Clinical and laboratory findings of the first imported case of Middle East respiratory syndrome coronavirus (MERS-CoV) into the United States

Minal Kapoor, Kimberly Pringle, Alan Kumar, Stephanie Dearth, Lixia Liu, Judith Lovchik, Omar Perez, Pam Pontones, Shawn Richards, Jaime Yeadon-Fagbohun, Lucy Breakwell, Nora Chea, Nicole J. Cohen, Eileen Schneider, Dean Erdman, Lia Haynes, Mark Pallansch, Ying Tao, Suxiang Tong, Susan Gerber, David Swerdlow, Daniel R. Feikin

Division of Infectious Diseases (Kapoor) and Department of Emergency Medicine (Kumar), Community Hospital, Munster, Indiana; Indiana State Department of Health, Indianapolis, Indiana (Dearth, Liu, Lovchik, Perez, Pontones, Richards, Yeadon-Fagbohun); Epidemic Intelligence Service, Division of Scientific Education and Professional Development (Pringle, Breakwell, Chea), Division of Global Migration and Quarantine, National Center for Emerging and Zoonotic Infectious Diseases (Cohen), Division of Viral Diseases (Schneider, Erdman, Haynes, Pallansch, Tao, Tong, Gerber, Feikin), National Center for Immunization and Respiratory Diseases (Swerdlow), Center for Disease Control and Prevention, Atlanta, Georgia

Contact: Daniel Feikin, 1600 Clifton Rd. MS-A34, Atlanta, GA 30030. drf0@cdc.gov. 4046394443

Summary -- The first U.S. case of MERS-CoV was confirmed on May 2, 2014 in a 65-year old physician who worked in Saudi Arabia and presented to an Indiana hospital on day of illness 11. He had bilateral pneumonia and recovered fully.
Abstract.

Background. The Middle East respiratory syndrome coronavirus (MERS-CoV) was discovered September 2012 in the Kingdom of Saudi Arabia (KSA). The first U.S. case of MERS-CoV was confirmed on May 2, 2014.

Methods. We summarize the clinical symptoms and signs, laboratory and radiologic findings, and MERS-CoV-specific tests.

Results. The patient is a 65 year-old physician who worked in a hospital in KSA where MERS-CoV patients were treated. His illness onset included malaise, myalgias and low-grade fever. He flew to the U.S. on day of illness (DOI) 7. His first respiratory symptom, a dry cough, developed on DOI 10. On DOI 11, he presented to an Indiana hospital dyspneic, hypoxic, and with a right lower lobe infiltrate on chest x-ray. On DOI 12 his serum tested positive by real-time reverse transcription-polymerase chain reaction (rRT-PCR) for MERS-CoV and showed high MERS-CoV antibody titers, while his nasopharyngeal swab was rRT-PCR-negative. Expectorated sputum was rRT-PCR-positive the following day with a high viral load (5.31 x 10^6 copies/ml). He was treated with antibiotics, intravenous immunoglobulin and oxygen by nasal cannula. He was discharged on DOI 22. The genome sequence was similar (>99%) to other known MERS-CoV sequences, clustering with those from KSA in June-July 2013.
Conclusions. This patient had a prolonged nonspecific prodromal illness before developing respiratory symptoms. Both sera and sputum were rRT-PCR-positive, when nasopharyngeal specimens were negative. U.S. clinicians must be vigilant for MERS-CoV in patients with febrile and/or respiratory illness with recent travel to the Arabian Peninsula, especially among health-care workers.
The Middle East respiratory syndrome coronavirus (MERS-CoV) was first reported in September 2012 in a Saudi Arabian patient with pneumonia. (1) As of May 12, 2014, 536 MERS-CoV patients had been confirmed by WHO, all related to residence, recent travel or contact with a recent traveler from the Arabian Peninsula. (2) Initial reports of clinical course among MERS-CoV case-patients from Saudi Arabia revealed high case-fatality proportions (3, 4), but subsequent increases in testing of symptomatic and asymptomatic persons as part of contact investigations has revealed that approximately one-fifth to one-quarter of cases are mildly symptomatic or asymptomatic. (5, 6) As of April 2014 travel-associated cases have been detected in eight countries outside the Arabian Peninsula. (7) We report here on the clinical course and laboratory findings from the first case of MERS-CoV in the U.S.

