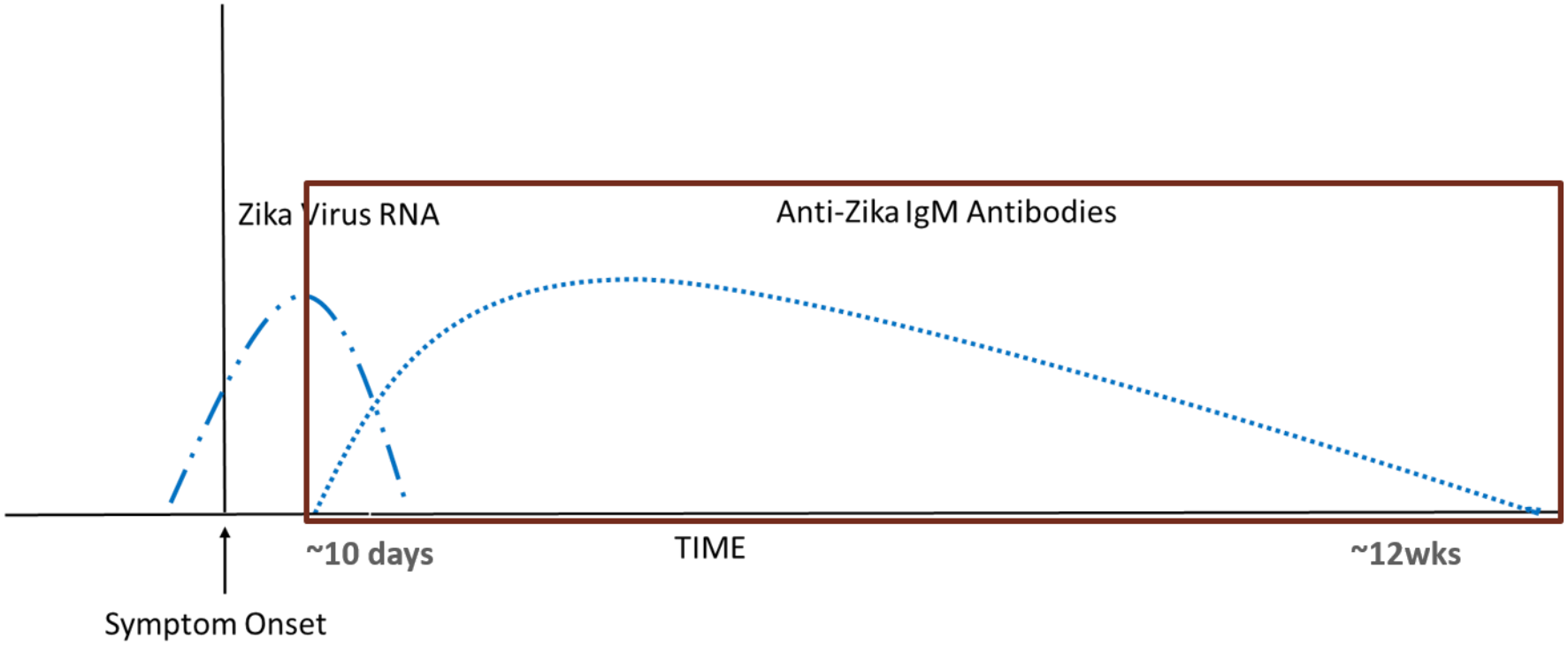
- *Should health care providers still collect serum?*

Updated Guidance for US Laboratories Testing for Zika Virus

- Issued November 16, 2016
- Expands laboratory testing parameters
- Addresses use of currently available commercial assays
- Clarification for testing algorithms

http://www.cdc.gov/zika/laboratories/lab-guidance.html

Detecting Zika Virus Infection



Zika Diagnostic Assays

- Detection of Zika virus RNA is performed using Nucleic Acid Tests (NATs).

