This memo is intended to provide the latest information to all North Carolina clinicians regarding the Middle-East Respiratory Syndrome Coronavirus or MERS-CoV, including specimen testing requirements. MERS-CoV infections are reportable in North Carolina. Physicians are required to contact their local health department or state Communicable Disease Branch (919-733-3419) as soon as MERS-CoV infection is reasonably suspected.

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- STD Services
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Physicals:
- Sports
- Work
- College
- DOT
- Women’s Health

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- Monitoring & Reducing Health Hazards
- Reducing Specific Disease and Injury
- Providing Emergency Preparedness and Response
- Issuing Health Advisories & News Releases
- Implementing Policies, Processes, and Environmental Changes to Improve Health
- Providing Health Education & Information
- Planning Partnerships with Health Care Providers
- Improving Healthy Eating, Active Living and Tobacco-free Living
- Improving Access to Health Care

Environmental Health:
- Ensuring Water Quality
- Monitoring Waste Disposal
- Fighting Pollution
- Ensuring Sanitation
- Enforcing Health and Safety Codes

To: All North Carolina Health Care Providers  
From: Erica Wilson, MD, MPH, Medical Epidemiologist  
       Scott Shone, PhD, HCLD(ABB), Laboratory Director  
Re: Middle-East Respiratory Syndrome Coronavirus (MERS-CoV) (3 pages)

This memo is intended to provide the latest information to all North Carolina clinicians regarding the Middle-East Respiratory Syndrome Coronavirus or MERS-CoV, including specimen testing requirements.

This version has been modified to include links to updated recommendations for monitoring and movement of persons with potential exposure to MERS-CoV, as well as specimen testing requirements at the NC State Laboratory of Public Health.

Summary
MERS-CoV is a coronavirus that was first identified in 2012 and has been associated with severe respiratory infections among persons who live in or have traveled to the Middle East and persons (including health care providers) exposed to MERS cases outside of the Middle East. The first travel-associated cases in the United States were confirmed in May, 2014. There has been clear evidence of person-to-person transmission both in household and healthcare settings, but no evidence of sustained person-to-person transmission within the community.

Case Investigation and Testing

- A person meeting both the clinical features and epidemiological criteria listed below should be considered a Patient Under Investigation (PUI).

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Epidemiologic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severe illness</strong></td>
<td>A history of travel from countries in or near the Arabian Peninsula(^2) within 14 days before symptom onset, or close contact(^3) with a symptomatic traveler who developed fever(^1) and acute respiratory illness (not necessarily pneumonia) within 14 days after traveling from countries in or near the Arabian Peninsula(^2). – or – A member of a cluster of patients with severe acute respiratory illness (e.g., fever(^1) and pneumonia requiring hospitalization) of unknown etiology in which MERS-CoV is being evaluated, in consultation with state and local health departments in the US.</td>
</tr>
<tr>
<td>Fever(^1) and pneumonia or acute respiratory distress syndrome (based on clinical or radiological evidence)</td>
<td></td>
</tr>
<tr>
<td><strong>Milder illness</strong></td>
<td>A history of being in a healthcare facility (as a patient, worker, or visitor) within 14 days before symptom onset in a country or territory in or near the Arabian Peninsula(^2) in which recent healthcare-associated cases of MERS have been identified.</td>
</tr>
<tr>
<td>Fever(^1) and symptoms of respiratory illness (not necessarily pneumonia; e.g., cough, shortness of breath)</td>
<td></td>
</tr>
<tr>
<td>Fever(^1) or symptoms of respiratory illness (not necessarily pneumonia; e.g., cough, shortness of breath)</td>
<td>Close contact(^3) with a confirmed MERS case while the case was ill.</td>
</tr>
</tbody>
</table>
• Clinicians caring for patients meeting these criteria should immediately contact their local health department or the state Communicable Disease Branch (919-733-3419; available 24/7) to discuss laboratory testing and control measures.

• Persons who meet criteria should also be evaluated for common causes of community-acquired pneumonia, if not already done. (Note: Viral culture should not be attempted in cases with a high index of suspicion.) MERS-CoV infection should still be considered even if another pathogen is identified, since co-infections have been reported.

