

Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Information and Guidance for Clinicians

**Clinician Outreach and
Communication Activity (COCA)
Conference Call
June 13, 2013**



Objectives

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

- ❑ Describe the key components in the surveillance case definition for a patient under investigation for MERS-CoV infection**
- ❑ Identify specimens to be obtained and the appropriate laboratory test to diagnose a patient with MERS-CoV infection**
- ❑ List infection control measures appropriate for control of MERS-CoV**

TODAY'S PRESENTER



Susan I. Gerber, MD

Medical Epidemiologist
Respiratory Virus Program
Division of Viral Diseases

National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

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Alexander Kallen, MD, MPH

Medical Officer

Division of Healthcare Quality Promotion

National Center for Emerging and Zoonotic Infectious Diseases

Centers for Disease Control and Prevention

Emergence of a Novel Coronavirus in the Arabian Peninsula, Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

Susan I. Gerber, MD

Medical Epidemiologist
Respiratory Virus Program
Division of Viral Diseases

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Objectives

- Describe the clinical spectrum of disease caused by MERS-CoV
- Identify the key components in the surveillance case definition for a patient under investigation for MERS-CoV
- Identify specimens to be obtained and the appropriate laboratory test to diagnose a patient with MERS-CoV
- List infection control measures appropriate for control of MERS-CoV

Coronaviruses (CoVs)

- Enveloped positive strand RNA virus
- Human CoVs isolated in the 1960s
- Six human CoVs (HCoVs) have been identified to date:
 - HCoV-229E
 - HCoV-OC43
 - HCoV-NL63
 - HCoV-HKU1
 - SARS-CoV
 - **Middle East Respiratory Syndrome Coronavirus (MERS-CoV)**

Coronavirus Classification

- Alpha
 - Human examples: HCoV-229E, HCoV-NL63
 - Pig, dog, and cat CoVs
- Beta
 - HCoV-OC43, HCoV-HKU1, HCoV-SARS
 - MHV, rat, pig and cow CoVs
 - **MERS-CoV**
- Gamma
 - Chicken and turkey CoVs
- Delta
 - Bird CoVs

Clinical Spectrum of Illness: HCoV: 229E, NL-63, OC-43, HKU1

- Most often associated with upper respiratory tract infections in children
- Pneumonia and lower tract infections in immunocompromised individuals and the elderly
- May play a role in exacerbations of underlying respiratory diseases

Epidemiology: HCoV's: 229E, NL-63, OC-43, HKU1

- Worldwide
- Seasonality: Winter and spring in temperate climates
- Exposure common in early childhood
- Transmission likely to be droplet, contact, and indirect contact
- Symptoms and viral loads high first few days of illness
- Incubation period 2-5 days

Clinical Spectrum of Illness: SARS

- Fever, myalgia, headache, chills 1-2d, followed by a nonproductive cough and shortness of breath 5-7d after onset
- Most identified illnesses recognized in adults
- ~25 % diarrhea
- 20-30% management in ICUs
 - ARDS, mechanical ventilation
- ~ 10-15 % mortality rate, higher in adults >60y

Epidemiology: SARS

- First recognized Nov., 2002 as sporadic cases in Guangdong province, China
- Outbreak period 2002-2003
- Hong Kong hotel contributed to spread of virus to several countries
- 8,098 probable SARS cases
 - 774 deaths

Epidemiology: SARS

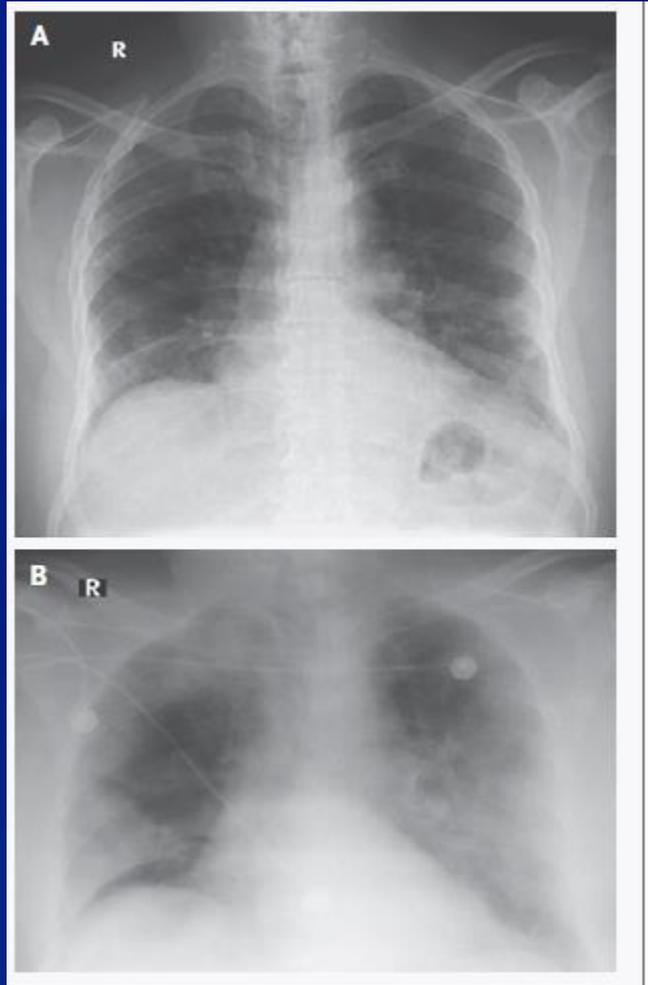
- Incubation period is 2-10d* (median 4d)
- Transmission through droplets
 - Aerosol spread?
 - Fomites?
 - Fecal- respiratory transmission at an apartment complex in Hong Kong
- Transmission most likely during 2nd week of illness
- Super spreading events

First Reported MERS-CoV Case

- 60 year old Saudi man
- Presented on June 13th with 7d h/o fever and cough; recent shortness of breath
- Increasing blood urea nitrogen (BUN) and creatinine, starting day 3 of admission
- White cell count normal on admission (but 92.5% neutrophils) and increased to a peak of 23,800 cells per cubic millimeter on day 10 with neutrophilia, lymphopenia, and progressive thrombocytopenia

First Case: Chest Radiographs

A: On admission
B: 2 days later



Bilateral enhanced pulmonary hilar vascular shadows (more prominent on the left) and accentuated bronchovascular lung markings. Multiple patchy opacities in middle and lower lung fields

Opacities more confluent and dense

First Case Outcome

- Patient developed acute respiratory distress syndrome (ARDS) and multiorgan dysfunction syndrome
- Died June 24th
- No close contacts with severe illnesses reported

Second Case

- 49 year old Qatari national
- Onset of illness September 3rd with mild respiratory symptoms
- September 9th- admission to Qatar hospital with bilateral pneumonia- subsequent intubation
- September 12th admitted to London ICU with respiratory failure and renal failure
- Fully dependent on ECMO
- History of travel to Saudi Arabia July 31- Aug. 18, where noted to have URI symptoms (and traveling companions)
- History of farm (camels and sheep) exposure, but no history of direct contact with these animals

