

Hospital Infection Control & PREVENTION

The Trusted Source for the Infection Preventionist for More Than Four Decades

September 2013

Volume 40, No. 9

Pages 97-108

Have virus, will travel: U.S. hospitals must be vigilant for incoming cases of MERS, H7N9 as seasonal flu hits

'International travel is incredibly frequent. No community is really immune to this.'

By Gary Evans, Executive Editor



MERS coronavirus

With the approaching flu season complicated by possible introductions of an emerging coronavirus in the Middle East and a novel H7N9 flu strain in China, clinicians in U.S. hospitals may need to rely more on gumshoe epidemiology than available diagnostics.

As this issue went to press no cases of Middle East Respiratory Syndrome (MERS) coronavirus nor

IPs watchful for emerging viruses: This is not a drill

We follow the report in our July 2013 issue — “Infection prevention in an era of emerging pandemics” with a real world example of this new normal. We approach an influenza season that may be confounded by two potential pandemic diseases with strikingly similar symptoms of severe respiratory disease. The CDC is warning of possible introductions of both Middle East Respiratory Syndrome (MERS) coronavirus and a novel H7N9 avian flu strain that has emerged in China. Both viruses are deadly and have pandemic potential, but neither has made its way to a hospital emergency room in the United States. That situation could change rapidly, as the lessons of SARS remind. The CDC is particularly concerned about MERS infections in hospitalized patients with underlying chronic conditions, as the novel coronavirus has caused mortality rates in the 60% range in that vulnerable population. ■

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Financial Disclosure:
Executive Editor **Gary Evans**, Consulting Editor **Patrick Joseph**, MD, and **Kay Ball**, Nurse Planner, report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

novel avian influenza A (H7N9) had been reported in North America. H7N9 seems to have particularly dropped off the radar, but the Centers for Disease Control and Prevention is urging vigilance in what could be a chaotic season for respiratory infections. The respective viruses both appear to need a further mutation to transmit effectively in the community, but they remain simmering with pandemic potential due to their novel nature and high mortality rates in confirmed cases. As infection preventionists are well aware, both influenza and coronaviruses have the ability to genetically reassort and mutate in ways that could make them more transmissible.

The immediate threat to hospitalized patients in the U.S. is clearly MERS, which in its present form is capable of causing a nosocomial outbreak. MERS has caused fatal and life-threatening infections in patients with underlying medical conditions and has shown the ability to spread to both patients and health care workers in hospital outbreaks in the Middle East. Though there are some distinctions, MERS is something of a pathogenic cousin to the Severe Acute Respiratory Syndrome (SARS) coronavirus that emerged dramatically in 2002-2003. An outbreak that began in China spread globally, eventually causing more than 8,000 infections and some 775 deaths. Then, like some violent squall at sea, SARS vanished as rapidly as it arose.

Only a smattering of cases occurred in the U.S., but Toronto, Canada was hit particularly hard with some 400 infections and 44 deaths in patients and health care workers. The Toronto outbreak began with a case of unrecognized SARS in an infected contact of a recent traveler



Allison McGeer
MD, FRCPC

to the Hong Kong epicenter. The patient was admitted to a community hospital, resulting in a large nosocomial outbreak that included a total of 128 patients, health care workers, household or social contacts, and hospital visitors.¹ Indeed, hospital transmission was a primary accelerator of SARS infections during the brief pandemic, accounting for 72% of cases in Toronto and 55% of probable cases in Taiwan.²

Allison McGeer, MD, FRCPC, has now seen the grim handiwork of both viruses, having battled SARS in her own hospital and traveled recently to Saudi Arabia to consult on a MERS outbreak at Al Ahsa Hospital and several other health care facilities. (*See related story, p. 103.*)

"Although there are some differences, there

Hospital Infection Control & Prevention®, including **Infection Control Consultant**™ and **Healthcare Infection Prevention**™ (ISSN 0098-180X), is published monthly by AHC Media, LLC, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices. Web: www.ahcmedia.com

POSTMASTER: Send address changes to **Hospital Infection Control & Prevention**®, P.O. Box 105109, Atlanta, GA 30348.

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This activity is effective for 36 months from the date of publication.

Target audience: Infection control practitioners and infectious disease physicians.

Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

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Subscription rates: U.S.A., one year (12 issues), \$499. Add \$17.95 for shipping & handling. Outside U.S., add \$30 per year, total prepaid in U.S. funds. Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue date. **Back issues**, when available, are \$78 each. (GST registration number R128870672.)