Methods.

Clinical history and physical findings.

The patient’s clinical history and possible exposures to MERS-CoV were elicited by direct interview with the patient and family members. His physical findings, and laboratory and radiologic findings were extracted from his medical record.

MERS-CoV laboratory testing and genome sequencing

Specimens were drawn at the hospital and sent on ice to the Indiana Department of Health (IDH) laboratory or CDC. Initial testing by real-time reverse transcription-polymerase chain reaction (rRT-PCR) was performed at the IDH laboratory with confirmatory sequencing
performed at CDC. The CDC rRT-PCR screening assay consists of two signatures that target a region upstream of the MERS-CoV envelope protein gene (upE) and the nucleocapsid gene (N2).(8) A positive test result with either or both assays is then confirmed with a third rRT-PCR assay also targeting the nucleocapsid gene (N3). Serology was done using a recombinant MERS-CoV nucleocapsid protein based ELISA developed by CDC. This ELISA was developed using a modified version of the HKU5.2 N ELISA as described.(9) Briefly, sera were considered positive when the optical density (OD) values were at or above the 0.36 cut-off value (mean absorbance at 405nm of sera from U.S. blood donors plus 3 standard deviations). The overall specificity of the assay was determined after screening 555 serum samples from donors in the U.S., the Middle East and persons with other non-MERS respiratory infections (e.g. HCoV-OC43, HCoV-229E, SARS-CoV, HCoV-NL63, rhinovirus, HMPV, H1N1). The assay specificity was 98.1% (544/555). Serum from HKU1 human serum was not available for evaluation; however, HKU1 mouse hyper immune serum did not cross-react with the MERS-CoV N protein. At a screening dilution of 1:400, sera with OD values at or near the cut-off were titered with serial two to four-fold dilutions (1:100-1:6400). The assay sensitivity was determined by screening a limited number of serum samples from individuals with confirmed MERS-CoV infection (sera provided by Public Health England, Robert Koch Institute and the Jordan Ministry of Health).

Confirmatory testing for MERS-CoV specific antibodies was done on all positive ELISAs by MERS-CoV immunofluorescence and microneutralization assays.(10) Both confirmatory assays were evaluated using similar panels of sera as described above with similar specificities. Serologic testing was done at CDC.
Full genome sequence was determined from RNA obtained directly from sputum collected on day of illness (DOI) 13 by generating tiling amplicons across the virus genome followed by Sanger sequencing. The sequence was deposited into the GenBank database under accession number KJ813439 named Indiana/USA-1_Saudi Arabia_2014.

Results

Clinical History

The patient is a 65 year-old male physician living in the Kingdom of Saudi Arabia (KSA) who reported onset of fatigue and mild myalgia on April 18, 2014 (DOI 1), which curtailed his daily exercise program. He reported a low grade fever of < 38.0°C but no respiratory symptoms. On DOI 1, the patient began acetaminophen and naproxen for myalgias and also began a five-day course of ciprofloxacin due to a history of prostatitis with no improvement. He went to the Emergency Department in KSA on DOI 2, where he had a normal complete blood count (CBC) and normal CXR by report. He was not tested for MERS-CoV.

The patient flew from KSA to London on April 24 (DOI 7) and then from London to Chicago, arriving the same day. He took a bus to his family’s home in Indiana. Upon arrival, the patient’s sister noticed that he appeared fatigued, which she attributed to jet lag. On DOI 8, the patient recorded an oral temperature of 38.6°C, and family suggested that he start oseltamivir for possible influenza. A non-productive cough developed on DOI 10, and on DOI 11 he developed
visible dyspnea and tachypnea. He used an albuterol meter-dosed inhaler on both days without improvement, which prompted his sister to drive him to the ED of a local hospital.

Past Medical History

The patient has hypertension and coronary artery disease for which he had two stents placed 5 and 17 years ago. He also has benign prostatic hypertrophy and had prostatitis 2 years ago. His medications include valsartan, atenolol, atorvastatin, and clopidogrel. He does not smoke or drink alcohol.