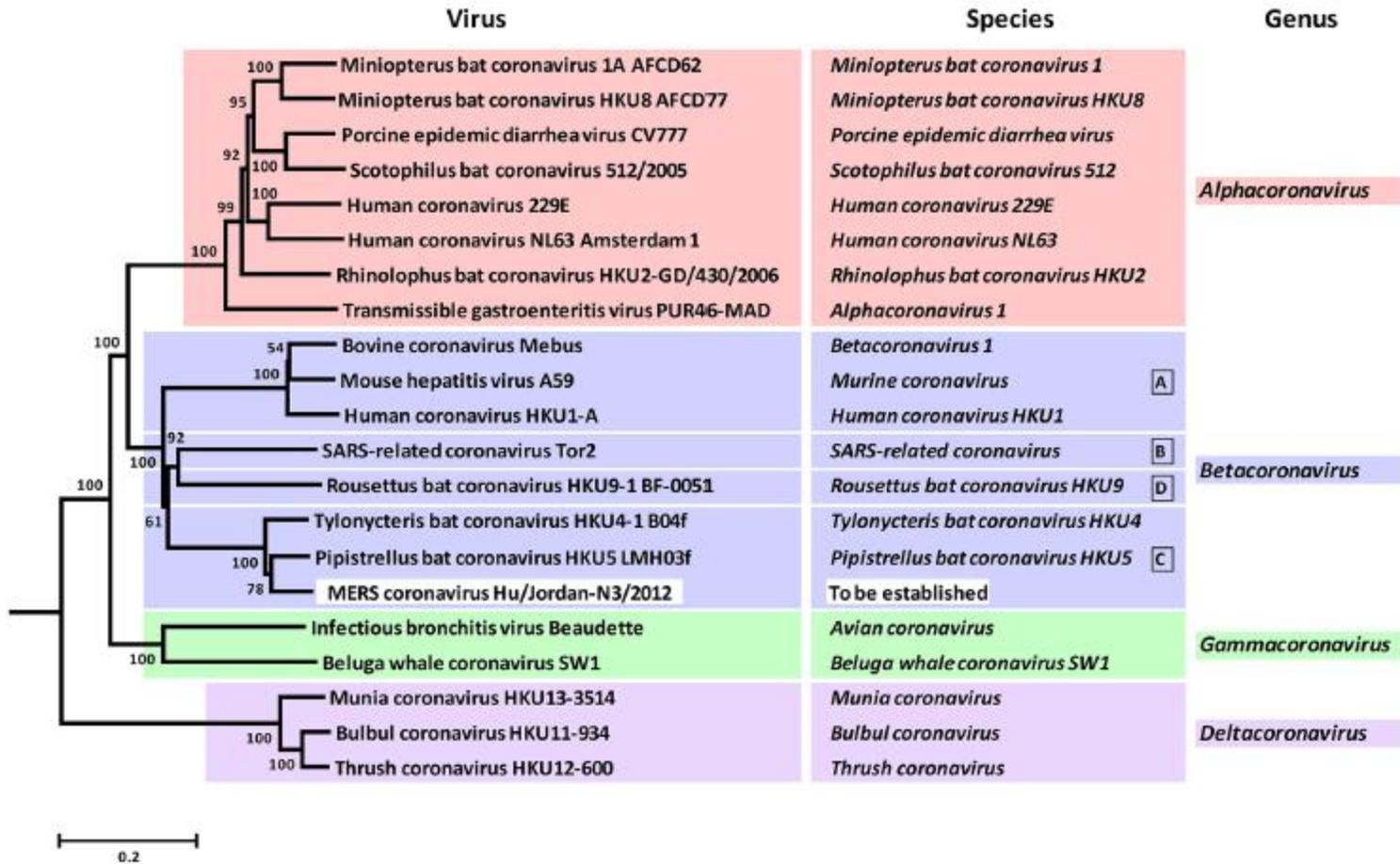
Second Case: Management

- Airborne precautions
- Close contacts monitored for at least 10d
- 64 contacts identified among healthcare personnel (HCP), family, and friends
 - No severe acute respiratory illnesses identified
 - 13 HCP with mild respiratory symptoms
 - 10 HCP negative for MERS-CoV

MERS-CoV: Link

- Virus from second case compared to virus isolated from lung tissue of first case
- 99.5% identity: One nucleotide mismatch over regions (replicase) compared
- Genome sequence: JX869059.1

Middle East Respiratory Syndrome Coronavirus (MERS-CoV)



Emergence of a Novel Virus



Recognition of a novel coronavirus, Saudi Arabia and Qatar



UK family cluster



Healthcare facility cluster, Saudi Arabia



April, 2012

Sept., 2012

Nov., 2012

Feb., 2013

March, 2013

April, 2013

May, 2013

Jordan cluster



1st family cluster, Saudi Arabia



Imported UAE case into Germany



Healthcare facility cluster, France



Saudi Arabia Household Cluster

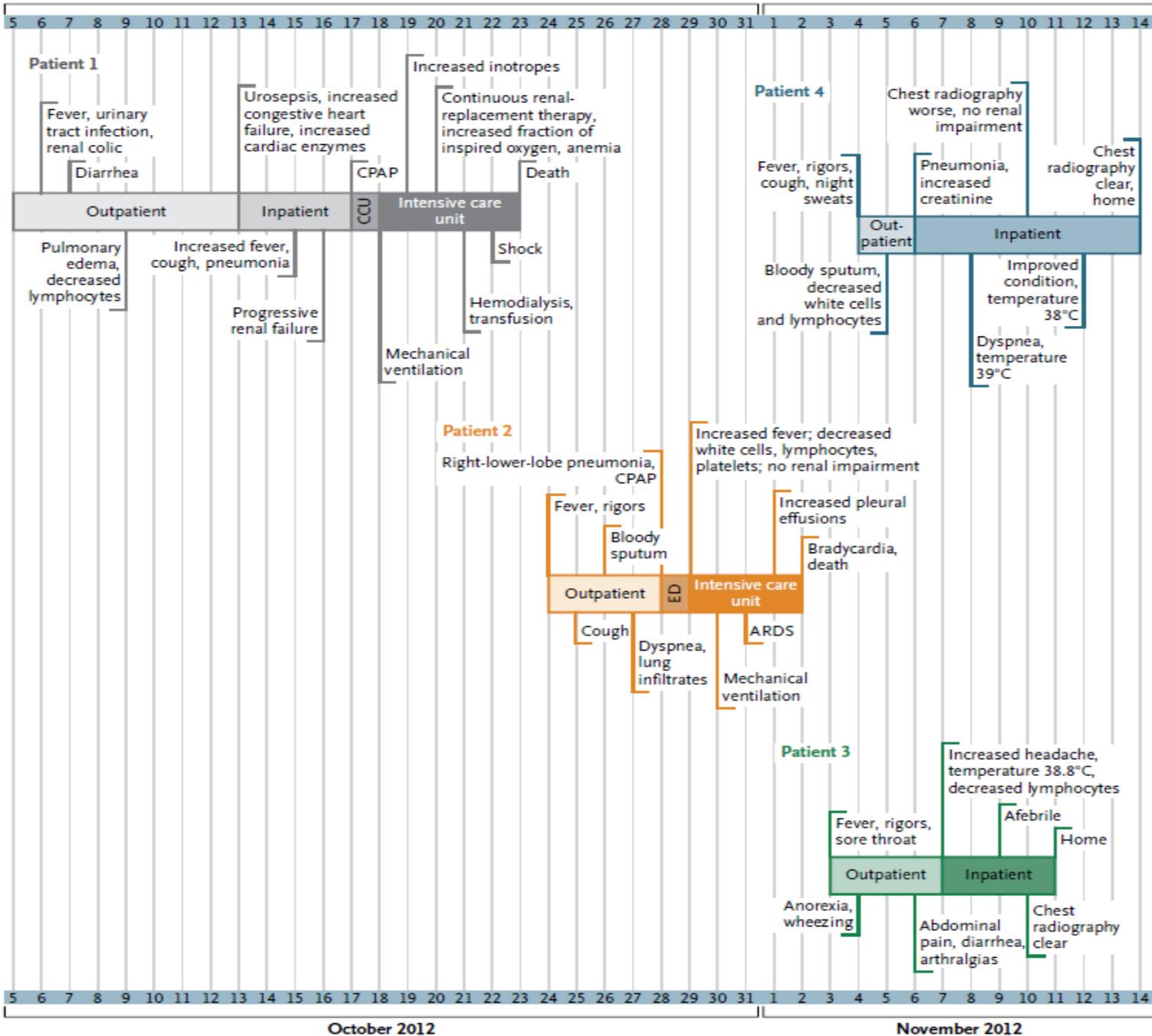
- A cluster of 4 respiratory illnesses in a family who lived in an apartment
 - All males; ages 16-70y
- All hospitalized
- 3 of 4 confirmed with MERS-CoV
- 3 of 4 patients with gastrointestinal symptoms: diarrhea, abdominal pain, anorexia)
- 2 deaths

Saudi Arabia Household Cluster: Virus Detection

- Patient 1: Positive bronchial lavage specimen
- Patients 2 and 4: Sputum positive
- Patient 3's illness milder and no lower respiratory tract specimens available; upper respiratory tract swabs negative