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are some really striking similarities between MERS and SARS," says McGeer, a microbiologist and infectious disease consultant at Mount Sinai Hospital in Toronto. "I am not particularly worried about introductions because we know what rules this virus lives by. But we are having that discussion here in Ontario — are we prepared to identify the first case of MERS? I think our ability to detect travel-associated cases in hospitals — which is the critical issue — is probably pretty good. If it presents in a household contact of a traveler — which is how we got into trouble with SARS — then that will be more difficult."

Since MERS first appeared in September 2012, there have been 94 laboratory-confirmed infections (as of August 19, 2013) reported in Saudi Arabia, Qatar, Jordan, the United Arab Emirates, the United Kingdom, France, Tunisia, and Italy. All the European and North African cases had a connection to the Middle East. However, France, Italy, Tunisia and the UK cases included limited local transmission among close contacts that had not travelled to the region. There have also been sixteen probable cases. Likewise, an unknown number of mild or asymptomatic cases have likely occurred, but MERS currently has a 50% mortality rate in the confirmed cases with 47 deaths among the 94 patients. Evidence of the MERS coronavirus has been found in bats and camels, but other animals may also serve as a reservoir or intermediate host. (See *related story*, p. 105)

Look for the 'epi' link

As with SARS, infection control measures can effectively contain MERS once suspect or identified cases are placed in patient isolation, McGeer says. Compliance with infection control measures is critical because no vaccine or effective antiviral treatment is currently available for MERS. Given that and the unknown routes of transmission of MERS, the CDC essentially pulled out all stops in recommending a combination of standard, contact, and airborne precautions for patients hospitalized with known or suspected MERS. Hospitals should use airborne infection isolation rooms with health care workers donning gloves, gowns, eye protection and N95 respirators.

"Once you identify it — as the hospital in Al Ahsa did — it is completely controllable," McGeer says. "But you have to be looking for it very carefully and recognize that you will export cases to other hospitals. You have to understand that this

is a regional thing as opposed to a single hospital outbreak. You have to be watching more broadly than you usually do for cases of transmission, but none of it is that difficult if you are ready to go. If you haven't dealt with SARS, it is an interesting challenge and people could get into some trouble, though I don't think as much trouble as we got into with SARS."

Some hard-earned wisdom gained from that trouble was to "think epidemiologically," McGeer adds. "The first thing about detecting cases is that at presentation in the hospital emergency department you really need to be able to detect the 'epi' risk," she says. "Thinking epidemiologically when you first see people is something that has taken all of us a while to learn because it is not the traditional clinical approach to things."

Hospital outbreaks of both SARS and MERS underscore the epidemiological consequences of patient movement, and the cost of failed communication between facilities.

"It is not just the patients who have disease," she says. "Who are the other patients in the ICU who were exposed and are no longer there? Have exposed patients in your hospital gotten sick and then turned up in another hospital? Now of course unless you are on top of it and telling that other hospital — they have no idea there is an 'epi' link. Not a clue."

An immediate challenge for American IPs and clinicians will be discerning between a panoply of severe respiratory infections with similar symptoms that may include fever and pneumonia requiring hospitalization. The CDC has developed a checklist for frontline workers that include using "source control" measures like putting a face mask on suspect cases until they can be placed in an isolation room. (See *related story*, p. 101.)

"The clinicians are really going to be the first line of defense for a case of MERS, H7N9 or seasonal flu," says **Terri Rebmann**, PhD, RN, CIC, associate professor in the Institute for Biosecurity at Saint



Louis (MO) University. "They are going to have to be really thorough in their history taking, ask the right questions and then follow up with prompt reporting to the health department."

While flu tests may help guide decision making,



William Schaffner, MD,

the rapid tests lack sensitivity and can result in false negatives, she says. "The CDC instructs clinicians to interpret negative lab result findings with caution, and to base treatment decisions on signs and symptoms as well as lab test results,"

Rebmann notes.

Epidemiologically, travel history is the immediate triage point between suspect MERS cases and those with seasonal flu or some other serious respiratory infection.

"It is a small world today and people are within 12 hours of most places on the globe," says **William Schaffner**, MD, chairman of preventive medicine at Vanderbilt University Medical Center in Nashville. "International travel is incredibly frequent. There is no community that is really immune to this."

