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Infectious Disease [ALERT]

Incisive Commentary and Clinical Abstracts on Current Issues in Infectious Diseases

ABSTRACT & COMMENTARY

U.S. MERS cases worked in Saudi hospitals

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University, Hospital Epidemiologist, Sequoia Hospital, Redwood City, CA, Editor of Infectious Disease Alert

SOURCE: CDC. Middle East Respiratory Syndrome (MERS). http://www.cdc.gov/features/novelcoronavirus/

SYNOPSIS: The first U.S. case of MERS-CoV infection diagnosed in the U.S. has been identified in an individual traveling from Saudi Arabia.

An American health care worker flew from Riyadh, Saudi Arabia, to Chicago on a connecting flight from London on April 24, 2014. This was followed by an approximately 30-mile bus ride to Munster, Indiana. Three days later, on April 27, he developed fever, cough, and breathlessness and he presented to the Emergency Department of the 427--bed Community Hospital in Munster on the evening of the following day and was admitted as an inpatient. Middle East respiratory syndrome coronavirus (MERS-CoV) infection was suspected. As a consequence, the patient was managed with appropriate isolation precautions and specimens were sent to the CDC, which confirmed the diagnosis on May 2nd.

In order to detect possible secondary cases, family members and health care workers with significant contact with the patient underwent daily monitoring for 14 days, which is considered the outer limit of the incubation period of the infection. CDC began contacting the patient's airplane and bus co-passengers on May 3rd. (For an update of this story with details on the second U.S. MERS case see p. 105.)

■ COMMENTARY

As of May 12th, CDC reported a total of 538 confirmed MERS-CoV cases that include 145 deaths. The fact that 200 new cases were reported by Saudi Arabia and the United Arab Emirates in the single month of April 2014 has appropriately raised concerns that viral mutations had led to enhanced adaptation to human hosts.[1]

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The available evidence, however, has not, to date, confirmed this fear. Rather, it has been suggested that at least part of the reason has been increased recognition of the disease. Another suspected factor is the mass birthing of dromedary camels (the one-humped type) that occurs every winter in breeding facilities.

The virus, like the SARS coronavirus, has been found in bats. The role of these mammals in the transmission of MERS-CoV is uncertain, but dromedary camels are an important reservoir of the virus. For instance, a country-wide survey in Oman led to its detection in conjunctival and nasal secretions in high concentration in 5 of 76 of the ungulates tested and the finding that the viruses were closely related to MERS-CoV of human origin detected in the same geographic area.[2] In a few cases, closely related MERS-CoV has been identified in humans and camels with which they had had contact. Thus, it has been suggested that human infections may result from contact with the camels, eating camel meat, and the common practice of eating unpasteurized camel milk. Human-to-human transmission also occurs, with cases occurring in those with close contact with cases, including family members and health care workers. Fortunately, sustained transmission has not been observed.

Autochthonous cases of infection have occurred in 6 countries in or near the Arabian Peninsula: Saudi Arabia (where the bulk of cases have occurred), Oman, Kuwait, United Arab Emirates, Qatar, and Jordan. The U.S. is the 12th country to which the virus has been exported and, in our globally connected world, it will not be the last.

Fatal cases, in particular, mostly occurred in those with significant comorbidities such as chronic renal insufficiency and diabetes mellitus. Treatment of rhesus macaques experimentally infected with MERS-CoV with ribavirin and interferon-α2b, which are active against the virus in vitro, was associated with somewhat improved outcomes.[3] Monoclonal antibodies with neutralizing activity have also been developed.

One last thing — congratulations to the alert clinicians at Community Hospital in Munster for rapidly recognizing the possibility of MERS-CoV infection in their patient!

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3. Falzarano D, et al. Treatment with interferon-α2b and ribavirin improves outcome in MERS-CoV-infected rhesus macaques. Nat Med 2013; 19:1313-7. ■

ABSTRACT & COMMENTARY

Pertussis Outbreak in a Newborn ICU costs $100,000 to Contain

By Philip R Fischer, MD, DTM&H

Professor of Pediatrics, Department of Pediatric and Adolescent, Medicine, Mayo Clinic, Rochester, MN.

Dr. Fischer reports no financial relationships in this field of study.