October 2012

November 2012



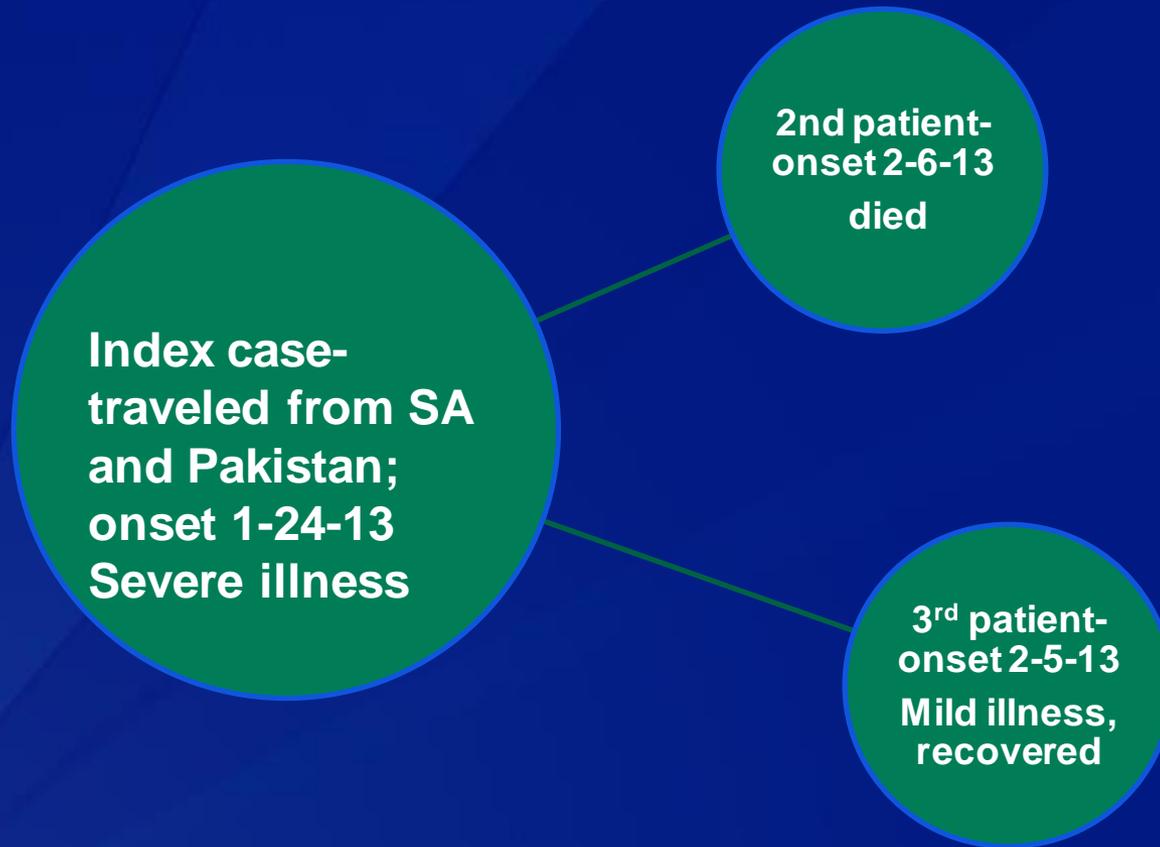
124 healthcare workers remained healthy as of Jan., 2013

Memish ZA et al. NEJM epub May 29, 2013

Jordan Cluster, April, 2012

- 2 confirmed cases reported retrospectively
- Both cases fatal
- Occurred at the same time as a cluster of severe respiratory illness among healthcare workers, N=13

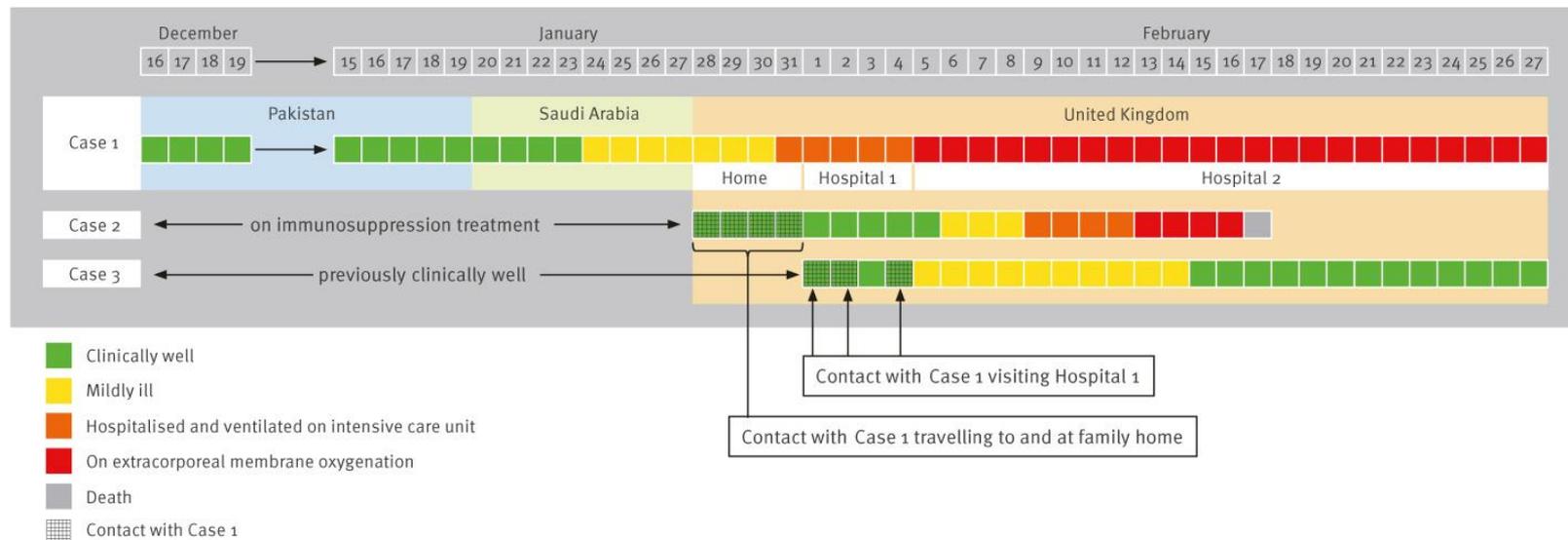
UK Cluster



Timeline of UK Cluster

FIGURE 1

Timeline of three novel coronavirus cases, United Kingdom, December 2012 to February 2013



UK Cluster: Public Health Implications

- Evidence of person-to-person transmission
- Coinfection with influenza (index case) and parainfluenza type 2 (both secondary cases)
- No sustained chains of transmission
- Incubation period may be 1-9 days

Nosocomial Transmission in France, Index Patient

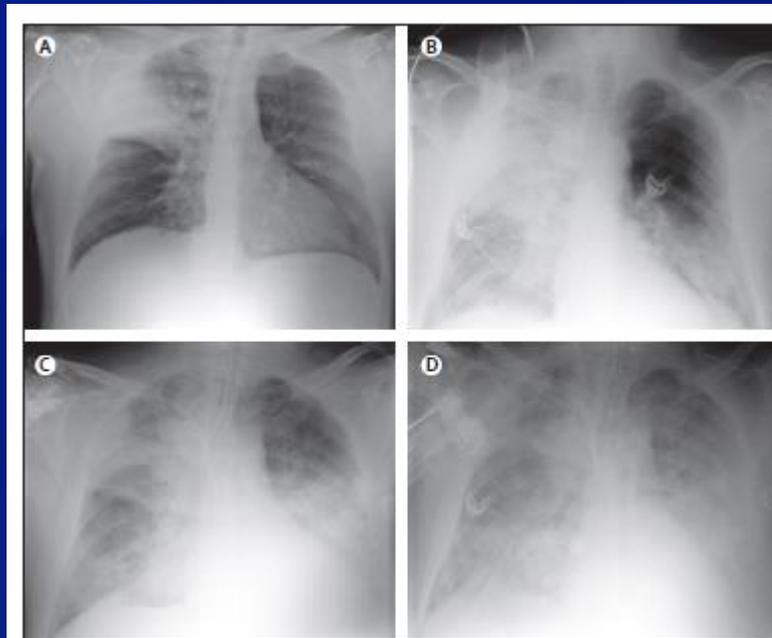
- 64 year old man, returned from travel to Dubai 5 days earlier
- History of renal transplantation
- Onset of symptoms: Diarrhea, fever, chills
- Abdominal CT showed pulmonary infiltrates 2d after onset
- Developed cough and dyspnea 4d after onset; initial NP swab deemed negative, but bronchoalveolar lavage specimen positive
- Respiratory failure, renal failure- death, 36 days after onset of illness