The CDC advises considering MERS if a patient with severe respiratory symptoms has been to the Middle East in the last 14 days. Similarly, patients with severe respiratory infections should be considered for novel H7N9 flu if they have travelled to China in the last 10 days.

"We're back to doing things as in the SARS era with travel histories," Schaffner says. "Certainly we did that then and we will be doing this going forward here at Vanderbilt — reminding all of our providers that when they see patients with respiratory illness ask them the simple question: 'Have you been traveling out of country, and if so where?' That's very simple. It's easy to do and costs no money — you just have to remind your practitioners to do that."

Widening the net

Concerned that some MERS introductions could be missed, the CDC recently revised its guidance for the coronavirus.³ In the previous guidance the CDC did not recommend MERS testing for people whose illness could be explained by another etiology. The new guidance states that, in patients who meet certain clinical and epidemiologic

criteria, testing for MERS and other respiratory pathogens can be done simultaneously. Moreover, positive results for another respiratory pathogen should not necessarily preclude testing for MERS, the CDC said.

"We just want to make it clear that it is not essential to rule out other causes

of a severe acute respiratory infection," says **Susan Gerber**, MD, a medical epidemiologist in the CDC Respiratory Virus Program. "Clinicians may order testing for MERS coronavirus while also investigating other causes. A

lot of symptoms for severe respiratory infections overlap and that's why testing is so important. Severe influenza infection and community-acquired pneumonias may also be due to streptococcal infections or legionella. Many of these symptoms and clinical presentations [are similar to] the MERS coronavirus."

Hospitals that have a suspect case of MERS should contact their state and local health department for testing. Lab tests using polymerase chain reaction for MERS-CoV detection have been distributed to state health departments by the CDC. The CDC has not changed the case definition of a confirmed MERS case, but the criteria for laboratory confirmation were recently clarified. The CDC has also revised its definition of a "probable case" so that identification of another etiology does not exclude someone from being classified as a probable case of MERS.

"The way I read this is that MERS is a continuing and potentially growing problem," Schaffner says. "They want to increase their capacity to pick up cases that are imported into the United States. In effect, they're widening the net."

At the risk of putting too fine a point on it, the CDC guidelines suggest that a hypothetical patient positive for seasonal flu could still be worked up for MERS if he had traveled to the Middle East in the prior two weeks.

"If it were a sufficiently serious illness, that's correct," Schaffner says. "If you have a rapid



Susan Gerber, MD

[positive] test for flu but that patient has just come back from Yemen, you would think seriously of getting another specimen and getting it off to CDC for MERS testing.”

The new CDC guidance also clarifies recommendations for investigating unexplained clusters of severe acute respiratory illness when there is no apparent link to a MERS case. Clusters of patients with severe acute respiratory illness should be evaluated for common respiratory pathogens and reported to local and state health departments. If the illness remains unexplained, testing for MERS should be considered in consultation with state and local health departments, the CDC recommends.

“This is an illness that has the potential to spread from person to person [in the community] so if there is a cluster of serious respiratory illness that immediately doesn’t have an answer as to etiology, MERS ought to be considered,” Schaffner says. “This is another way to think of how possible introductions may present themselves.”

Though testing for MERS if a patient has another etiology for severe respiratory infection may be exercising an abundance of caution, in

general the CDC guidelines fall within reasonable epidemiological parameters, says **Stanley Perlman, MD, PhD**, a microbiology professor who studies coronavirus pathogenesis at the University of Iowa in Iowa City.



Stanley Perlman
MD, PhD

“As an infectious disease physician I would have done this anyway,” he says. “If I had somebody in my clinic who was sick and just traveled to Saudi Arabia I would certainly be thinking in the back of my mind they could have MERS. But if it’s the middle of December and somebody from Saudi

CDC triage tips for incoming MERS

Front-line healthcare providers in the United States should be prepared to evaluate patients for new and emerging infectious diseases such as Middle East Respiratory Syndrome (MERS) coronavirus, the Centers for Disease Control and Prevention advises.

The following CDC checklist highlights key steps for healthcare providers to take in preparation for transport and arrival of patients potentially infected with MERS.