SYNOPSIS: In a neonatal intensive care unit in Arizona, five infants and ten health care providers were found to have pertussis during a two month period. The outbreak cost the involved hospital nearly $100,000 in expenses and could likely have been prevented by careful implementation of staff

vaccination policies, limitation of symptomatic staff and family members from contact with neonatal patients, and application of established environmental management policies.

SOURCE: Yasmin S et al. Healthcare-Associated Pertussis Outbreak in Arizona: Challenges and Economic Impact, 2011. J Pediatr Infect Dis Soc 3:81-84, 2014.

The index case, a four-week-old girl born prematurely after a 28 week gestation, was hospitalized at an unnamed neonatal intensive care unit. She developed apnea that was attributed to gastro-esophageal reflux and then developed a cough that lasted 26 days. Only after being transferred to a different facility was pertussis testing done; both PCR and culture were positive.

The index case shared two nurses with the premature newborns in the adjoining beds. The space between beds was 16 inches. Those two adjacent babies also developed pertussis. Ten health care providers in the neonatal intensive care unit had, it was retrospectively determined, coughing illnesses that fulfilled a case definition of pertussis; each kept working through the illness. A fourth infant case was visited by an older sibling with symptomatic pertussis at the time of the visit.

The intensive care unit was evaluated by an outbreak investigation team. Of eight sinks in the area, access to two was obstructed by carts and trash cans. Hospital policies required health care providers with acute respiratory illnesses to take personal leave, but those policies were not enforced. Visitors to the neonatal intensive care unit were not screened for respiratory symptoms, and no signage warned ill visitors to postpone their visits.

After identification of the outbreak, costs were evaluated. More than half of costs were due to missed work after a diagnosis of pertussis, but there were also costs of testing and treatment of symptomatic individuals as well as for vaccination of incompletely immunized employees. The total cost of the outbreak came to approximately $100,000 (separate from patient care costs).

■ COMMENTARY

Since the era of Semmelweis, astute clinicians have recognized an increased risk of infection in some inpatient settings. Fortunately, there have been significant improvements in the quality and safety of healthcare offered in hospitals since then. Nonetheless, there are still risks of getting sick in healthcare facilities.

The Arizona NICU pertussis outbreak documents the risk of staff spreading infection to the smallest and most vulnerable of patients. More importantly, it also provides clear guidance toward the prevention of such tragedies. As noted in the paper by Yasmin and colleagues, "standard" policies might have been effective if they had been implemented. Health care providers should refrain from working when they are ill with acute respiratory infections (as was the policy at the involved hospital; unfortunately, the policy had not been followed). Visitors should be warned not to visit when they are symptomatic with respiratory illnesses. And, clinicians should suspect pertussis in infants with cough, especially chronic cough. (Of the five infected babies in the Arizona outbreak, symptoms had persisted from seven to 51 days before testing was done.)

Aware of the specific need to prevent children from becoming sick in hospitals, the Society for Healthcare Epidemiology of America Pediatric Leadership Council has been working for four years to reduce the burden of infection in residential healthcare facilities, of central line-associated bloodstream infection, and of *Clostridium difficile* infection.[1] Opportunities, however, remain; there is still a need to better study infection prevention implementation strategies.

Infection control is particularly challenging in resource-limited settings where even hand hygiene is relatively costly and where isolation rooms and materials are incompletely available. This is seen in newsworthy outbreaks such as Ebola (reported in May 2014 in *Infectious Disease Alert*) as well as in the more common outbreaks of measles and meningitis.

Despite the challenges, the Arizona outbreak reminds us that infection is often more expensive than prevention. Careful attention to and implementation of hospital infection control measures are still needed.

Reference

1. Sandora TJ. Hospital Epidemiology and Infection Control for Children: Report from the Society for healthcare Epidemiology of America Pediatric Leadership Council. J Pediatr Infect Dis Soc 3:4-6, 2014. ■

ABSTRACT & COMMENTARY

Neurological Manifestations of Influenza in the Era of the new Pandemic (H1N1) Strain

By Dean L. Winslow, MD, FACP, FIDSA

Clinical Professor of Medicine and Pediatrics Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Associate Editor of Infectious Disease Alert

Dr. Winslow is a consultant for Siemens Diagnostic.

SYNOPSIS: 25 cases of neurologic complications of influenza were reported from Great Britain beginning in 2011. 84% of cases were seen in children. A variety of distinct neurological manifestations were seen. 80% of patients required intensive care, 68% had poor outcomes, and 4 patients (16%) died.