Nosocomial Transmission in France, Patient 2

- 51 year old man with history of myocardial infarction, arterial hypertension, and steroid therapy for histamine-induced angioedema. Also had history of several episodes of deep venous thrombosis
- Shared a hospital room with index patient during day 4-day 7 of index patient's illness (index patient mostly confined to bed, while Patient 2 moved around)
- Shared bathroom
- NP swabs inconclusive; induced sputum positive for MERS-CoV
- No aerosolizing procedures performed for index patient
- No suspicion of MERS-CoV

Radiographs of Patient 2

A. Consolidation of right upper lobe, 1 day after onset of illness



B. 4 days after onset of illness, Ground glass opacity and consolidation of left lower lobe

C and D. Bilateral ground-glass opacities and consolidation, 7 days and 9 days after onset of illness, respectively

Figure 2: Radiographs of the chest of patient 2
(A) Chest radiograph obtained on May 9 showed a systematic consolidation of the upper right lung lobe. (B) On May 12, ground-glass opacity and consolidation could also be seen in the lower left lobe. Bilateral ground-glass opacities and consolidation were noted afterwards on May 15 (C) and May 17 (D).

Timeline of French Cluster

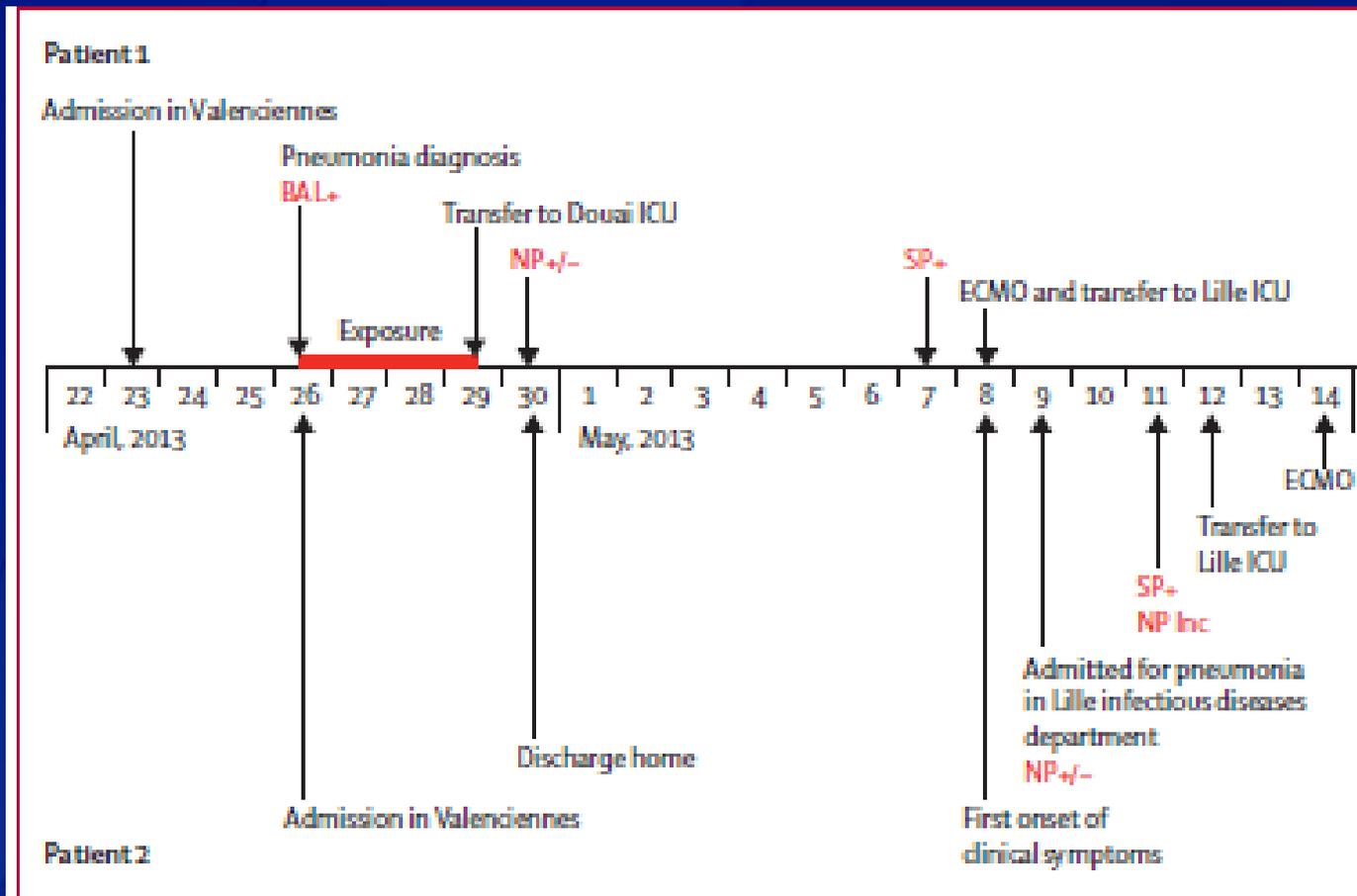


Figure 3: Timeline of pertinent exposure, dates of illness, and virological findings in patients 1 and 2. Exposure (bold red line) shows the period during which the two patients shared the same room. BAL=bronchoalveolar lavage. NP=nasopharyngeal swab. SP=sputum. Inc=Inconclusive. ECMO=extracorporeal membrane oxygenation. ICU=intensive-care unit.

French Cluster: Public Health Implications

- Nosocomial transmission
- Initial presentation without respiratory symptoms
- Incubation period up to 9-12 days
- Lower respiratory tract specimens may be preferred samples for detection of MERS-CoV

MERS-CoV Outbreak in Saudi Arabia

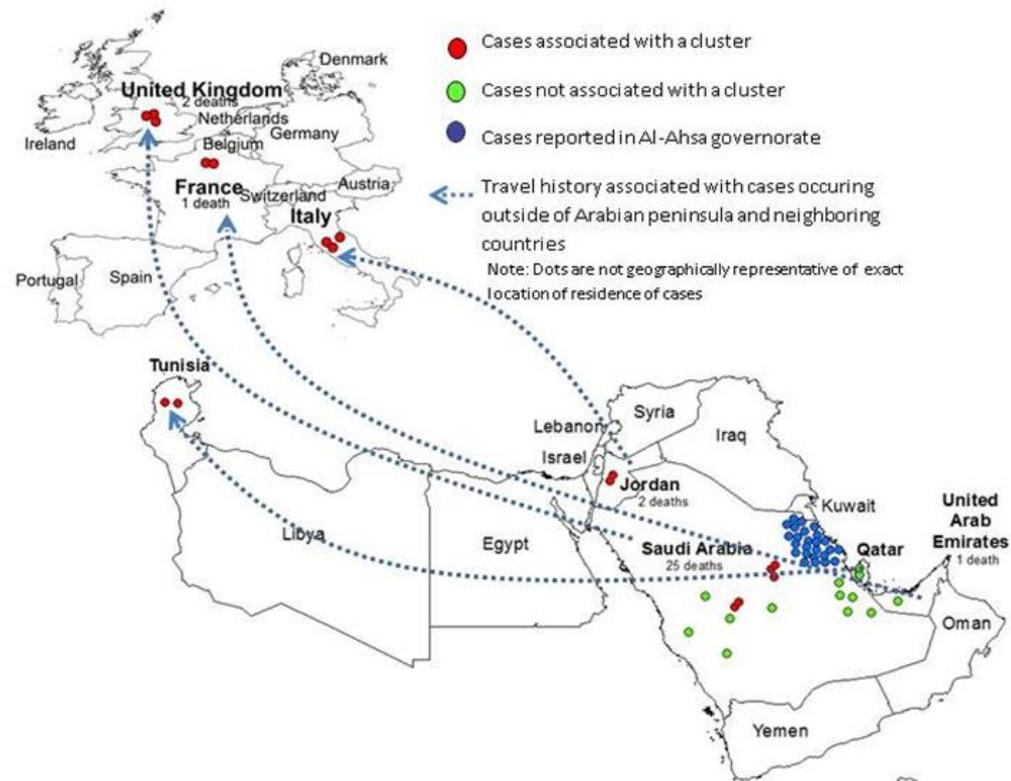
April – May 2013

- Al-Ahsa governorate in eastern region
- Cluster currently being investigated
- 25 confirmed cases, 14 confirmed deaths
- 18 males, 7 females; Ages 14 - 94 years, median age: 58
- Initial cases associated with one hospital but now also:
 - Family contacts
 - Healthcare workers
 - Cases with no link to hospital
- Most cases with comorbidities