- Stay up to date on the latest information about signs and symptoms, diagnostic testing, and case definitions for MERS disease (<http://www.cdc.gov/coronavirus/mers/case-def.html>)
- Review your infection control policies and CDC infection control recommendations for MERS (<http://www.cdc.gov/coronavirus/mers/infection-prevention-control.html>) for these important areas:
 - Assessment and triage of acute respiratory infection patients
 - Patient placement
 - Visitor management and exclusion
 - Personal protective equipment (PPE) for

healthcare personnel

- Source control measures for patients (e.g., put facemask on suspect patients)
- Requirements for performing aerosol generating procedures
 - Be alert for patients who meet the MERS case definition (<http://www.cdc.gov/coronavirus/mers/case-def.html>)
 - Promptly implement source control for potential MERS patients before transport or upon entry to the facility and triage according to facility plans (e.g., place in private room) for evaluation
 - Know how to report a potential MERS case or exposure to facility infection control leads and public health officials
 - Know who, when, and how to notify and when to seek evaluation by occupational health following an unprotected exposure (i.e., not wearing recommended PPE) to a suspected or confirmed MERS patient
 - Know how to contact and receive information from your state or local public health agency
 - Remain at home if you are ill ■

Arabia is positive for a flu culture I would probably think they had the flu.”

On the other hand, if a patient came back from the Middle East and had a positive culture for a rhinovirus, MERS testing would be considered, Perlman says. “What they are saying makes some sense, it just can’t be crazy.”

Occam’s razor

Indeed, at some point in all of this it may be useful to invoke “Occam’s razor,” a principle of parsimony and logic that essentially says if you have competing hypotheses, the one with the fewest assumptions is likely correct.

“Most of us — if we had a cluster of patients with severe respiratory disease and we didn’t know what was going on — would do widespread testing,” Perlman says. “The caveat here is that most people who have gotten sick [with MERS] had underlying diseases. If I have a group of people who just came back from scuba diving in San Diego — perfectly healthy otherwise and 25 years old — it is unlikely they have MERS even if one of them also traveled to Saudi Arabia.”

A more realistic concern for MERS exposures — and subsequent U.S. introductions by thousands of returning travelers — is the Hajj pilgrimage to

Saudi Arabia in mid-October. (*See related story, this page.*)

“That could be a major concern — some of the elderly pilgrims may be immune compromised,” Perlman says. “[MERS] could cause immediate infections with the possibility for dissemination.”

Overall, in the absence of another mutation, MERS appears to lack the staying power needed for true pandemic potential — the ability to spread in the community between people with competent immune systems. Researchers recently compared MERS to SARS using the classic epidemiological measure of reproductive ratio, the expected number of secondary infections from a single case. The reproductive ratio reaches a tipping point for further transmission at 1 or above, indicating secondary infections can sustain an outbreak. Researchers looked at 55 of the 64 laboratory-confirmed cases of MERS as of June 21, 2013. Under their most “pessimistic scenario,” they estimated a MERS reproductive ratio of .69, noting that pre-pandemic SARS was at .80. With recent implementation of effective contact tracing and isolation procedures in the affected regions, they concluded that MERS does not yet have pandemic potential.⁴

“The only thing that is worrying people in Saudi Arabia — if cases continue to be acquired—is if

CDC, Saudis advise risk groups to forgo Hajj

MERS poses risk to old, young, pregnant women

Among the largest mass gatherings in the world, the annual Hajj pilgrimage to Mecca, Saudi Arabia, will draw some 3 million Muslims from around the world this year to the epicenter of an emerging infection: Middle East Respiratory Syndrome (MERS) coronavirus.

The pilgrimage will take place from approximately October 13 to 18, and the Centers for Disease Control Prevention estimates that some 11,000 Americans typically attend the gathering. Because of the risk of MERS, the Saudi Arabian Ministry of Health has recommended that the following groups should postpone their plans for Hajj this year:

- People over 65 years old
- Children under 12 years old
- Pregnant women
- People with chronic diseases (such as heart disease, kidney disease, diabetes, or respiratory

disease)

- People with weakened immune systems
- People with cancer or terminal illnesses

The CDC is encouraging pilgrims traveling to Saudi Arabia to consider this advice and discuss their travel plans with their doctor. The virus that causes MERS can spread from person to person through close contact, so pilgrims living and traveling in crowded conditions may be at risk, the CDC notes.