• Any cluster of severe acute respiratory illness in healthcare workers in the United States should be thoroughly investigated. Occurrence of a severe acute respiratory illness cluster of unknown etiology should prompt immediate notification of local public health for further investigation and testing.

• Testing for MERS-CoV is available at the North Carolina State Laboratory of Public Health. Testing requires consultation and pre-approval from the state Communicable Disease Branch. Detailed information about specimen collection and transport is listed on the next page and at https://slph.ncpublichealth.com/bioterrorism/mers.asp.

Infection Control
• Transmission of MERS-CoV has been documented in healthcare settings. See CDC’s updated Interim Guidance for Healthcare Professionals at https://www.cdc.gov/coronavirus/mers/interim-guidance.html

• Standard, contact, and airborne precautions are recommended for management of patients in healthcare settings with known or suspected MERS-CoV infection. These include:
  o Use of fit-tested NIOSH-approved N95 or higher level respirators
  o Use of gowns, gloves and eye protection
  o Use of negative-pressure airborne infection isolation rooms if available

• A facemask should be placed on the patient if an airborne infection isolation room is not available or if the patient must be moved from his/her room.


Monitoring and Movement of Exposed persons
• Recommendations for public health monitoring and movement restrictions for healthcare personnel and others potentially exposed to MERS-CoV are based on the level of exposure (high risk, some risk, and low risk). Details are available at https://www.cdc.gov/coronavirus/mers/hcp/monitoring-movement-guidance.html.

Treatment
• No antivirals are currently available for treatment of MERS-CoV or other novel coronavirus infections.

Reporting
• MERS-CoV infections are reportable in North Carolina. Physicians are required to contact their local health department or the state Communicable Disease Branch (919-733-3419) as soon as MERS-CoV infection is reasonably suspected.

Recommendations may change as new information becomes available. Updated information and guidance are available from the CDC at http://www.cdc.gov/coronavirus/mers/index.html.

1Fever may not be present in some patients, such as those who are very young, elderly, immunosuppressed, or taking certain medications. Clinical judgement should be used to guide testing of patients in such situations.

2Countries considered in the Arabian Peninsula and neighboring include: Bahrain; Iraq; Iran; Israel, the West Bank, and Gaza; Jordan; Kuwait; Lebanon; Oman; Qatar; Saudi Arabia; Syria; the United Arab Emirates (UAE); and Yemen.

3Close contact is defined as: a) being within approximately 6 feet (2 meters) or within the room or care area of a confirmed MERS case for a prolonged period of time (e.g., healthcare personnel, household members) while not wearing recommended personal protective equipment (i.e., gowns, gloves, respirator, eye protection); or b) having direct contact with infectious secretions of a confirmed MERS case (e.g., being coughed on) while not wearing recommended personal protective equipment.
NCSLPH MERS-CoV Specimen Collection and Testing Guidelines

Testing Criteria
- All suspect or probable cases of MERS-CoV infections based on the clinical criteria described on page one should be reported to the NC DPH Communicable Disease Branch at (919) 733-3419 for prior approval for laboratory testing.

Testing Employed
- The NCSLPH has validated the CDC MERS-CoV rRT-PCR assay that has been granted FDA Emergency Use Authorization. Presumptive positive specimens will be forwarded to the CDC for confirmation.
- Estimated turn-around time for initial results is 5-48 hours, once specimens are received.
- USE APPROPRIATE PRECAUTIONS WHEN COLLECTING SPECIMENS FOR MERS-CoV TESTING: https://www.cdc.gov/coronavirus/mers/infection-prevention-control.html

To increase the likelihood of detecting infection, the CDC recommends collecting multiple specimens from different sites at different times after symptom onset, if possible.

All three specimen types (not just one or two of the three), lower respiratory, upper respiratory and serum specimens should be collected for the CDC MERS rRT-PCR assay.