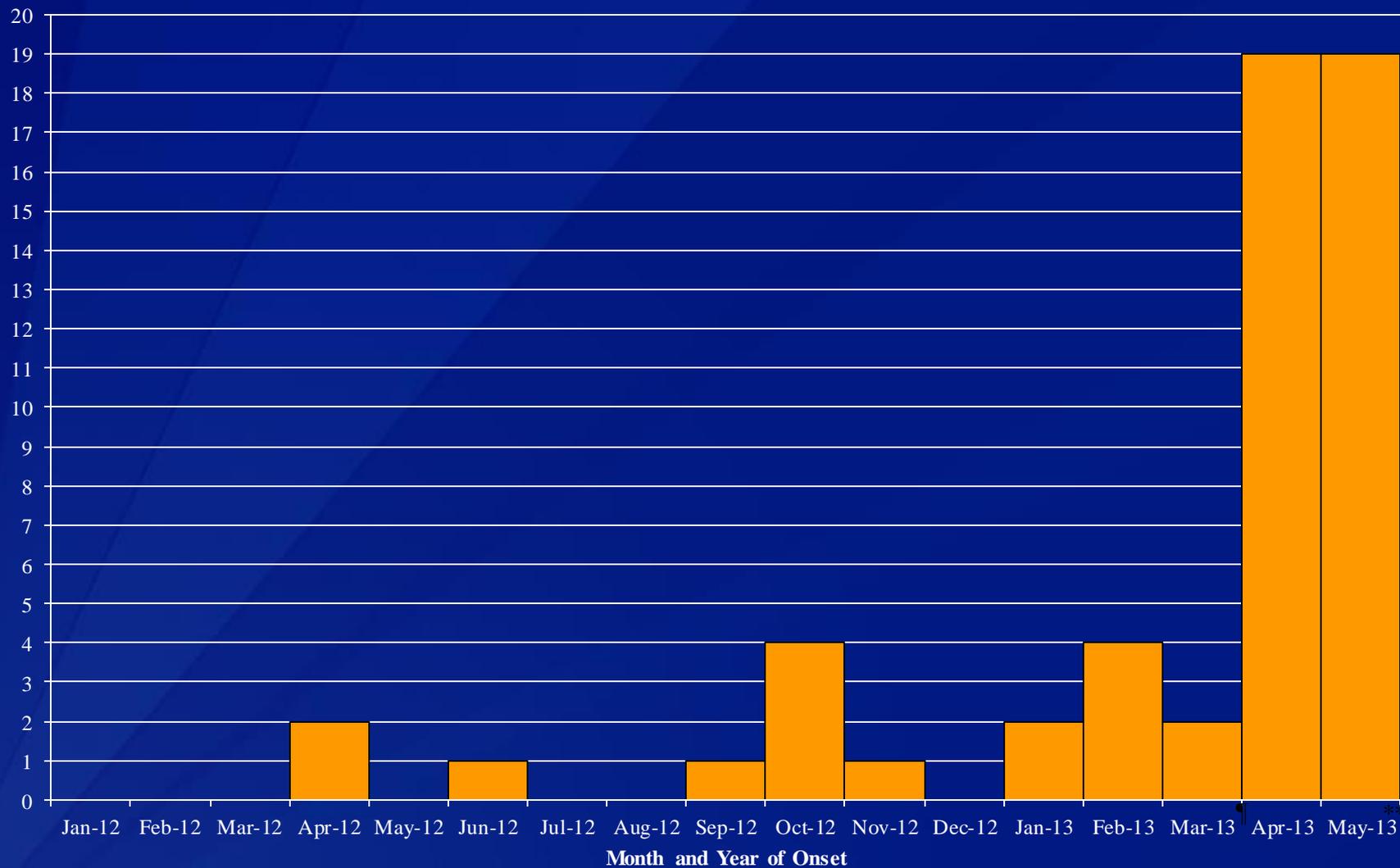
MERS-CoV- Overall Epidemiology

- Approximately 50% mortality rate
- Onsets between April 2012 and May 29, 2013
- Median age ~ 56 y
 - 2 pediatric cases reported
- Male predominance
- Most cases reported with comorbidities
- Cases by country of residence:
 - Saudi Arabia 40, UK 3, Jordan 2, Qatar 2, UAE 1, France 2, Tunisia 2, Italy 3
 - Three were returning travelers, 3 medical transfers

Confirmed cases of MERS-CoV (n=55) and history of travel from the Arabian Peninsula



MERS-CoV Confirmed cases 2012-2013



2012

2013

CDC Case Definition: Surveillance

- A Patient Under Investigation (PUI) is a person with
 - an acute respiratory infection, which may include fever ($\geq 38^{\circ}\text{C}$, 100.4°F) and cough; AND
 - suspicion of pulmonary parenchymal disease (e.g., pneumonia or acute respiratory distress syndrome based on clinical or radiological evidence of consolidation); AND
 - history of travel from the Arabian Peninsula or neighboring countries within 14 days; AND
 - not already explained by any other infection or etiology, including all clinically indicated tests for community-acquired pneumonia according to local management guidelines.

CDC Case Definition: Surveillance

- Persons who develop severe acute lower respiratory illness of known etiology within 14 days after travel from the Arabian Peninsula or neighboring countries but do not respond to appropriate therapy; OR
- Persons who develop severe acute lower respiratory illness who are close contacts of a symptomatic traveler who developed fever and acute respiratory illness within 14 days after travel from the Arabian Peninsula or neighboring countries. Close contact is defined as providing care for the ill traveler (e.g., a healthcare worker or family member), or having similar close physical contact; or stayed at the same place (e.g. lived with, visited) as the traveler while the traveler was ill.

CDC Case Definition: Close Contact

- Close contact is defined as:
 - Any person who provided care for the patient, including a healthcare worker or family member, or had similarly close physical contact.
 - Any person who stayed at the same place (e.g. lived with, visited) as the patient while the patient was ill.

CDC Case Definitions:

Probable Case

- Any person who-
 - meets the criteria above for “[Patient Under Investigation](#)” and has clinical, radiological, or histopathological evidence of pulmonary parenchyma disease (e.g. pneumonia or ARDS), but no possibility of laboratory confirmation exists, either because the patient or samples are not available or there is no testing available for other respiratory infections, AND
 - is a close contact with a laboratory-confirmed case, AND
 - has illness not already explained by any other infection or etiology, including all clinically indicated tests for community-acquired pneumonia according to local management guidelines.
- OR any person with-
 - severe acute respiratory illness with no known etiology, AND
 - an epidemiologic link to a confirmed MERS case.

Confirmed Case

- A person with laboratory confirmation of infection with MERS-CoV.

Interim Infection Prevention and Control Recommendations for Hospitalized Patients

Alexander Kallen, MD, MPH

Medical Officer
Division of Healthcare Quality Promotion
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

Interim Infection Prevention and Control Recommendations for Hospitalized Patients

- Standard, contact, and airborne precautions are recommended for management of hospitalized patients with known or suspected MERS-CoV infection
- These recommendations are consistent with those recommended for the coronavirus that caused severe acute respiratory syndrome (SARS)
- As information becomes available, these recommendations will be re-evaluated and updated as needed

Infection Control Recommendations for Hospitalized Patients

- These recommendations are for hospitalized patients who meet the case definition and are based on the following issues:
 - Poorly characterized clinical signs and symptoms, and a suspected high rate of morbidity and mortality among infected patients
 - Unknown modes of transmission of MERS-CoV
 - Lack of a vaccine and chemoprophylaxis
 - Evidence of limited, not sustained, human-to-human transmission
 - Absence of confirmed or probable MERS-CoV cases in the United States

Patient Placement

- Airborne Infection Isolation Room (AIIR)
 - If an AIIR is not available, the patient should be transferred as soon as is feasible to a facility where an AIIR is available.
 - Pending transfer, place a facemask on the patient and isolate him/her in a single-patient room with the door closed.
 - The patient should not be placed in any room where room exhaust is recirculated without high-efficiency particulate air (HEPA) filtration.
- Once in an AIIR, the patient's facemask may be removed.
- When outside of the AIIR, patients should wear a facemask to contain secretions.