Pilgrims can help protect themselves from respiratory diseases by washing their hands often; not touching their mouth, nose, or eyes; and avoiding contact with sick people. They should pay attention to their health when traveling in the Arabian Peninsula and seek medical care if they develop a fever with cough or shortness of breath within 14 days after returning from their trip, the CDC advises. ■

MERS achieves a reproductive ratio above 1 in the community," McGeer says. "If it's above 1 in the community then we're in trouble because as an endemic disease, MERS would be a very difficult problem. You couldn't tell who was coming in [with it]. But as long as it is just travel related I'm quite optimistic that we have enough global experience with these viruses to contain it."

Perlman made the same point in a recent editorial, though warning of the potential for MERS mutation.⁵

"Basically if the virus spreads to fewer people than it initially infected then it is going to go away," he says. "[But] with these coronaviruses you have to be wary about being too optimistic because they do mutate so easily."

For example, a mutated coronavirus that has been previously seen in Europe is currently infecting swine in the U.S., he notes.

"There is a huge outbreak now in North America of this porcine epidemic diarrhea (PED) coronavirus," Perlman says. "It probably came from Europe and it probably mutated with something else to allow this virus to cause severe infections in pigs. The point is that MERS has the potential to do that. During the SARS epidemic, we realized [the virus] changed during the course of the epidemic. So it could still mutate, but the good news is that we are now many months in with this virus and that really has not happened."

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Until cases recognized, MERS a formidable bug

21 cases of person-to-person spread

The rapid transmission and high attack rate of Middle East Respiratory Syndrome (MERS) coronavirus in a hospital dialysis unit in Al-Hufuf, Saudi Arabia "raises substantial concerns about the risk of health care-associated transmission of this virus," a team of researchers recently reported.¹

A team of experts that included SARS veteran **Allison McGeer**, MD, a microbiologist and infectious disease consultant at Mount Sinai Hospital in Toronto, reviewed an outbreak of MERS that occurred between April 1 and May 23, 2013. A total of 23 confirmed cases and 11 probable cases were part of a single outbreak involving several health care facilities. There was strong evidence of person-to-person transmission as patients moved between units and facilities.

"Epidemiologic and phylogenetic analyses support person-to-person transmission; however, it is not possible to be certain about whether there were single or multiple introductions from the community," the authors found. "Similarly, we are unable to determine whether person-to-person transmission occurred through respiratory droplets or through direct or indirect contact and whether the virus was transmitted when the contact was more than [1 meter] away from the case patient."

Because some patients presented with gastrointestinal symptoms, and transmission appeared to occur between rooms on the ward, the current WHO recommendations for surveillance and control should be regarded as the minimum standards, they noted. Hospitals should use contact and droplet precautions and should consider the follow-up of persons who were in the same ward as a patient with MERS infection, they recommended.

"One of the patients who was in the ICU at the time — who was exposed and got infected — was in fact a dialysis patient at another dialysis unit," McGeer says. "So by the time he got tracked down he was already sick and he had been dialyzed. He exposed people in the other dialysis unit, and subsequently two or three of those

patients got sick.”

As part of the investigation, medical records were reviewed for clinical and demographic information and determination of potential contacts and exposures. Case patients and contacts were interviewed and viral RNA was sequenced. Symptoms in the 23 MERS patients included fever in 20 patients (87%), cough in 20 (87%), shortness of breath in 11 (48%), and gastrointestinal symptoms in 8 (35%). Twenty of them presented with abnormal chest radiographs. As of June 12, a total of 15 patients (65%) had died, 6 (26%) had recovered, and 2 (9%) remained hospitalized.

“A total of 21 of the 23 cases were acquired by person-to-person transmission in hemodialysis units, intensive care units, or in-patient units in three different health care facilities,” the authors found.

‘Super spreaders’ a la SARS

Sequencing data from four isolates revealed a single monophyletic clade, meaning all the organisms were closely related. Among 217 household contacts and more than 200 health care worker contacts, MERS infection developed in five family members (three with laboratory-confirmed cases) and in two health care workers (both with laboratory-confirmed cases).

“The apparent heterogeneity in transmission, with many infected patients not transmitting disease at all and one patient transmitting disease to seven others, is reminiscent of SARS,” the team reported.

This so called “super spreader” phenomenon was further evidenced by a patient that transmitted MERS to three people and four patients who transmitted infection to two persons each. Super spreaders were also reported during the SARS pandemic, but McGeer questions whether the label really provides any actionable information.