SOURCE: Goenka A, et al. Neurological manifestations of influenza infection in children and adults: results of a national British surveillance study. CID 2014; 58: 775-84.

A 2-year surveillance study was conducted in British neurological surveillance units beginning in 2011. 21 children and 4 adults with influenza virus infection were identified. PCR of respiratory samples identified influenza A in 21 patients (of which 20 were H1N1) and influenza B in 4 patients. 12 children had encephalopathy (1 with movement disorder), 8 encephalitis, and 1 meningoencephalitis. Two adults had encephalopathy with movement disorder, 1 encephalitis, and 1 had Guillain-Barre syndrome. Specific acute encephalopathy syndromes included 4 with acute necrotizing encephalopathy, 1 acute infantile encephalopathy affecting frontal lobes, and 1 acute hemorrhagic leukoencephalopathy. 80% of patients required intensive care, 68% had poor neurologic outcomes, and 16% died.

■COMMENTARY

This is a very interesting study from the UK, which presents detailed evaluations of 25 cases of well-documented influenza-associated neurologic complications. The authors very carefully evaluated the specific neurologic manifestations observed clinically and in most cases were able to correlate these with neuro imaging studies including MRI scans. In contrast to the large study of influenza-associated neurologic complications published by Glaser et al[1] in 2012 (which reported on 77 such patients with neurologic complications associated with pandemic H1N1 in California who became ill during the 2009-2010 season and tended to have good outcomes), this British study seemed to show much more severe disease and worse neurologic outcomes. However, as was the case in the study by Glaser and colleagues, neurologic complications were seen primarily in children.

It seems clear that influenza A H1N1 strains circulating since 2009, in particular, appear to be more neurovirulent than influenza strains circulating in previous years. In the Glaser paper influenza-associated neurologic complications were seen in 4% of cases of fatal or severe 2009 H1N1 influenza. Sadly, most of these cases were potentially preventable. In the British surveillance study, none of the patients reported had received influenza vaccine. The pathogenesis of this apparent increased neurovirulence is not known.

Reference

1. Glaser CA, et al. A population-based study of neurologic manifestations of severe influenza A (H1N1) pdm09 in California. Clin Infect Dis 2012; 55: 514-20. ■

ABSTRACT & COMMENTARY

HIV Infection and Subclinical Coronary Artery Disease

By Joseph F John, Jr., MD

Dr. John reports no financial relationships.

SOURCE: Post WS, Budoff M, Kingsley L et al. Associations between HIV infection and subclinical coronary artery disease. Ann Intern Med 2014 160:458-467.

This study comes from the legacy Multicenter AIDS Cohort Study (MACS) of almost 7000 men who have sex with men, both HIV-infected and non-HIV, for 3 decades. The current study asks the question whether HIV infected men have more asymptomatic coronary artery disease than matched non-HIV infected men. A large proportion were studied using coronary angio and all subjects had the use of non-contrast cardiac CT as a total measure of coronary artery disease. There were 618 infected and 383 uninfected men. The blinded readers reported several parameters of coronary artery disease (CAD): presence, size and composition of the plaque and also the degree of luminal compromise in all coronary segments. A complex statistical analysis was used to arrive at an Agatson score of coronary involvement. The HIV infected group were a bit younger and more likely to be African American but were otherwise well matched. About one third of all men used lipid-lowering agents.

The major findings were as follows:
• The prevalence of non-calcified plaques was higher in the HIV-positive group with both non-contrast and contrast studies.
• With contrast studies, there was a coronary artery stenosis of >50% was more likely in their group but there was no difference when stenosis of >70% was compared.
• When any plaque was present, total coronary plaque and non-calcified plaque, but not calcified plaque, were more common in the HIV group.
• For variables of HAART therapy, a longer duration of HAART therapy was associated with stenosis >50%.
• Stenosis of >50% was also associated lower nadir CD4+.
• Despite these results, relatively few coronary events have occurred.

■COMMENTARY

HIV infection and long term HAART therapy in the HIV-infected in the MACS cohort was associated with asymptomatic coronary disease. The authors hesitate to use the term early coronary disease but that is what we are talking about here since the presence of more advanced disease, that characterized by calcified coronary plaques, was the same in the infected and the non-infected groups. The design of the study emphasizes the need for very complex statistical analysis and some of the language describing the analysis is very difficult for most practicing physicians.