- Zika MAC-ELISA is used for the detection of Zika IgM antibodies.
  - Cross-reaction with related flaviviruses (e.g., dengue) is common.

- Specimens tested with the Zika MAC-ELISA that are presumptive positive, equivocal or uninterpretable are further analyzed using plaque reduction neutralization tests (PRNT).
  - *PRNT confirmation is not currently routinely recommended in Puerto Rico.*

CDC Zika Diagnostic Assays

- FDA has issued Emergency Use Authorizations (EUAs) for two CDC assays
  - Zika MAC-ELISA for presumptive detection of Zika IgM antibodies
    - *Specimens positive for Zika MAC-ELISA are further analyzed by using PRNT.*
  - Trioplex rRT-PCR to detect Zika, dengue, and chikungunya viral RNA

- CDC Zika diagnostic assays are distributed in the United States through the Laboratory Response Network (LRN).

- CDC Zika diagnostic assays have also been distributed internationally.

http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika

CDC EUA Updates

- Trioplex rRT-PCR, September 21, 2016

  Addition of:

  - Whole blood as a specimen type
  - Two new extraction instruments
    - MagNA Pure Compact
    - BioMerieux easyMAG
  - Large volume (1 mL) extraction preferred for serum, urine, CSF, and amniotic fluid (using authorized instrumentation)
- Patient and healthcare provider fact sheets updated

Additional Capacity for Zika Diagnostic Testing

- Ten commercial diagnostic manufacturers have received an EUA for a molecular test for Zika virus RNA.
  - FDA reference panel sent to all manufacturers for blind testing and test performance evaluation.
- One commercial diagnostic manufacturer has received an EUA for a serologic test for Zika virus infection
  - Three independent laboratories are conducting performance evaluation of three manufacturers' Zika serological assays, as another commercial MAC-ELISA option.
- Three commercial laboratories (Quest, LabCorp, and Mayo) have been qualified to use CDC Zika MAC-ELISA.

Nucleic Acid-based EUAs

Test	Specimen Type	EUA Issuance
CDC Trioplex Real-time RT-PCR	Serum, CSF, Whole Blood, Urine, and Amniotic Fluid	March 17, 2016
Zika Virus RNA Qualitative Real-Time RT-PCR Focus Diagnostics, Inc.(Quest)	Serum	April 28, 2016
RealStar Zika Virus RT-PCR Kit U.S. Altona Diagnostics GmbH	Serum or Urine	May 13, 2016
Hologic Aptima Zika Virus assay (transcription-mediated amplification test)	Serum, Plasma, Urine	June 17, 2016
Viracor-IBT Laboratories, Inc.'s Zika Virus Real-time RT-PCR Test	Serum, Plasma, Urine	July 19, 2016
VERSANT® Zika RNA 1.0 Assay (kPCR) Kit Siemens Healthcare Diagnostics Inc.	Serum, Plasma, Urine	July 29, 2016
xMAP® MultiFLEX™ Zika RNA Assay Luminex Corporation	Serum, Plasma, Urine	August 4, 2016
LightMix® Zika rRT-PCR Test Roche Molecular Systems, Inc.	Serum or Plasma	August 26, 2016
Sentosa® SA ZIKV RT-PCR Test Vela Diagnostics USA, Inc.	Serum, Plasma, Urine	September 23, 2016
Zika Virus Detection by RT-PCR Test ARUP Laboratories	Serum, Plasma, Urine	September 28, 2016
Abbott RealTime Zika Assay Abbott Molecular Inc.	Serum, Plasma, Urine	November 21, 2016

http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika

Zika MAC-ELISA EUAs

Test	Specimen Type	EUA Issuance
CDC Zika MAC-ELISA	Serum, CSF	June 29, 2016
ZIKV Detect™ IgM Capture ELISA (InBios, USA)	Serum	August 17, 2016

http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika

Additional Capacity for Zika Diagnostic Testing

In addition, CDC is

- Meeting with states with a high risk of local transmission
- Developing capacity to meet potential testing demand
- Providing reagents to support testing for the Zika virus through the International Reagent Resource (IRR) program
    - Including support for approved domestic and US territories (including Puerto Rico)