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Optimal Collection Time</th>
<th>Specimen Volume</th>
<th>Shipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Lower Respiratory:</td>
<td>As soon as possible after symptoms begin – ideally within 7 days, and before antiviral medication.</td>
<td>2–3 mL fluid contained in a sterile leak-proof cup</td>
<td>Refrigerated (4°C), placed on cold packs if shipment is to be received within 72 h of collection. For delays exceeding 72 h, freeze at -70°C &amp; ship on dry ice.</td>
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<tr>
<td>Bronchoalveolar lavage (preferred specimen), tracheal aspirate, pleural fluid, and/or sputum (patient should rinse mouth with water prior to collection for sputum samples)</td>
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<tr>
<td>2. Upper Respiratory:</td>
<td>&lt;14 days; optimally, collected during the first 10-12 days after symptom onset</td>
<td>Adults: 3–5 mL Infants: 0.5-1 mL</td>
<td>NP and OP swabs can be combined in 2 – 3 mls viral transport media</td>
</tr>
<tr>
<td>Nasopharyngeal (NP) AND oropharyngeal (OP) swabs (preferred specimens), NP wash/aspirate, or nasal aspirates</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Use only synthetic fiber swabs with plastic shafts in viral transport media</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>3. Serum</td>
<td>&lt;14 days; optimally, collected during the first 10-12 days after symptom onset</td>
<td>Adults: 3–5 mL Infants: 0.5-1 mL</td>
<td>See above</td>
</tr>
<tr>
<td>Serum (for serologic testing)</td>
<td>Convalescent: ≥ 14 days after symptom onset</td>
<td>Adults: 3–5 mL Infants: 0.5-1 mL</td>
<td></td>
</tr>
</tbody>
</table>

Appropriate Specimens for MERS-CoV Testing Conducted at the CDC

All specimen submissions must have a completed BTEP Specimen Submission Form

CONTACT THE BTEP UNIT (919-807-8600) PRIOR TO ANY SHIPMENT OR IF YOU HAVE QUESTIONS.

Additional Information:
- Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from PUIs for MERS-CoV - v2.1
- NC Division of Public Health Epidemiology Section - MERS-CoV Information:
**Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Patients Under Investigation (PUIs) for Middle East Respiratory Syndrome Coronavirus (MERS-CoV) – Version 2.1**

**Summary of Changes in Version 2.1**

This is an updated version of the interim guidance document issued by the Centers for Disease Control and Prevention (CDC) January 2014. CDC has revised the interim guidance based on comments received from public health partners, healthcare providers, professional organizations, and others. CDC will continue to update the document as necessary to incorporate new information that increases our understanding of MERS-CoV.

Updates:

*Minor changes were made to clarify specimen type and collection procedures.*

1. Emphasized the recommendation to collect all 3 specimen types (lower respiratory, upper respiratory, and serum) if possible and not just one or two of the three specimen types for testing using the CDC MERS rRT-PCR assay
2. Deleted the recommendation to collect a stool specimen for MERS-CoV testing
3. Provided additional information for collection and processing serum specimens

Before collecting and handling specimens for Middle East Respiratory Syndrome Coronavirus (MERS-CoV) testing, determine whether the person meets the current definition for a “patient under investigation” (PUI) for MERS-CoV infection prepared by the Centers for Disease Control and Prevention (CDC). See case definitions (www.cdc.gov/coronavirus/mers/case-def.html).

**Specimen Type and Priority**

To date, little is known about pathogenic potential and transmission dynamics of MERS-CoV. To increase the likelihood of detecting infection, CDC recommends collecting multiple specimens from different sites at different times after symptom onset, if possible.

**Points to consider when determining which specimen types to collect from a patient under investigation for MERS include:**

- The number of days between specimen collection and symptom onset
- Symptoms at the time of specimen collection

**Additional points to consider:**

- Maintain proper infection control when collecting specimens
- Use approved collection methods and equipment when collecting specimens
- Handle, store, and ship specimens following appropriate protocols

**Collection of all three specimen types (not just one or two of the three), lower respiratory, upper respiratory and serum specimens for testing using the CDC MERS rRT-PCR assay is recommended.** Lower respiratory specimens are preferred, but collecting nasopharyngeal and oropharyngeal (NP/OP) specimens, and serum, are strongly recommended depending upon the length of time between symptom onset and specimen collection. Respiratory specimens should be collected as soon as possible after symptoms begin – ideally within 7 days. However, if more...
than a week has passed since symptom onset and the patient is still symptomatic, respiratory samples should still be collected, especially lower respiratory specimens since respiratory viruses can still be detected by rRT-PCR. For example,

1. if symptom onset for a PUI with respiratory symptoms was less than 14 days ago, a single serum specimen (see Section II. Serum), an NP/OP specimen and lower respiratory specimen (see Section I. Respiratory Specimens) should be collected for CDC MERS rRT-PCR testing.
2. if symptom onset for a PUI with an ongoing respiratory tract infection, especially lower, was 14 or more days ago, a single serum specimen for serologic testing (see Section II. Serum) in addition to a lower respiratory specimen and an NP/OP specimen (see Section I. Respiratory Specimens) are recommended.