The authors are reluctant to advise the use of coronary CT in asymptomatic HIV+ patients as a screening test. In a patient-centered world, however, the patients in question may press for such a study since they may feel they would have the opportunity to reduce their risk for symptomatic cardiac events. Providers of HIV care, then, are left with this knowledge that many of their patients may have evolving coronary artery disease. Further studies will define the best course of interventions and therapies. Presently, we need to warn HIV-infected men, homosexual, bisexual or not, that they may have increasingly with time and with HAART a greater risk of CAD than their non-HIV-infected counterparts. Short of actually documenting the status of the coronary arteries with coronary CT or angiography, informed medical decision making of patient and provider will dictate the best interventions until further studies are available. ■

ABSTRACT & COMMENTARY

Neuraminidase Inhibitor Therapy of Influenza Virus Infections — Yes or No?

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University, Hospital Epidemiologist, Sequoia Hospital, Redwood City, CA, Editor of Infectious Disease Alert

SOURCE: Jefferson T, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. Cochrane Database Syst Rev 2014 Apr 10;4:CD008965. PubMed PMID: 24718923.

SYNOPSIS: A Cochrane review questions the value of osletamivir and zanamivir in the treatment of influenza virus infections – but the CDC and IDSA disagree.

Jefferson and colleagues examined data from all available results, including unpublished data, from randomized placebo controlled trials of therapy and prophylaxis of influenza virus infection with neuraminidase inhibitors in both children and adults in order to determine their safety and efficacy. Overall, 107 clinical trials were examined.

Treatment — Adults:
Oseltamivir reduced the time to initial alleviation of symptoms in adults from a mean of 7 days to one of 6.3 days, a mean reduction of 16.8 hours (95% CI, 8.4 to 25.1 hours; P<0.0001). Zanamivir reduced this measure from 6.6 to 6.0 days, a 0.60 day reduction (95% CI, 0.39 to 0.81 days; P<0.00001). Neither oseltamivir nor zanamivir had a significant effect on hospitalizations or serious complications; this endpoint was not reported in zanamivir studies. Oseltamivir and zanamivir each significantly reduced "unverified" pneumonia, but not more stringently defined pneumonia in the few studies in which this was analyzed. Oseltamivir was associated with an increased risk of nausea and vomiting but decreased risks of diarrhea and cardiac events during treatment.

Treatment — Children:
Oseltamivir reduced the time to initial alleviation of symptoms in previously healthy children by a mean of 29 hours (95% CI, 12 to 47 hours; P=0.001), but the effect in children with asthma was non-significant. There was also no significant effect of oseltamivir on hospitalizations, serious influenza complications, or unverified pneumonia. Oseltamivir was associated with an increased risk of vomiting

Prophylaxis — Adults and Children:
Oseltamivir significantly reduced the risk of symptomatic influenza in individuals (risk difference [RD] 3.05%, 95% CI 1.83 to 3.88) with a number needed to treat (NNT) of 33. The risk in households was also significantly reduced (RD 13.6%, 95% CI 9.52 to 15.47) with an NNT of 7. The results with zanamivir were similar.

The authors concluded that, overall, the benefit of neuraminidase therapy in these outpatient studies were small, and that there was no evidence of prevention of serious outcomes. There was, however, apparent benefit of prophylaxis in the prevention of symptomatic infection.

■ COMMENTARY

CDC has carefully considered this analysis but nonetheless indicates that it does not alter their existing recommendations for influenza treatment that "emphasize initiation of antiviral treatment as soon as possible for patients who are severely ill and for those who are at greatest risk for complications from influenza. This includes hospitalized patients with suspected or confirmed influenza, those with severe or progressive illness, and outpatients who are at high risk of influenza complications (for example, young children, people aged 65 years and older, pregnant women, and persons with certain underlying chronic medical conditions). In addition, because other reviews of randomized clinical trials and observational studies have found consistent clinical benefit of early oseltamivir treatment in reducing the risk of lower respiratory tract complications such as those requiring antibiotics, persons with uncomplicated influenza who are not in a high risk group and who present within 48 hours of illness onset can be treated with antiviral medications based upon clinical judgment."[1]