Summary

- Updated laboratory guidance released in November 2016
- Expands testing parameters, such as whole blood (CDC Trioplex NAT)
  - *Recommend collect whole blood (improved sensitivity)*
  - *Large volume (1.0 mL) extraction is preferred (serum, urine, CSF, amniotic fluid to improve sensitivity)*
  - *Must still collect serum for serologic assays*
- CDC-developed and several commercial assays authorized under FDA EUA for Zika virus testing

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Diagnostic Testing for Zika Virus in Clinical Laboratories

Matthew J. Binnicker, Ph.D., D(ABMM)

Director of Clinical Virology, Mayo Clinic

Chair, ASM Professional Development Committee

Controlling Zika – A TEAM Effort

- Success will depend on careful *coordination* and *cooperation* among providers, public health, and clinical laboratories.
- Involvement of local/private labs and reference laboratories is essential:
  - Closest to the patient
  - Reduce burden of testing on public health labs

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Diagnostic Assays for Zika Virus

- Currently require Emergency Use Authorization (EUA) from the FDA prior to use.
- CDC assays first to receive EUA
  - TrioPlex rRT-PCR* – molecular test for detection of Zika, dengue and chikungunya viruses from:
    - Serum (preferred)
    - Whole blood
    - CSF
    - Urine
    - Amniotic fluid

    } Zika testing only
  - MAC-ELISA** – serology for detection of IgM

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*Available in CDC-designated public health labs
**Available in CDC-designated public health and reference labs

Diagnostic Assays for Zika Virus

- Several commercial assays are now available:

Laboratory/Company	Method	Sample type(s)
Focus/Quest Diagnostics	Real-time RT-PCR	Serum, urine
altona Diagnostics	Real-time RT-PCR	Serum, urine
Hologic	TMA	Plasma, serum, urine
Viracor-IBT	Real-time RT-PCR	Plasma, serum, urine
Siemens	Real-time RT-PCR	Plasma, serum, urine
Luminex	Real-time RT-PCR	Plasma, serum, urine
Roche	Real-time RT-PCR	Plasma, serum
InBios	IgM Capture ELISA	Serum

How should these tests be used?

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Case #1

- A 27 year-old female returns from vacation in Jamaica. Seven days after arriving home, the patient takes a pregnancy test, which is positive. The patient is asymptomatic.

- Is Zika testing recommended, and if so, what testing should be performed?

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Case #1 – Testing recommended

<14 days after return from travel or exposure?

>14 days (2-12 weeks) after return from travel or exposure?