Exposure history

The patient works full-time at a large hospital in Riyadh. He attends patients in both the outpatient and inpatient setting, including the Emergency Department. He does not recall directly treating any patients with known MERS-CoV infection from April 1-23, but was aware of MERS-CoV positive patients in the hospital during the month of April. He entered the rooms of several intubated patients as part of his work, but did not have extensive direct contact with these patients. He recalls examining a few patients while they were undergoing nebulizer treatments, while wearing a surgical mask. He denies being present during intubations or respiratory suctioning. His last day of work was April 23, the day before he travelled.
In Saudi Arabia, he lives with three family members and a household employee, none of whom were ill in the two weeks before his symptom onset. The patient denied contact with known MERS-CoV patients outside of work. He also denied physical contact with or consumption of camels or camel products.

Physical exam and clinical course.

On presentation to the Emergency Department of an Indiana hospital on April 28 (DOI 11), the patient had an oral temperature of 37.1°C, blood pressure 158/93 mm Hg, heart rate 83 beats/minutes, respiratory rate 20 breaths/minute and oxygen saturation (O2Sat) of 90% on room air (RA). Pulmonary exam revealed right lower quadrant rhonchi with decreased breath sounds. Cardiovascular, abdominal, skin, neurological and musculoskeletal exams were unremarkable.

His admission laboratory data were remarkable for lymphopenia (total lymphocyte count of 0.81 x 10⁹/L), mildly elevated liver function tests, slight hyponatremia, and mildly elevated inflammatory markers (Table 1). Other laboratory results were within normal limits. His CXR on admission showed right lower lobe infiltrates (figure 1a).

The patient was initially placed on 2 L/min of O₂ with nasal cannula (NC), given antibiotics (vancomycin, piperacillin/tazobactam) for hospital acquired pneumonia, and admitted to the medical floor. The patient had a maximum temperature of 38.6°C on DOI 12, when his O₂
requirement increased to 6L/min. A CT of the chest from DOI 12 showed bilateral infiltrates predominantly in the lower lobes (Figure 2).

On DOI 13, levofloxacin was added for coverage of atypical pneumonia pathogens given his continued fevers, but was replaced with ceftriaxone on DOI 14 when his Legionella and Mycoplasma pneumoniae tests returned negative. On DOI 14, the patient was afebrile and had a decreasing O₂ requirement (5L/min) while maintaining an O₂Sat of 95%. He also received two doses of 100mg/kg of Intravenous Immunoglobulin on DOI 14 and 15. On DOI 16, the patient was thought to have volume overload; a CXR showed worsening bilateral infiltrates and he had an increasing O₂ requirement to 10L/min. The same day furosemide was started with brisk diuresis via a Foley catheter, and the O₂ was weaned rapidly to 6 L/min, and oral antibiotics (linezolid and levofloxacin) were started. On DOI 18 the patient no longer required oxygen (O₂Sat of 96-97% on RA), and had an improving CXR on DOI 21(Figure 1b).

His total lymphocyte count remained low throughout the hospital stay with a nadir of 0.69 x 10⁹/L and a discharge value of 1.44 x 10⁹/L. All other elements of the CBC and electrolytes, including renal function, remained within normal limits on subsequent testing. He had several other microbiology tests apart from MERS-CoV testing, including a negative blood culture from DOI 11, negative sputum culture from DOI 12, negative multiplex-PCR for common respiratory pathogens (Biofire Diagnostics, Utah) from April 29, negative urine antigen tests for pneumococcus, Mycoplasma pneumoniae and Legionella pneumophila from DOI 12.
The patient was discharged home in stable condition on DOI 22.

**MERS-CoV testing and genome sequencing**

The patient was initially positive by rRT-PCR for MERS-CoV in the serum at the first collection on April 29 (DOI 12), although the nasopharyngeal (NP) sample was negative on that date. The serum antibody titer was 1:3200. The patient had 3 additional positive samples – sputum (DOI 13), oropharyngeal swab (DOI 14) and plasma (DOI 15) (Table 2)(8). The viral load in sputum on DOI 13 was $5.31 \times 10^6$ copies/ml. On DOI 16 viral load decreased to $1.26 \times 10^5$ copies/ml in the sputum sample, and antibody titers were greater than 1:6400. Antibody titers remained high until the last day of collection (DOI31). Stool and urine tested negative for MERS-CoV. To date, attempts to culture the virus from sputum (DOI 13) sample have been unsuccessful.