“We know enough now about shedding of influenza and other respiratory viruses to know that there is a fair amount of heterogeneity in what kind of particle sizes you put out and what concentration of virus you put out,” she says. “The difficulty is that it doesn’t help in the sense that I can’t really tell you by looking at a person whether they are going to be somebody that sheds lot of virus and particles of the right size. I don’t think we are really further ahead on what makes a ‘super spreader,’ but there was evidence from that outbreak that there does seem to be heterogeneity in the way people transmit.”

The incubation period of confirmed cases was 5.2 days, which may partially explain why cases occurred despite the use of infection control measures. For example, between April 14 and April 30, MERS infection was confirmed in nine patients who were undergoing hemodialysis. Of those, eight had an onset of disease before or within 24 hours after infection-control interventions were implemented on April 21.

“I don’t think we have evidence to say that transmission occurred *through* precautions,” McGeer says.

The interventions included monitoring hand hygiene, implementing droplet and contact precautions for febrile patients, testing patients with fever for MERS, putting masks on all patients undergoing hemodialysis, not allowing patients with suspected MERS infection into the dialysis unit, enhancing environmental cleaning, and excluding visitors and nonessential staff.

“The 65% case fatality rate in this outbreak is of concern,” the researchers conclude. “We and others have found that the severity of illness associated with MERS infection ranges from mild to fulminant. The clinical syndrome is similar to SARS, with an initial phase of nonspecific fever and mild, nonproductive cough, which may last for several days before progressing to pneumonia. Some patients with MERS infection also had gastrointestinal symptoms, a finding similar to that with SARS.”

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MERS deadly to patients with underlying conditions

Hits those with diabetes, chronic disease

While a number of mild cases are likely going unrecognized — the bottom of the iceberg if you will — the serious MERS infections that are being detected are striking people with underlying medical conditions and killing more than half of them.

A recently published case series — the largest to date — includes 47 cases (46 adults, 1 child) of confirmed Middle East Respiratory Syndrome

(MERS) coronavirus.¹ Of the 47 cases, 36 (77%) were male. The case fatality rate for all patients was 60%, with 28 of the 47 patients dying. The case-fatality rate rose with increasing age. Only two of the 47 cases were previously healthy, with the remaining 45 cases having underlying comorbid medical disorders that included 32 (68%) with diabetes; 23 (49%) with chronic renal disease; 16 (34%) with hypertension; and 13 (28%) with chronic cardiac disease. All patients had abnormal findings on chest radiography, ranging from subtle to extensive unilateral and bilateral abnormalities.

The findings underscore the need for improved tests to detect a wider epidemiologic spectrum of disease and minimize spread from suspected milder cases to those with underlying conditions that may be at higher risk.

"Infection control measures within hospitals seem to work," said co-author **Ali Zumla**, MD, a professor at University College in London.

The identification of milder or asymptomatic cases of MERS in health care workers, children, and family members of contacts of MERS cases indicates that "we are only reporting the tip of the iceberg of severe cases and there is a spectrum of milder clinical disease which requires urgent definition," he said. "Ultimately the key will be to identify the source of MERS infection, predisposing factors for susceptibility to infection, and the predictive factors for poor outcome."

The case study findings also show a clear distinction between the emerging infection and SARS, another novel corona virus that spread to North America and other areas of the globe after emerging in China in 2002.

"In contrast to SARS — which was much more infectious, especially in healthcare settings and affected a healthier and younger age group — MERS appears to be more deadly, with 60% of patients with co-existing chronic illnesses dying, compared with the 1% toll of SARS," explains **Ziad Memish**, MD, the Deputy Minister for Public Health from the Kingdom of Saudi Arabia, who led the research.

Again, the high mortality rate with MERS is "probably spurious" because only severe cases are being detected, he said. "[Though we] are only picking up severe cases and missing a significant number of milder or asymptomatic cases, so far there is little to indicate that MERS will follow a similar path as SARS."

The researchers analyzed epidemiological, demographic, clinical, and laboratory data from confirmed cases of sporadic, household, com-

munity, and health-care-associated MERS infections reported from Saudi Arabia between Sept 1, 2012, and June 15, 2013. Common symptoms of MERS patients at presentation were fever

(98%), fever with chills or rigors (87%), cough (83%), shortness of breath (72%), and myalgia (15 [32%]). Gastrointestinal symptoms were also frequent, including diarrhea (26%), vomiting (21%), and abdominal pain (17%).

Despite sharing some clinical similarities with SARS (e.g., fever, cough, incubation period), there are also some important differences in MERS. Those include a rapid progression to respiratory failure — up to 5 days earlier than SARS, the researchers found.