**General Guidelines**

For short periods (≤ 72 hours), most specimens should be held at 2-8°C rather than frozen. For delays exceeding 72 hours, freeze specimens at -70°C as soon as possible after collection (with exceptions noted below). Label each specimen container with the patient’s ID number, specimen type and the date the sample was collected.

**I. Respiratory Specimens**

**A. Lower respiratory tract**

*Bronchoalveolar lavage, tracheal aspirate, pleural fluid*

Collect 2-3 mL into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container. Refrigerate specimen at 2-8°C up to 72 hours; if exceeding 72 hours, freeze at -70°C and ship on dry ice.

*Sputum*

Have the patient rinse the mouth with water and then expectorate deep cough sputum directly into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container. Refrigerate specimen at 2-8°C up to 72 hours; if exceeding 72 hours, freeze at -70°C and ship on dry ice.

**B. Upper respiratory tract**

*Nasopharyngeal swab AND oropharyngeal swab (NP/OP swab)*

Use only synthetic fiber swabs with plastic shafts. Do not use calcium alginate swabs or swabs with wooden shafts, as they may contain substances that inactivate some viruses and inhibit PCR testing. Place swabs immediately into sterile tubes containing 2-3 ml of viral transport media. **NP/OP specimens can be combined, placing both swabs in the same vial.** Refrigerate specimen at 2-8°C up to 72 hours; if exceeding 72 hours, freeze at -70°C and ship on dry ice.

*Nasopharyngeal swab* - Insert a swab into the nostril parallel to the palate. Leave the swab in place for a few seconds to absorb secretions. Swab both nasopharyngeal areas.

*Oropharyngeal swab (e.g., throat swab)* - Swab the posterior pharynx, avoiding the tongue.

*Nasopharyngeal wash/aspirate or nasal aspirate*

Collect 2-3 mL into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container. Refrigerate specimen at 2-8°C up to 72 hours; if exceeding 72 hours, freeze at -70°C and ship on dry ice.
II. Serum

Serum (for serologic testing)

For serum antibody testing: Because we do not want to delay detection of MERS infection and since the prevalence of MERS in the US is low, serologic testing on a single serum sample collected 14 or more days after symptom onset may be beneficial. This is in contrast to serologic testing for many other respiratory pathogens which require collection and testing of acute and convalescent serum specimens. Serologic testing is currently available at CDC upon request and approval. Please be aware that the MERS-CoV serologic test is for research/surveillance purposes and not for diagnostic purposes - it is a tool developed in response to the MERS-CoV outbreak. Contact CDC’s Emergency Operations Center (EOC) (770-488-7100) for consultation and approval if serologic testing is being considered.

Serum (for rRT-PCR testing)

For rRT-PCR testing (i.e., detection of the virus and not antibodies): A single serum specimen collected optimally during the first 10-12 days after symptom onset is recommended. Note: The kinetics of MERS-CoV are not well understood. Once additional data become available, these recommendations will be updated as needed.

Minimum serum volume needed: The minimum amount of serum required for MERS-CoV testing (either serologic or rRT-PCR) is 200 µL. If both MERS-CoV serology and rRT-PCR tests are planned, the minimum amount of serum required is 400 µL (200 µL for each test). Serum separator tubes should be stored upright for at least 30 minutes, and then centrifuged at 1000–1300 relative centrifugal force (RCF) for 10 minutes before removing the serum and placing it in a separate sterile tube for shipping (such as a cryovial). Refrigerate the serum specimen at 2-8°C and ship on ice-pack; freezing and shipment of serum on dry ice is permissible.

Children and adults: Collect 1 tube (5-10 mL) of whole blood in a serum separator tube.

Infant: A minimum of 1 mL of whole blood is needed for testing pediatric patients. If possible, collect 1 mL in a serum separator tube.