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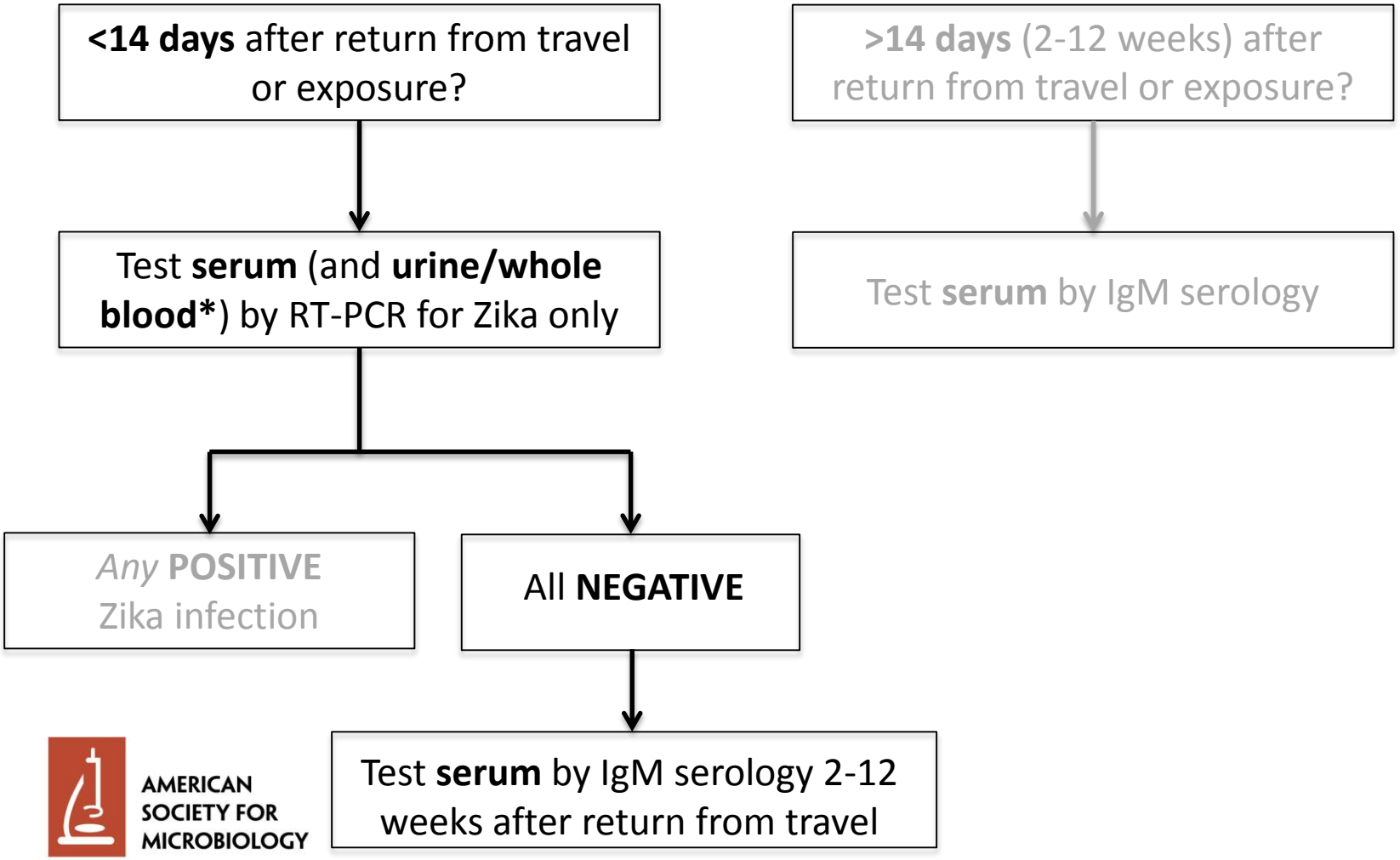
Case #1 – Testing recommended



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*Optional; must be accompanied by paired serum

Case #2

- A 45 year-old male from Honduras visits his family in Texas. He was well during his first 7 days in the U.S., but has experienced an intermittent low grade fever, rash and mild joint pain over the past 2.5 weeks.

- Is Zika testing indicated?

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Case #2 – Testing indicated

<14 days following symptom onset?

>14 days following symptom onset?