The genome sequence (30123 nt) was similar (>99%) to other known MERS-CoV sequences and clustered most closely with human derived MERS-CoV strains obtained in Riyadh and Hafr-Al-Batin from summer 2013 (Figure 3 and Figure S1).

**Infection control procedures**

The patient spent 2.5 hours in the Emergency Department, although the entire time was spent in a private triage room. He was admitted to the General Medical floor into a private room without airborne or contact precautions for approximately 20 hours. He was placed on airborne
precautions on DOI 12 (Hospital Day 2) but remained in a private room that was not negative pressure relative to the hallway. On DOI 13 contact precautions were added and the patient was moved to a negative pressure room; these precautions were maintained throughout the remainder of his hospital stay.

Discussion.

We report on the first case of MERS-CoV in the United States. There are several aspects of this patient’s clinical presentation and course that provide insight into MERS-CoV disease. First, he had a relatively prolonged period of systemic symptoms of malaise, myalgia and low-grade fever, which lasted ten days, before he developed his first respiratory symptoms. Although in a series of critically ill MERS-CoV patients, the median time from illness onset to admission was one day, a protracted, non-respiratory illness of over a week has been described in a patient who eventually had significant bilateral lung infiltrates as this patient did.(3, 11, 12) Although the patient in Indiana eventually developed a dry cough, which has occurred in approximately half of MERS-CoV patients, the cough was never prominent despite extensive lung parenchymal involvement.(4)

Second, the patient’s clinical presentation, radiologic and laboratory findings had no distinguishing features of a MERS-CoV infection and could easily have been diagnosed as other more common viral or bacterial pneumonia etiologies. While this patient had the three most prevalent symptoms observed in the largest series of 47 MERS-CoV patients from Saudi
Arabia – fever (98%), cough (83%) and shortness of breath (72%) – he lacked upper respiratory tract (e.g. sore throat, rhinorrhea) and gastrointestinal tract symptoms (e.g. diarrhea, vomiting), which have been seen in approximately a quarter of MERS-CoV patients.

The patient’s laboratory data were unremarkable except for a mild elevation in liver enzymes, which has been seen in up to 15% of patients, lymphopenia, which has been seen in 34-86% of patients, and mild elevation in inflammatory markers. The key feature to the diagnosis of MERS-CoV in this patient was the history of his being a healthcare worker with recent travel and practice in KSA. At the time of this case, approximately 88% of the MERS-CoV cases worldwide had occurred in KSA and infection among healthcare workers is well-documented. The number of confirmed MERS-CoV cases identified in KSA increased substantially from March to early May 2014 (318 cases confirmed by the World Health Organization from March 1-May 12). When MERS-CoV cases are prevalent in the Arabian Peninsula, U.S. clinicians need to be ever more vigilant for MERS-CoV among patients with compatible clinical presentation (e.g. fever and severe respiratory illness), travel history (i.e. illness onset within 14 days after travel to the Arabian Peninsula or nearby countries) and close contact with a confirmed or probable case. (Although this patient did not recall close contact, his work in a healthcare setting in KSA suggested the potential for unrecognized close contact.) Ten days after this patient’s confirmed diagnosis, a second imported case of MERS-CoV was detected in Florida in another healthcare worker who also had worked in KSA. No other US cases have occurred to date.