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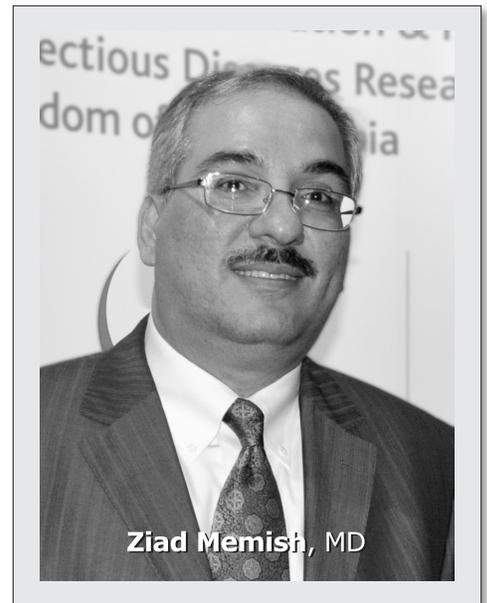
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Is the camel the culprit? Signs of past MERS infection

'These viruses can effectively mate with each other and develop new variants'

By **Gary Evans**, Executive Editor

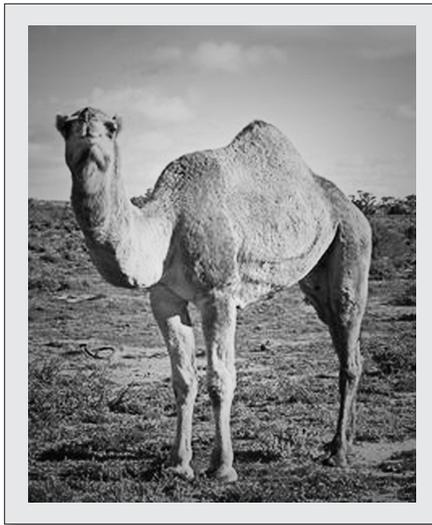
Camels may play an important role as an intermediate or "bridge" host for Middle East Respiratory Syndrome (MERS) coronavirus, possibly allowing it to move from a suspected bat reservoir to humans. Other animals may also serve as a reservoir or intermediate host for the



Ziad Memish, MD

coronavirus, but there is now clear evidence regarding camels.

Researchers found antibodies for MERS in camels in Oman, an Arab state on the southeast coast of the Arabian Peninsula. In a blood culture study, they found that 50 of 50 (100%) sera from Omani camels and 15 of 105 (14%) from Spanish camels had protein-specific antibodies against the MERS coronavirus.¹ Though no MERS virus was detected, the presence of antibodies suggests the animals were able to mount an immune response and survive infection with the coronavirus.



Camel meat serves as a source of protein and the Bedouins and other nomadic tribes have consumed camel milk for centuries. Moreover, camels are imported in the Middle East from Australia and Africa; with the southern regions of the latter continent being the home of a bat species (*Neoromicia cf. zuluensis*) that carries a virus that closely matches MERS, another group of researchers found. Researchers from Germany reported the coronavirus of the South African bat is genetically more closely related to MERS than any other known virus.²

The findings form the framework of a working theory for a classic progression of an emerging virus from an animal reservoir (bat), to an intermediate host (camel), and then eventually into humans in contact with the domesticated animal. There have been a few thinly described encounters between camels in some of the human MERS cases, including one account of a man in the United Arab Emirates who died after treating a sick racing camel (which recovered).³ Another published report mentions that a man in a family MERS cluster in Riyadh, Saudi Arabia had “attended the slaughtering of a camel.”⁴ Though the article gives no additional detail, camels are among the animals ritually sacrificed in the Islamic religious observation of Eid Al-Adha or the “Festival of Sacrifice.” “In a symbolic act, Muslims who can afford it slaughter a cow, goat, sheep or camel, keeping a portion to feed themselves and distributing the rest to friends, family and the needy.”⁵

Could such encounters have allowed MERS to cross species lines? It is now known that HIV moved from chimpanzees to humans during the slaughter and consumption of bush meat. However, camel exposures have not been

described in the majority of MERS cases, suggesting that other animal reservoirs may be contributing to the case count along with the limited episodes of clear human-to-human transmission. No MERS antibodies were found in European sheep, goats, and cattle tested in the aforementioned study.