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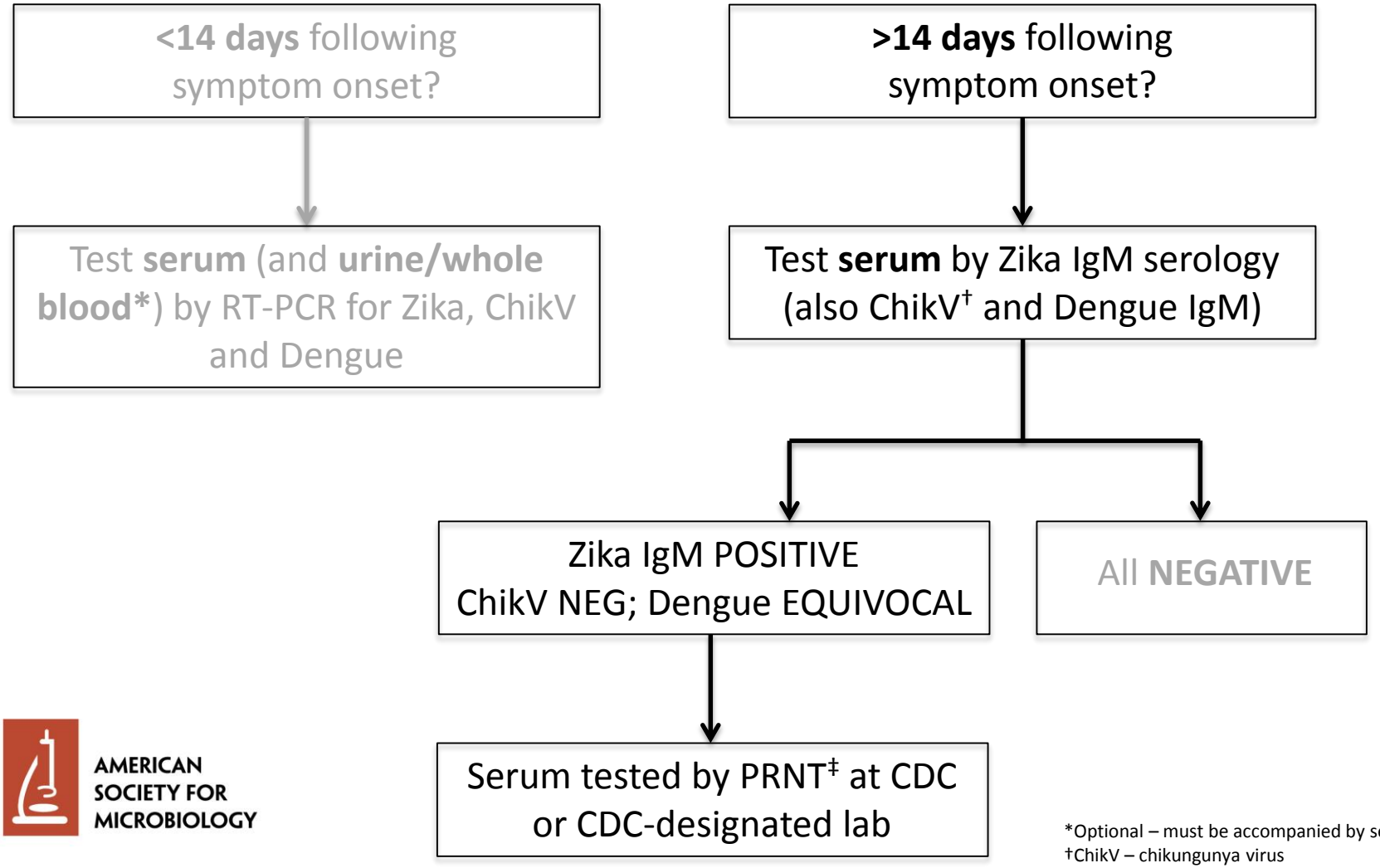
Case #2 – Testing indicated



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*Optional – must be accompanied by serum
†ChikV – chikungunya virus
‡PRNT – plaque reduction neutralization test

Case #3

- A 57 year-old female from Des Moines, IA visits Haiti as part of a church mission trip. Two days after returning home, she contacts her primary care provider and requests testing for Zika. The patient is asymptomatic.

- Is Zika testing recommended?

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Case #3

- "Diagnostic" testing is ***not*** recommended in asymptomatic, non-pregnant individuals.
- Caveat: Blood donors (Organ/tissue donors**)

  On August 26, 2016, the U.S. FDA recommended that all donated blood be screened for Zika virus
- Currently, two screening tests available:
  - Nucleic acid amplification tests (Roche and Hologic)

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**No definitive guidance; however, may be screened. Recommended screening test (PCR vs. serology) unclear.