Patient Placement

- Limit transport and movement of the patient outside of the AIIR to medically-essential purposes.
- Implement staffing policies to minimize the number of personnel who must enter the room.

Personal Protective Equipment (PPE) for Healthcare Personnel (HCP)

- Gloves
- Gowns
- Eye protection (goggles or face shield)
- Respiratory protection that is at least as protective as a fit-tested NIOSH-certified disposable N95 filtering facepiece respirator

Personal Protective Equipment (PPE) for Healthcare personnel (HCP)

- Recommended PPE should be worn by HCP upon entry into patient rooms or care areas.
- Upon exit from the patient room or care area, PPE should be removed and either:
 - Discarded, or
 - For re-useable PPE, cleaned and disinfected according to the manufacturer's reprocessing instructions.

Environmental Infection Control

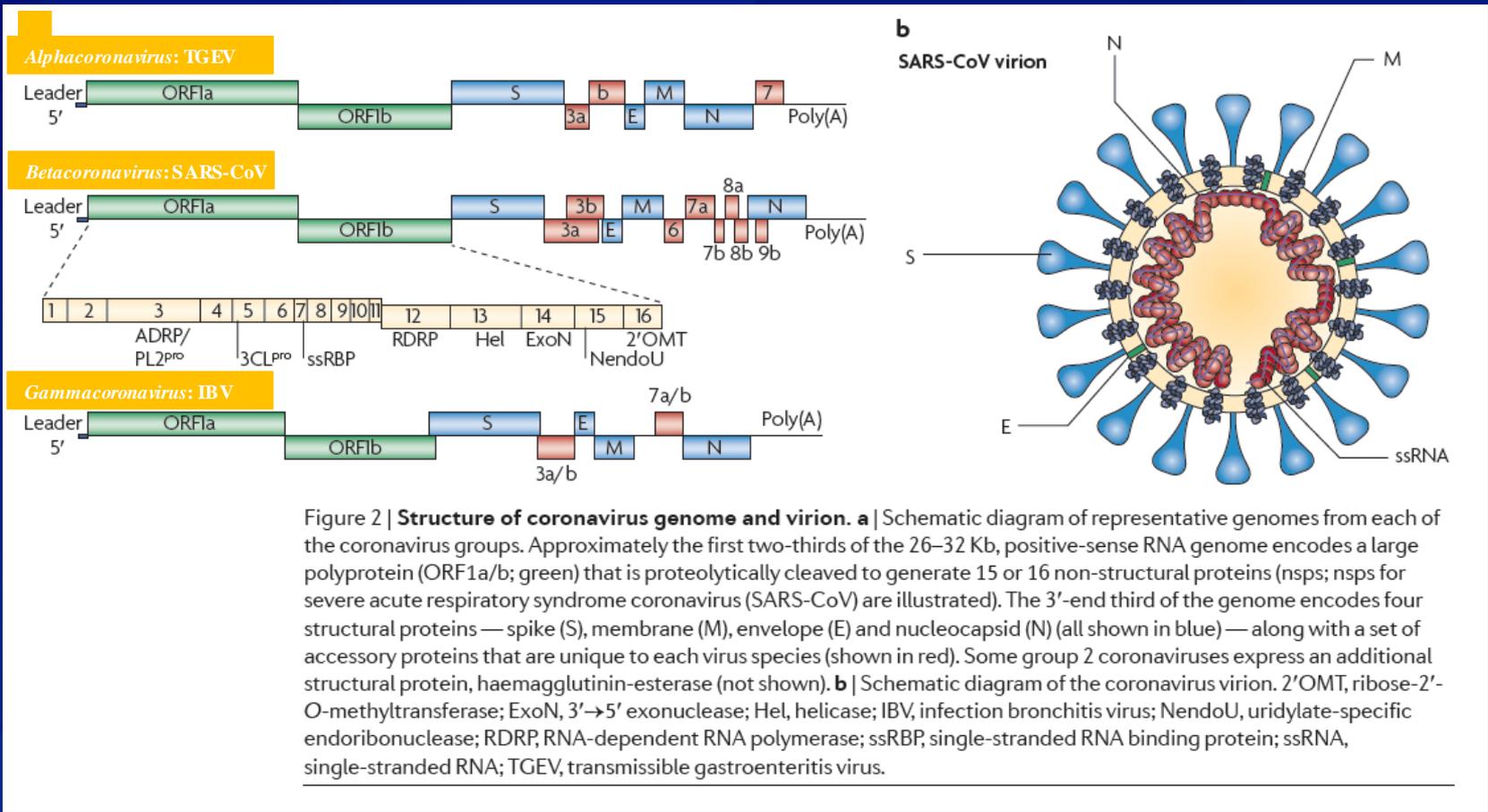
- Follow standard procedures, per hospital policy and manufacturers' instructions, for cleaning and/or disinfection of:
 - Environmental surfaces and equipment
 - Textiles and laundry
 - Food utensils and dishware