The Viral Storm

In a recent interview with **Nathan Wolfe**, PhD, founder of the Global Viral Forecasting Initiative, we asked about the importance of detecting animal

reservoirs of emerging viruses.

“It is very important because if we really understand the animal reservoirs and the nature of how these viruses are jumping into human populations, we are going to be much more likely to be able to catch future events, which is, of course, the Holy Grail for our field,” he says.

The author of *The Viral Storm* warned that viruses may continue to mutate and change even as they continue emerging from animals to man.

“You can have a situation where an agent crosses from an animal to human populations — starts spreading within the human population — and yet new strains, new genetic diversity might continue to come from animal populations to enrich the pool,” Wolfe said. “These viruses can effectively mate with each other and develop new variants, and that diversity ends up being quite critical.”

Camels have been suspected previously as an intermediate viral host, possibly allowing smallpox to move from rodents to humans. Camelpox is the most closely related pox virus to smallpox in nature.⁶

“It’s interesting that we are really not 100% certain of the origins of smallpox, which is arguably the most important historical infection of human populations,” Wolfe said. “We simply don’t really know where it came from. The suspicion — because there is so much diversity in these viruses in rodents — is that perhaps [smallpox] is a rodent



virus. Once a virus has adapted to a mammalian system its probability of jumping into humans is greater. So domesticated animals can act as bridges and you can have pathogens that infect multiple animal hosts. These things really don't respect species boundaries that well, or political boundaries for that matter."

Meanwhile, the search for other animal reservoirs of MERS continues. As this issue went to press, scientists reported finding a 100% match to MERS coronavirus in a bat in Saudi Arabia called the Egyptian tomb bat, but since few case patients have reported bat contacts there was still suspicion of other animal reservoirs and intermediate hosts. A World Health Organization interview questionnaire for MERS cases includes questions on animal contact, including:

- Describe any contact with live or dead animals you have had including visiting places where animals are kept, even if you didn't have direct contact with them:
 - Did you have close contact with domestic (including household pets) or wild animals?
 - Were any of these animals sick or dead?
 - Were you aware of any other animals/excreta that are not usually present inside or outside your household (e.g. bats, rodents, stray cats/dogs, foxes, reptiles, etc.)?
 - Did you visit a market selling live animals?

References

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3. Sick camel linked to MERS virus death in UAE has recovered. *7 Days in Dubai* <http://www.7daysindubai.com/Sick-camel-linked-MERS-virus-death-UAE-recovered/story-19397041-detail/story.html>

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4. Memish, ZA. Zumla AI, Al-Hakeem, RF, et al. Family Cluster of Middle East Respiratory Syndrome Coronavirus Infections. *N Engl J Med* 2013;368:2487-2494 ■

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To earn credit for this activity, please follow these instructions.

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CNE/CME Objectives

Upon completion of this educational activity, participants should be able to:

- Identify the clinical, legal, or educational issues encountered by infection preventionists and epidemiologists;
- Describe the effect of infection control and prevention issues on nurses, hospitals, or the health care industry in general;
- Cite solutions to the problems encountered by infection preventionists based on guidelines from the relevant regulatory authorities, and/or independent recommendations from clinicians at individual institutions. ■

COMING IN FUTURE MONTHS

■ Joint Commission supplement for Infection Control

■ Active surveillance cultures for MRSA – case closed?

■ Universal decolonization study gets pushback

■ Is there a CMS infection control survey in our future?

■ Breaking news from IDWeek aka “Bug Stock”

CNE/CME Questions

1. The Centers for Disease Control and Prevention recommends which of the following infection control measures for Middle East Respiratory Syndrome (MERS) coronavirus?
 - A. airborne infection isolation rooms
 - B. gloves, gowns and eye protection
 - C. N95 respirators.
 - D. All of the above
2. A CDC checklist for frontline workers recommends using MERS "source control" measures, such as:
 - A. triage tent outside emergency room
 - B. administering antivirals as prophylaxis
 - C. putting a face mask on suspect cases
 - D. barring visitors during flu season
3. According to new CDC guidelines, positive test results for another respiratory pathogen should not necessarily preclude testing for MERS if the patient has traveled to the Middle East in the last 14 days.
 - A. True
 - B. False
4. According to a recently published MERS case series, the coronavirus had a particularly high mortality rate in patients with which underlying condition?
 - A. diabetes
 - B. hypertension
 - C. chronic renal disease
 - D. all of the above

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