Case #4

- A 29 year-old female with laboratory confirmed Zika virus infection delivers her first child. Clinical exam of the infant reveals no evidence of abnormalities.

- Is Zika testing of the infant recommended?

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Case #4 – Testing indicated

- Lab testing is recommended for:
  - Infants born to mothers with lab evidence of Zika
  - Infants with findings suggestive of congenital Zika AND a maternal epidemiologic link (regardless of maternal test results)
- Initial testing of infant should include:
  - rRT-PCR of serum and urine (whole blood/CSF optional)
  - Zika virus IgM on serum

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Case #4 – Interpretation

- Interpretation of results of lab testing in cases of possible congenital Zika virus infection:

Zika rRT-PCR	Zika IgM	Interpretation
Positive*	**Positive** or Negative	Confirmed congenital Zika infection
Negative	**Positive**	Probable congenital Zika infection
Negative	Negative	Negative for congenital Zika infection

*Infant serum, urine or cerebrospinal fluid

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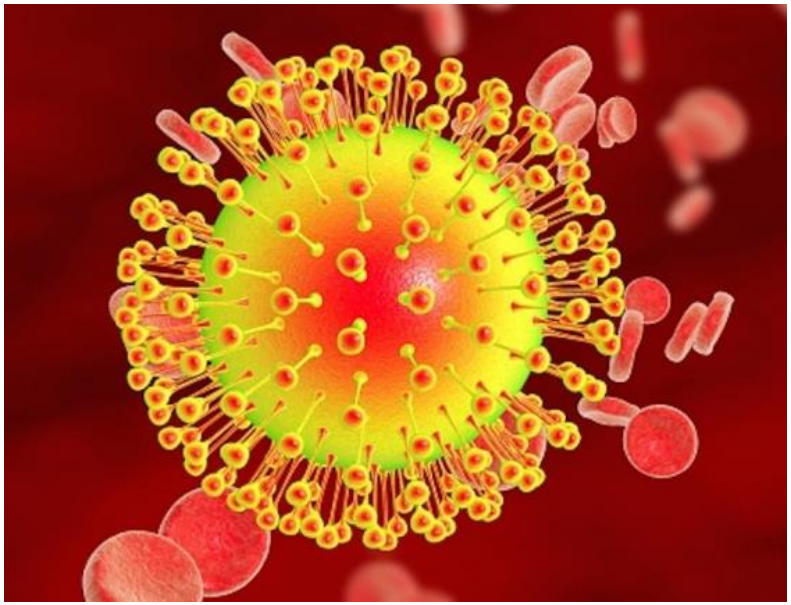
Summary

- Zika virus poses a significant challenge to public health and clinical laboratories.
- Coordinated effort is needed to identify cases and control the outbreak.
- Evolving process – new data will continue to guide diagnostic algorithms.



All Hands Response for Zika Testing

Grace Kubin, Ph.D.
Texas Department of State Health Services
Director of Laboratory Services

Parallels to the Ebola Response

Ebola

- Not much known about virus
- Confusion surrounding testing
- Confusion about specimen shipment
- Many different health care professionals involved

Zika

- Not much known about virus
- Confusion surrounding testing
- Confusion about specimen shipment
- Many different health care professionals involved

Where to Get Testing

- **Public Health Laboratories**
  - **Check city, county, or state health department websites for testing specifics**
- **Commercial and private laboratories**
  - **See current assay availability at FDA Medical Device EUA website**
  - **Check individual lab websites for which tests are offered**

Specimen Submission

- **Specimen handling requirements**
  - **Check recommendations for each lab**
- **Specimens approved for testing based on patient signs and symptoms and travel history**
  - **Extra information needed for determining if patient meets testing criteria**
  - **This information is also required for additional testing at CDC**

Where are my Results?