CDC points out that the studies analyzed by Jefferson and colleagues were not powered to detect the effects of therapy on severe outcomes such as hospitalization and death. Furthermore, patients at highest risk of severe outcome are often not included in randomized trials and, since a virological diagnosis was often not required, many included patients with influenza-like illness may not actually have had influenza virus infection. The trials included in the Cochrane analysis involved outpatients — there are no randomized trials in hospitalized patients — but there are a number of observational studies that have reported benefit from therapy. Thus, Muthuri and colleagues performed a metaanalysis of the effects of neuraminidase inhibitor therapy of hospitalized patients, examining 78 studies and >29,000 patients.[2] They found that administration of a neuraminidase inhibitor was associated with a significantly decreased risk of mortality (adjusted odds ratio [OR] 0•81; 95% CI 0•70 to 0•93; p=0•0024). Initiation of treatment within 2 days of symptom onset was associated with a reduction in mortality risk (adjusted OR 0•48; 95% CI 0•41—0•56; p<0•0001) when compared to later initiation and, when compared to no treatment, a halving of the risk of mortality (adjusted OR 0•50; 95% CI 0•37—0•67; p<0•0001). The benefit was greater in adults than in children.

The Infectious Diseases Society of America has issued a statement which concurs with the CDC recommendation confirming the benefit of neuraminidase inhibitors in both the prevention and treatment of influenza virus infection.[3]

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1. CDC Recommendations for Early Influenza Antiviral Medications Remain Unchanged.

http://www.cdc.gov/media/haveyouheard/stories/Influenza_antiviral2.html

2. Muthuri SG, et al. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. Lancet Resp Med Early Online Publication, 19 March 2014 doi:10.1016/S2213-2600(14)70041-4.

3. Statement by the Infectious Disease Society of America (IDSA) on the recent publication on "Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children" http://www.idsociety.org/Influenza_Statement.aspx ■

FDA Advisory Committee Recommends Approval of Tedizolid and Dalbavancin

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University, Hospital Epidemiologist, Sequoia Hospital, Redwood City, CA, Editor of Infectious Disease Alert

On March 21, 2014, two new antibiotics with activity against methicillin-resistant Staphylococcus aureus (MRSA) each received unanimous recommendations from FDA Advisory Committees for approval for treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by Gram-positive organisms.[1,2]

Tedizolid is, like linezolid, an oxazolidinone with once daily administration by either the oral or intravenous route that was evaluated in 2 randomized clinical trials which have been reviewed by O'Riordan and colleagues.[3] In ESTABLISH-1, 667 patients were randomized to receive tedizolid 200 mg daily orally for 6 days or linezolid 600 mg twice daily orally for 10 days. The primary endpoint, cessation of increase in size of the lesion at 48-72 hours and absence of fever, was met in 79.5% and 79.4%, respectively. In ESTABLISH-2, an examination of IV to oral switch was evaluated. Patients received tedizolid 200 mg daily for 6 days or linezolid for 10 days with, in each case, at least the first 2 doses administered intravenously, but with freedom to change to the oral route thereafter. The primary endpoint, a >20% reduction in lesion size at 48-72 hours, was achieved in 85.2% of tedizolid recipients and 82.6% of those given linezolid.

Thus, a 6 day course of once daily tedizolid was non-inferior to a 10 day course of linezolid. There was also no significant difference in overall adverse events. While tedizolid is reported to be a weaker inhibitor of monoamine oxidase, translation of this difference into clinical benefit is unproven.

Dalbavancin is a lipoglycopeptide for intravenous administration that has a remarkably prolonged serum elimination half-life that reportedly ranges from 147-258 hours.

In both DISCOVER 1 and 2, patients with ABSSSI were randomized to receive 2 intravenous doses of dalbavancin one week apart (1000 mg on day 1 and 500 mg on day 8) or to receive vancomycin 1000 mg or 15 mg/kg every 12 hours with an option to switch to orally administered linezolid after 3 days.[4] The primary endpoint in each trial was the cessation of increase in size of the lesion at 48-72 hours and absence of fever. In DISCOVER 1, this endpoint was achieved in 83.3% of dalbavancin and 81.8% of vancomycin/linezolid recipients, while in DISCOVER 2, it was achieved in 76.8% and 78.3%, respectively.