Once the Indiana patient was suspected of having MERS-CoV infection, the diagnosis was made within 24 hours. This virus was first detected in the patient’s serum, when his NP swab was negative.\textsuperscript{(15, 16)} NP swabs, because of their ease of collection, have been the most common sample used in making a diagnosis of MERS-CoV.\textsuperscript{(4)} Nonetheless, there is evidence from some MERS-CoV cases that even when high load of virus is detected in lower respiratory tract specimens, upper respiratory tract specimens can be weakly positive or negative.\textsuperscript{(16, 17)} In this patient, the initial NP sample was negative at a time when the sputum was positive by rRT-PCR at MERS-CoV concentrations that were as high as those from tracheobronchial secretions in other patients who were more critically ill.\textsuperscript{(17)} Moreover, the sputum remained positive for up to two days longer than the pharyngeal samples. The serum was also positive by rRT-PCR on two occasions during a four day period, when the nasopharyngeal sample was negative, suggesting a prolonged viremia. Blood and sera have been found to be rRT-PCR-positive in other MERS-CoV patients, and these might be more sensitive diagnostic specimens in MERS-CoV patients than in SARS patients.\textsuperscript{(13, 16-19)} In contrast to SARS, as in this patient MERS-CoV has been rarely detected in stool, and when detected was present in relatively low concentration.\textsuperscript{(16, 17, 20)} For diagnostic testing of persons under investigation for MERS-CoV, CDC states that lower respiratory specimens, which can include induced or expectorated sputa, are preferred; however, collecting NP/OP specimens, as well as stool and serum, are also recommended as soon as possible after symptom onset.\textsuperscript{(21)} If symptom onset was 14 or more days ago, a single serum specimen for serologic testing in addition to a lower respiratory specimen and an NP/OP specimen are recommended, although the kinetics of the antibody response to MERS-CoV infection needs further clarification.\textsuperscript{(21)}
Despite having bilateral pulmonary infiltrates, the patient required supplemental oxygen only by nasal cannula and was able to be weaned to room air eight days after admission. There is no evidence yet for any effective treatment for MERS-CoV infection. In the case-series of 47 Saudi MERS-CoV patients, no bacterial coinfection was diagnosed. Although bacterial pneumonia superinfection commonly seen following influenza virus infection has not been demonstrated with novel coronaviruses, WHO has a permissive recommendation for antibiotics based on clinical judgment in patients with novel coronavirus infections. IVIG has not been evaluated in MERS-CoV patients, but is unlikely to have been effective in this patient’s recovery given his non-severe clinical status and the expected absence of MERS-CoV antibodies in pooled sera in the U.S. Any immunomodulatory effect of IVIG in this patient is unknown. Although IVIG was administered to patients with SARS-CoV infection during 2003, the effectiveness of IVIG treatment for SARS patients is unknown due to confounders, variable severity of illness when treatment was initiated, and the uncontrolled study design. Due to its potential risks and unknown benefit, IVIG is not recommended to treat MERS-CoV patients. Whereas interferon-alpha-2b and ribavirin combined therapy has shown some therapeutic potential in cell culture and animal experiments, these have not been shown to be effective in MERS-CoV patients. However, these agents have only been implemented late in the course of illness. Steroids are also not recommended for the treatment of MERS-CoV.