III. Shipping

Specimens from suspected MERS cases must be packaged, shipped, and transported according to the current edition of the International Air Transport Association (IATA) Dangerous Goods Regulations. Shipments from outside of the United States may require an importation permit that can be obtained from CDC.

Specimens should be stored and shipped at the temperatures indicated above. If samples are unable to be shipped within 72 hours of collection, they should be stored at -70°C and shipped on dry ice. When shipping frozen specimen from long distances or from international locations, it is best to use a combination of dry ice and frozen gel ice-packs. The gel ice-packs will remain frozen for a day or two after the dry ice has dissipated.

All specimens must be pre-packed to prevent breakage and spillage. Specimen containers should be sealed with Parafilm® and placed in ziplock bags. Place enough absorbent material to absorb the entire contents of the Secondary Container (containing Primary Container) and separate the Primary Containers (containing specimen) to prevent breakage. Send specimens with cold packs or other refrigerant blocks that are self-contained, not actual wet ice. This prevents leaking and the appearance of a spill. When large numbers of specimens are being shipped, they should be organized in a sequential manner in boxes with separate compartments for each specimen.

Additional useful and detailed information on packing, shipping, and transporting specimens can be found at Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Middle East Respiratory Syndrome Coronavirus (MERS-CoV) (http://www.cdc.gov/coronavirus/mers/guidelines-lab-biosafety.html).
CDC recommends against the following:

- **Do not place** any dry ice in the "Primary Container" or "Secondary Container", foam envelopes, ziplock bags, cryovial boxes, or hermetically sealed containers.
- **Do not place** Primary Containers sideways or upside down in ziplock bags.
- **Do not place** any paperwork in the Secondary Containers or ziplock bags, so as not to damage the paperwork.
- **Do not use** biohazard/autoclave bags to prepack your materials due to the inadequate seal of these bags.

*For additional information, consultation, or the CDC shipping address, contact the CDC Emergency Operations Center (EOC) at 770-488-7100. Specimens should be shipped for overnight delivery - if Saturday delivery is planned, special arrangements must be made with the shipping company.*

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**Summary of MERS-CoV rRT-PCR Testing Guidelines for Specimens**

Many state health department laboratories are approved for MERS-CoV testing using the CDC rRT-PCR assay. Contact your local/state health department to notify them of the PUI and to request MERS-CoV testing. If your state health department is unable to test, contact CDC’s EOC at 770-488-7100.

**Testing for MERS-CoV and other respiratory pathogens can be done simultaneously.** Virus isolation in cell culture and initial characterization of viral agents recovered in cultures of MERS-CoV specimens are **NOT recommended** at this time. However, if done, these activities must be performed in a BSL-3 facility using BSL-3 work practices.

**Test for MERS-CoV**

The laboratory must follow the protocol for the CDC rRT-PCR assay. “NEGATIVE” test results should be reported through the CDC Laboratory Response Network (LRN) within 24 hours. When a “PRESUMPTIVE POSITIVE” or “EQUIVOCAL” test result is obtained, CDC must be contacted immediately as per the assay protocol, and the result must also be reported to the LRN within 6 hours. Confirmation of a “PRESUMPTIVE POSITIVE” result by CDC is required, however this should not delay the local investigation and response, including the contact investigation.

**Test for Other Respiratory Pathogens**

Testing for common respiratory pathogens by molecular or antigen detection methods (**not by viral culture**) is **strongly recommended.** Common respiratory pathogens include 1) influenza A, influenza B, respiratory syncytial virus, human metapneumovirus, human parainfluenza viruses, adenovirus, human rhinovirus and other respiratory viruses; 2) *Streptococcus pneumoniae*, *Chlamydia pneumophila*, and other pathogens that cause severe lower respiratory infections. Clinical presentation, epidemiologic and surveillance information, and season should be considered when selecting which pathogens to test for. A few MERS-CoV cases have had other respiratory pathogens detected, so identification of a respiratory pathogen prior to MERS-CoV testing should not preclude testing for MERS-CoV, especially if MERS is strongly suspected. If your laboratory does not have molecular or antigen testing capability for respiratory pathogens, contact your state laboratory for assistance.

For most current version, see [www.cdc.gov/coronavirus/mers/guidelines-clinical-specimens.html](http://www.cdc.gov/coronavirus/mers/guidelines-clinical-specimens.html)