Thus, dalbavancin is not inferior to vancomycin/linezolid in the treatment of ABSSSI and has the advantage of requiring administration of only 2 doses given one week apart. It should be noted that oritavancin, which is under development has an even longer half-life than dalbavancin and is administered intravenously as a single dose. One wonders, however, with regard to dalbavancin, whether a second dose is truly necessary.

References:

1. Anti-infective Drugs Advisory Committee Meeting for Tedizolid. March 31, 2014. http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/anti-infectivedrugsadvisorycommittee/ucm392556.pdf

2. Anti-infective Drugs Advisory Committee Meeting for Dalbavancin. March 31, 2014.

http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/anti-infectivedrugsadvisorycommittee/ucm392559.pdf

3. O'Riordan W, et al. Tedizolid phosphate for the management

of acute bacterial skin and skin structure infections: efficacy summary. Clin Infect Dis 2014; 58 Suppl 1:S43-50.

4. Wilcox M, et al. An Integrated Analysis of the Efficacy of Dalbavancin for the Treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in the DISCOVER Program. IDWeek Poster #1339 (2013) ■

ABSTRACT & COMMENTARY

Chagas Disease as a Cause of Dilated Cardiomyopathy in New York City

By Dean L. Winslow, MD, FACP, FIDSA,

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Dr. Winslow is a consultant for Siemens Diagnostic.

SYNOPSIS: In a sample of New York City immigrants with dilated cardiomyopathy the point prevalence of infection with Trypanosoma cruzi was found to be 13%.

SOURCE: Kapelusznik L, et al. Chagas disease in Latin American immigrants with dilated cardiomyopathy in New York City. CID 2013; ePub Mar 28, 2014.

A point prevalence study was conducted at the Cardiology clinics of Mount Sinai Medical Center and Elmhurst Hospital Center between 2009-2011. All patients were eligible for inclusion if they were >= 18 years old, did not have evidence of ischemic cardiomyopathy (CM), had left ventricular ejection fraction (LVEF) < 45% and lived for >= 12 months in a Chagas disease (CD) endemic country. Serum samples from patients were sent to the Centers for Disease Control and Prevention for *T. cruzi* IgG testing. Samples were considered positive if both EIA and IFA tests were positive. If these assays were discordant/indeterminate if an immunoblot assay using trypomastigote excreted-secreted antigens (TESA) were positive, then the individual was judged to be infected.

Forty-four eligible persons were identified and 39 agreed to participate in the study. Mean age of patients was 62 years. Of the 39 patients, 5 (13%) were infected with *T. cruzi* and none had prior knowledge of infection. Premature ventricular contractions (VPC's) were more commonly seen on routine 12 lead EKG's in Chagas disease patients than in the uninfected participants but right bundle branch block (RBBB) prevalence was not significantly different between the two groups.

■ COMMENTARY

This study confirms the high point prevalence of CD as a cause of CM in patients from CD-endemic areas. A similar study conducted in Los Angeles in immigrants with CM primarily from Mexico and El Salvador found a CD infection rate of 15%.[1]

It is clear that CD is a common and often overlooked cause of dilated CM in the U.S. While antiparasitic treatment probably has little utility in patients who already chronic dilated CM, it has been shown that patients with CD as a cause of CM have longer survival following cardiac transplantation than patients with idiopathic dilated CM,2 suggesting that these patients should be considered favorably for transplantation.

It is also now apparent that Chagas disease is endemic in Texas. At a recent meeting we had earlier this year in San Antonio where we brought together a wonderful multidisciplinary team of dedicated USAF, US Army, and Texas Department of Public Health professionals I was made aware of the potential threat of CD in Texas. Dr. Thomas (Leo) Cropper and Dr. Bryant Webber (both USAF Public Health officers) are in the process of studying the potential threat of CD to military trainees in the San Antonio area. Chagas disease (including acute Chagasic myocarditis) has been demonstrated in military working dogs, U.S. Customs and Border Protection working dogs and in civilian veterinary practices in Texas (personal communication, Dr. E. Wozniak). This is of significance since early CD in dogs and humans can be effectively treated with antiparasitic agents. It has also been demonstrated that a high percentage of meso-mammal hosts (including white-tail deer, raccoons, striped skunks, opossums, and wood rats, etc.) in Texas