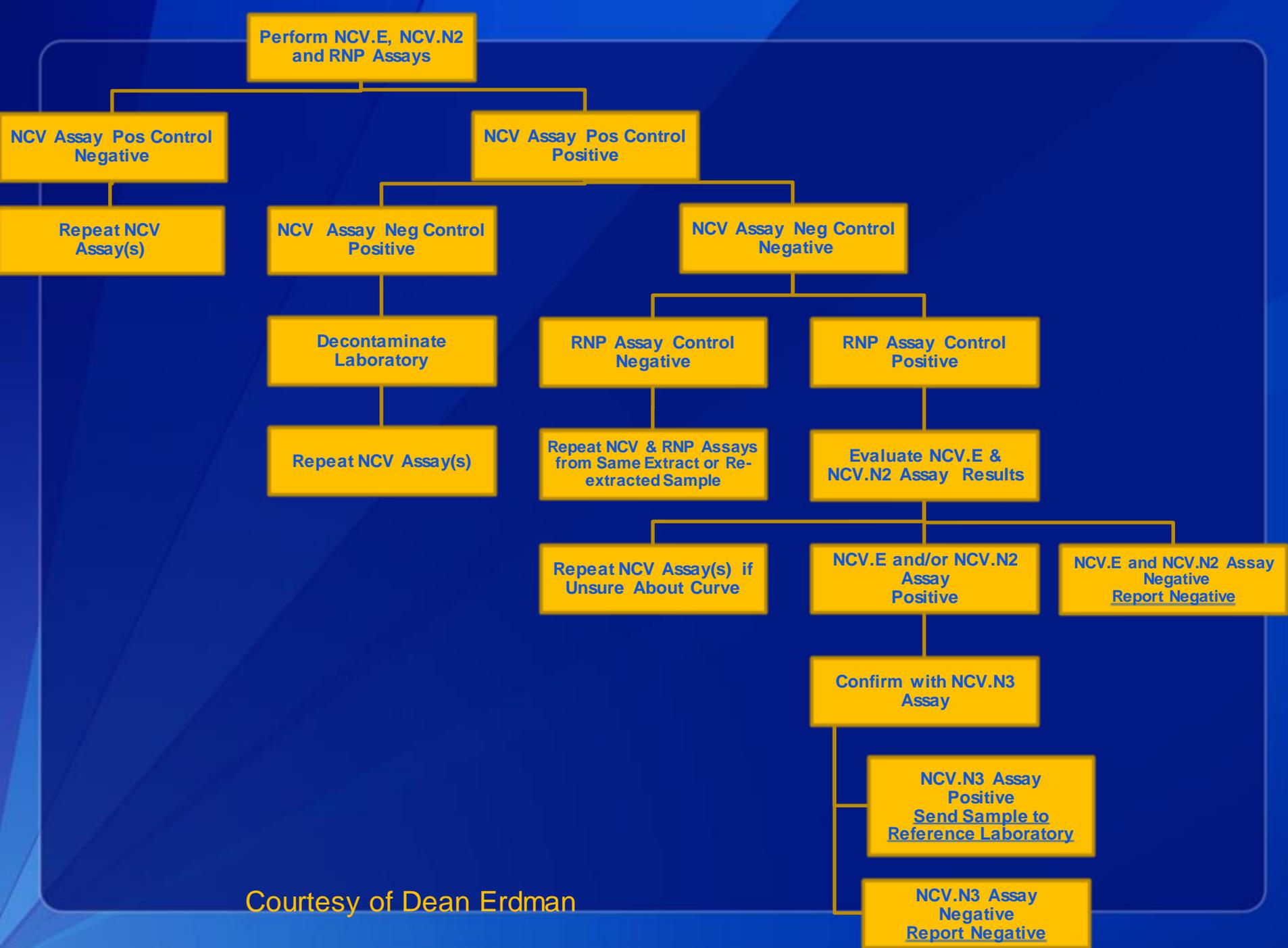
Laboratory Testing

- Lower respiratory specimens (sputum, bronchoalveolar lavage, endotracheal) are a priority respiratory specimen for real time reverse transcription polymerase chain reaction (RT-PCR) testing
- Respiratory (lower and upper tracts), stool, and serum specimens
- Specimen collection at different times

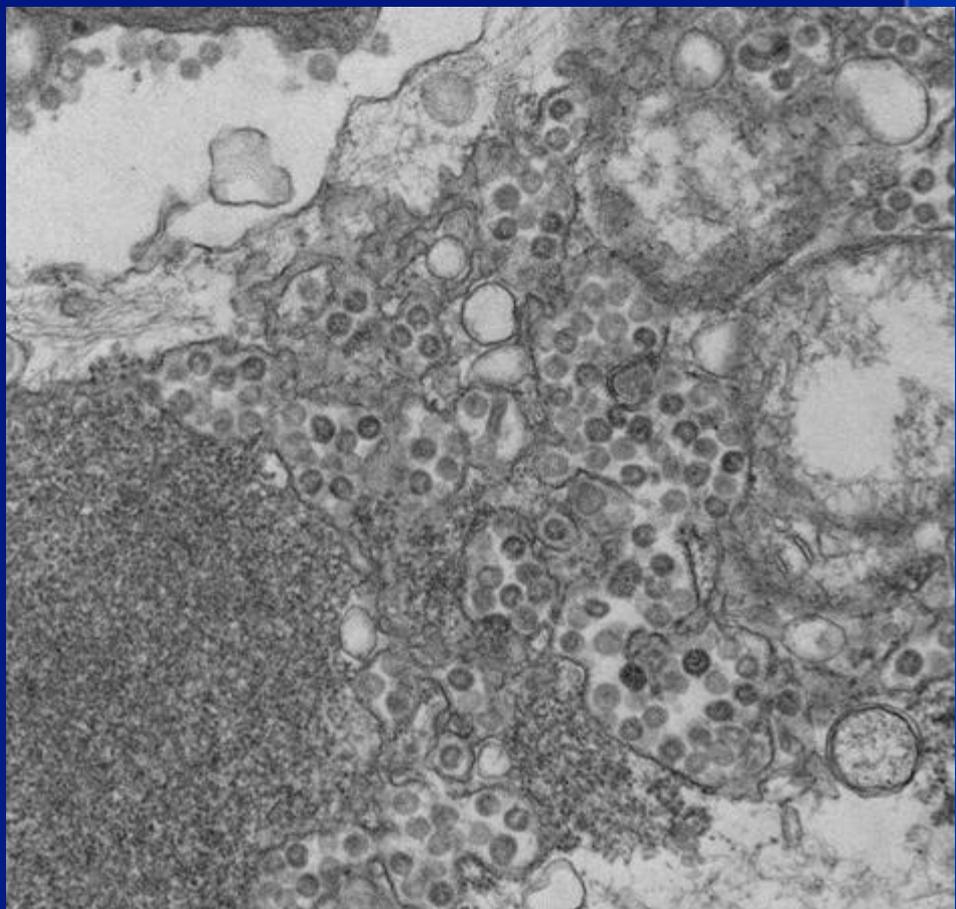
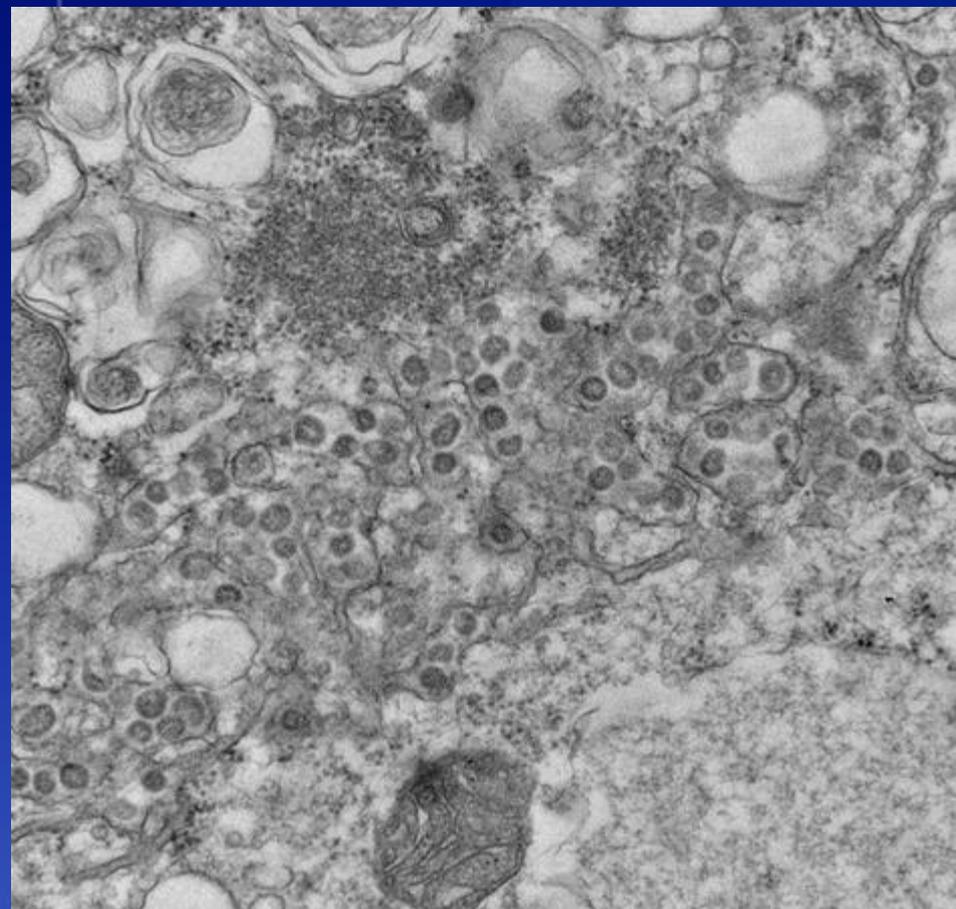
Emergency Use Authorization

- FDA issued an EUA on June 5, 2013, to authorize use of CDC's "Novel coronavirus 2012 real-time reverse transcription–PCR assay" to test for MERS-CoV in clinical respiratory, blood, and stool specimens.
- Assay will be deployed to Laboratory Response Network (LRN) laboratories in all 50 states over the coming weeks.