The most closely genetically related strain to this patient’s is from Riyadh in July 2013, which is where the Indiana patient lived and worked in a hospital. Of interest, the next most closely related virus is the June 2013 index case in a community cluster in Hafr Al-Batin, a town in
northeast KSA near the Kuwaiti border, approximately 500 km from Riyadh (Figure S1). Few sequences from 2014 are present in the GenBank database, particularly from Riyadh.

The ongoing threat of the spread of MERS-CoV into the U.S. requires the vigilance of astute clinicians and public health departments to detect MERS-CoV-infected patients and respond rapidly to prevent spread in healthcare facilities and the community.(14) People who are traveling to provide health care services in the Arabian Peninsula should be familiar with recommendations for infection control of confirmed or suspected MERS cases.

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The findings and conclusions are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

The authors have no other reported conflicts of interest related to the content of this manuscript.
Table 1. Admission laboratory results for MERS-CoV patient, April 28, 2014. Bolded values are outside of normal range.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>7.01 x 10^9/L</td>
<td>4.50-11 x 10^9/L</td>
</tr>
<tr>
<td>Neutrophil %, Count</td>
<td>80%, 5.62 x 10^9/L</td>
<td>55-72%, 2.48-7.92 x 10^9/L</td>
</tr>
<tr>
<td>Lymphocyte %, Count</td>
<td>11.6%, 0.81 x 10^7/L</td>
<td>20-40%, 1.5-4.0 x 10^7/L</td>
</tr>
<tr>
<td>Immature Granulocyte %, Count</td>
<td>0.7%, 0.05 x 10^9/L</td>
<td>0.0-0.4%, 0.0-0.04 x 10^9/L</td>
</tr>
<tr>
<td>Hemoglobin/Hematocrit</td>
<td>13.2/38.6%</td>
<td>13.5-16.5/41-50%</td>
</tr>
<tr>
<td>Platelets</td>
<td>224,000</td>
<td>100,000-450,000</td>
</tr>
<tr>
<td>Electrolytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>132 mEq/L</td>
<td>135-145 mEq/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.2 mEq/L</td>
<td>3.4-5.1 mEq/L</td>
</tr>
<tr>
<td>Chlorine</td>
<td>96 mEq/L</td>
<td>96 - 106 mEq/L</td>
</tr>
<tr>
<td>CO2</td>
<td>22 mEq/L</td>
<td>20-29 mEq/L</td>
</tr>
<tr>
<td>BUN</td>
<td>15 mg/dl</td>
<td>7-21 mg/dl</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.75 mg/dl</td>
<td>0.50-1.20 mg/dl</td>
</tr>
<tr>
<td>Glucose</td>
<td>167 mg/dl</td>
<td>&lt;140 mg/dl</td>
</tr>
<tr>
<td>Liver Function tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT (SGPT)</td>
<td>80 U/L</td>
<td>0-41 U/L</td>
</tr>
<tr>
<td>AST (SGOT)</td>
<td>95 U/L</td>
<td>0-37 U/L</td>
</tr>
<tr>
<td>Alkaline Phosphatase</td>
<td>270 U/L</td>
<td>35-116 U/L</td>
</tr>
<tr>
<td>Direct bilirubin</td>
<td>0.6 mg/dl</td>
<td>0.0-0.3 mg/dl</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>1.0 mg/dl</td>
<td>0.0-1.2 mg/dl</td>
</tr>
<tr>
<td>Inflammatory markers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythrocyte Sedimentation Rate</td>
<td>44 mm/h</td>
<td>0-15 mm/h</td>
</tr>
<tr>
<td>C-reactive Protein</td>
<td>10 mg/dl</td>
<td>0.0-0.5mg/dl</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>0.54 mg/dl</td>
<td>0.0-0.5 mg/dl</td>
</tr>
</tbody>
</table>
Table 2. MERS-CoV rRT-PCR test results of index patient specimen types with cycle threshold (CT) values for nucleocapsid protein gene signature (N2) in parentheses (8)

<table>
<thead>
<tr>
<th>Date of collection</th>
<th>NP</th>
<th>NP/OP</th>
<th>Sputum</th>
<th>Stool</th>
<th>Urine</th>
<th>Sera</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/29 (DOI 12)</td>
<td>Neg</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>Pos (36.0)</td>
</tr>
<tr>
<td>4/30 (DOI 13)</td>
<td>--</td>
<td>--</td>
<td>Pos (26.5)(^1)</td>
<td>Neg</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>5/1 (DOI 14)</td>
<td>--</td>
<td>Pos (31.2)(^2)</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>5/2 (DOI 15)</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>Pos (38.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/3 (DOI 16)</td>
<td>Neg</td>
<td>Neg</td>
<td>Pos (31.8)(^3)</td>
<td>--</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>5/4 (DOI 17)</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>Neg</td>
<td>--</td>
<td>Neg</td>
</tr>
<tr>
<td>5/5 (DOI 18)</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>5/7 (DOI 19)</td>
<td>Neg</td>
<td>--</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>--</td>
</tr>
</tbody>
</table>

\(^1\)upE target CT 28.1  
\(^2\)Only OP swab taken on this day.  
\(^3\)upE target CT 33.7  
Abbreviations. NP is nasopharyngeal. OP is oropharyngeal. DOI is day of illness.
Figure Legends

Figure 1. Chest x-rays of MERS-CoV patient on admission, Indiana, April 28, 2014 (1a) and on May 5, 2014 (1b)

Figure 2. Chest CT of MERS-CoV patient, Indiana, April 29, 2014

Figure 3. Phylogenetic analysis of the Indiana/USA-1_Saudi Arabia_2014 strain. The sequence alignment was generated using 56 nearly complete genome sequences published at i) GenBank, ii) the Health Protection Agency (HPA) website (http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1317136246479) and iii) the Institut Für Virologie (IFV) website (http://www.virology-bonn.de/index.php?id=46). The phylogenetic reconstructions were performed using MrBayes v3.2 under a General-Time-Reversible model of nucleotide substitution with four categories of gamma distributed rate heterogeneity and a proportion of invariant sites (GTR+4+I). The Indiana/USA-1_Saudi Arabia_2014 strain is highlighted in red. The camel MERS-CoV sequences were labeled with camel icon. The trees are drawn to scale, with branch lengths measured in the number of substitutions per site. The Bayesian posterior probabilities (> 0.5) are shown at nodes.
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