Reverse Transcriptase – Polymerase Chain Reaction (RT-PCR)

- Serum is preferred specimen
- Trioplex assay - urine, whole blood, CSF can be tested when submitted with paired serum
- Positive results are considered conclusive; no other testing required
- Results available approximately 2 -3 days after specimen arrives in the laboratory

Where are my Results?

IgM Antibody Capture enzyme-linked Immunosorbent Assay (MAC-ELISA)

- Serum is only suitable specimen
- Results available approximately 3 – 4 days after arrival in the laboratory
- Plaque-reduction neutralization test (PRNT) used to confirm positive or equivocal results
- Dengue and Chikungunya serology are recommended depending on where infected

Where are my Results?

Plaque-reduction neutralization test (PRNT)

- Serum is the preferred specimen
- Only CDC and a few CDC approved laboratories can perform this test
- Results should be interpreted in conjunction with the serology test results
- Test measures specific antibodies to Zika and other flaviviruses
- Test depends on virus growth which may be at least one week or more

Working With Partners

Commercial and Private Lab Coordination

- Private labs have contacted us regarding their implementation of RT-PCR testing and offered their testing capacity if needed
- Commercial labs are working with PHLs to provide surge capacity testing as part of a large scale investigation
- In some areas these labs can provide needed local capacity for specimen collection

Working With Partners

Military and Federal Lab Coordination

- Many military labs have implemented Zika RT-PCR and IgM testing and have indicated they would be available to provide surge testing
- Federal (CDC) labs provide PRNT testing for PHLs and other commercial labs; also have additional surge capacity to support local transmission investigations

Education and Outreach

Health Department Activities

- Media campaigns
- Webinars with health care providers
  - State Medical Association
  - State Pediatric Society
  - State Ob/Gyn Association
- Use of WIC sites for distribution of pamphlets and posting of educational materials

To Ask a Question

- **Using the Webinar System**
  - “Click” the Q&A tab at the top left of the webinar tool bar
  - “Click” in the white space
  - “Type” your question
  - “Click” ask

- **On the Phone**
  - Press Star (*) 1 to enter the queue
  - State your name
  - Listen for the operator to call your name
  - State your organization and then ask your question

Thank you for joining!

Centers for Disease Control and Prevention
Atlanta, Georgia
http://emergency.cdc.gov/coca

Today's webinar will be archived

When: A few days after the live call

What: All call recordings (audio, webinar, and transcript)

Where: On the COCA Call webpage

http://emergency.cdc.gov/coca/calls/2016/callinfo_120116.asp

Upcoming COCA Call
registration is not required

Risk Mitigation Strategies to Reduce Opioid Overdoses

- **Date: Tuesday, December 6, 2016**
- **Time: 2:00 – 3:00 pm (Eastern)**
- **Presenters:**
  - Deborah Dowell, MD, MPH—CDC
  - Jane C Ballantyne, MD, FRCA—University of Washington
  - Joseph O. Merrill MD, MPH—University of Washington

http://emergency.cdc.gov/coca

Upcoming COCA Call
registration is not required

Gearing up for the Travel Season: How Clinicians can Ensure Their Patients are Packed with Knowledge on Zika Prevention

- **Date: Thursday, December 8, 2016**
- **Time: 2:00 – 3:00 pm (Eastern)**
- **Presenters:**
  - Mary Tanner, MD, FAAP—CDC Zika Pregnancy and Birth Defects Task Force
  - Allison Taylor Walker PhD, MPH—CDC Zika Travelers' Health Branch

http://emergency.cdc.gov/coca

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Those who participated in today's COCA Call and who wish to receive continuing education should complete the online evaluation by December 31, 2016 with the course code WC2286. Those who will participate in the on demand activity and wish to receive continuing education should complete the online evaluation between December 31, 2016 and November 30, 2018 will use course code WD2286.

Continuing education certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CE's obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

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