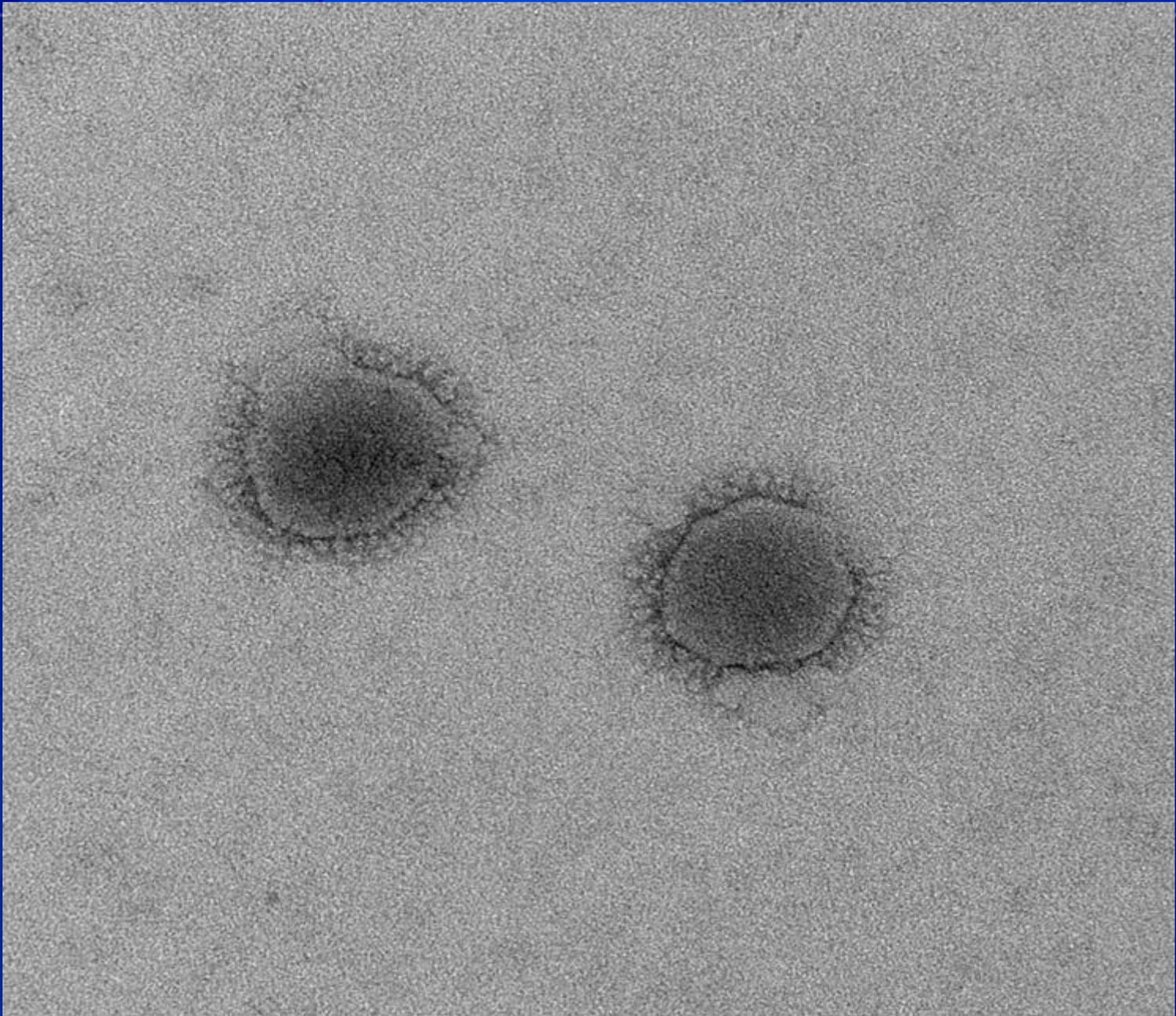




Courtesy of Dean Erdman



CS Goldsmith, MG Metcalfe, A Tamin

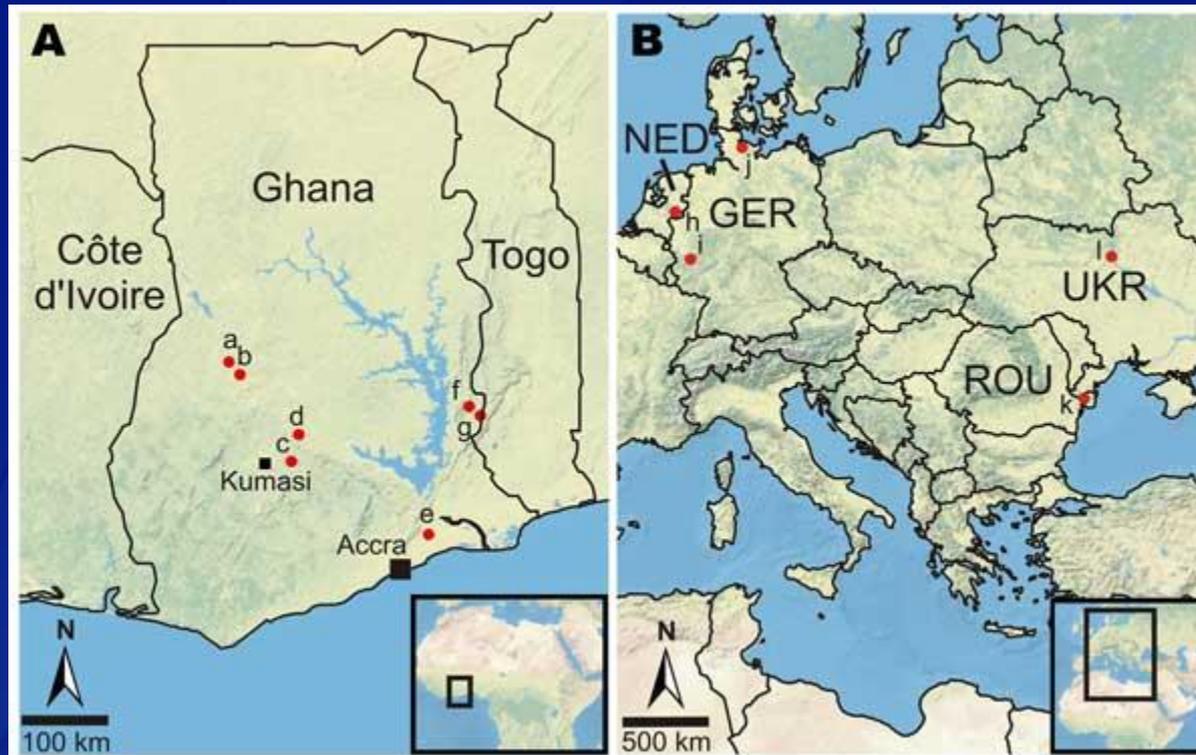


CS Goldsmith, MG Metcalfe, A Tamin

Approach to Serology

- Identify and generate candidate CoV antigens
 - Using proteins from similar bat viruses
- Develop ELISA-based assay
- Evaluate assay with an extensive panel of negative (specificity) and positive sera (sensitivity)

Location of Bat Sampling Sites



A- Ghana
B- Europe

Therapeutics

- No vaccines developed as of yet
- No antivirals identified as of yet
- Treatment is supportive

MERS-CoV Snapshot: June, 2013

- May cause mild to severe illness
- Evidence of person-to-person transmission
- Nosocomial spread with healthcare personnel transmission
- Focus in the Arabian Peninsula
- ~ 50% mortality rate
- No cases identified in the U.S.

Conclusions:

- MERS-CoV is a different virus than SARS-CoV, but also virulent
- More reported cases in past 2 months
- Persons with underlying health conditions at increased risk of severe disease
 - And transmission?

MERS Coronavirus Issues

- Human surveillance for additional cases
 - Laboratory diagnostics
 - Surveillance for severe acute respiratory infections
- Need for more investigations to understand human-to-human routes of exposure
- Animal surveillance
- Geography
- Management of patients under investigation
 - Rule out other etiologies
 - Infection control
 - Therapeutics

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



Centers for Disease Control and Prevention Atlanta, Georgia

Thank you for joining!

Please email us questions at coca@cdc.gov

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Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Information and Guidance for Clinicians

= No Continuing Education

Date: Thursday, June 13, 2013

Time: 2:00 - 3:00 pm (Eastern Time)

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Presenter(s):

Susan Gerber, MD
Medical Epidemiologist
Division of Viral Diseases
National Center for Immunization and Respiratory Disease
Centers for Disease Control and Prevention

Alexander Kallen, MD, MPH
Medical Officer
Division of Healthcare Quality Promotion
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

Overview:

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a newly identified virus that can cause severe acute respiratory illness and death. MERS cases have been linked to the Middle East, and there is documented spread of the virus internationally. So far, no cases of MERS have been reported in the United States. However, clinicians need to remain vigilant. Epidemiologic investigations have demonstrated that this unique virus spreads from person to person during close contact, such as within families and healthcare facilities. Clinicians have a critical role in recognizing and managing suspect cases of MERS. During this COCA call, a CDC subject matter expert will discuss the clinical signs, epidemiology and infection control recommendations for MERS-CoV.

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