are infected with T.cruzi (personal communication, Dr. M. Kramm) and the triatomine vectors show high rates of infection (personal communication, Dr. W. Roachell). Most importantly, several cases of autochthonous transmission to humans of CD have occurred in Texas (personal communication, Dr. C. Tully).
Chagas disease is clearly an under-recognized cause of cardiac disease in the U.S. While we eagerly await the results of the excellent science being done now in Texas by the U.S. military, Texas Department of Public Health and various academic institutions in Texas, I believe it is time that infectious diseases specialists, cardiologists, internists and family practitioners throughout the U.S. should start looking routinely for T.cruzi infection in patients from endemic areas (to include the Southern U.S. in addition to Latin America) who present with either dilated cardiomyopathy or acute myocarditis.

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2. Bocchi EA, et al. The paradox of survival results after heart transplantation for cardiomyopathy caused by Trypanosoma cruzi. Guidelines Group for Heart Transplantation of the Brazilian Society of Cardiology. Ann Thorac Surg 2001; 71: 1833-8. ■

Update: MERS in America

By Gary Evans, Executive Editor, IDA

As this issue went to press a second case of MERS was identified in Florida even as the Indiana case was being discharged in good condition. Here is what was known at press time.

Though unrelated to the recent MERS case in Indiana, the second U.S. case of the emerging coronavirus is also a health care worker who was apparently infected while working in a hospital in Jeddah, Saudi Arabia. The 44-year-old man is in good condition and under full MERS isolation measures at Orlando Health's Dr. P. Phillips Hospital, public health officials said May 12.

The Florida man was identified as a visitor from Saudi Arabia, where continuing hospital outbreaks have been "amplifying" MERS transmission and a quarter of the cases have been health care workers, according to a World Health Organization report.[1] The Indiana MERS case who was recently discharged from Community Hospital in Munsey also had been working at a Saudi hospital.

"We don't have exact numbers for individuals from the U.S. who work in the region," **Tom Frieden**, MD, MPH, director of the Centers for Disease Control and Prevention, said at May 12 press conference. "We do know it's not rare — one of the things that Saudi Arabia and other countries often do is to have [foreign] health care workers provide care. That's not just U.S. health care workers but health care workers from around the world. So this is an issue that is relevant for the World Health Organization and relevant for many countries that have, as we do, health care professionals working in the region."

The WHO report cited infection control breakdowns as a factor in MERS transmission to health care workers in Saudi hospitals. In contrast, the infection control measures in the two U.S. hospitals that have admitted MERS cases have been effective in blocking subsequent transmission.

"What we're seeing is the importance of two key concepts [for] MERS," Frieden said. "The first is the need for meticulous infection control in hospitals. And what has been done in Indiana and is being done in Florida is exactly what's needed to minimize the risk of spread. Rapid detection of a patient who's infected, rapid isolation and appropriate isolation of that individual, and then a furlough of health care workers who have had contact with that individual …so that if they become ill they will not create another chain of transmission."

Health care contacts and family members of the Florida MERS patient were placed under "voluntary home quarantine" for the 14-day incubation period, the same measures the CDC enacted for the Indiana case. "The protocol that we have followed for both Indiana and Florida is that the very close contacts — such as household contacts — will be staying home, away from others, monitoring their health until the end of the 14-day exposure period," **Anne Schuchat**, MD, director of CDC's National Center for Immunization and Respiratory Diseases, said at the press conference. "If they're going out they're wearing a mask."

FLORIDA PATIENT ILL WHILE TRAVELING

According to the CDC, on May 1st, the Florida patient departed Jeddah, Saudi Arabia, where hospital outbreaks of MERS have recently been reported. He flew to London and then on to Boston. The patient

then traveled from Boston to Atlanta, and finally on to Orlando.

"The patient began feeling unwell during the flight from Jeddah to London and continued to feel unwell on the subsequent flights with reported symptoms including fever, chills and a slight cough," Schuchat said.

Though the CDC said transmission was still unlikely, symptomatic patients are generally more likely to spread infection than those that are asymptomatic. The CDC is notifying some 500 passengers who may have been exposed during the patient's flights, she added. The CDC is individually contacting passengers on the flights rather than publically announcing the flight numbers.

On May 8th, the patient went to the emergency department of Phillips Hospital in Orlando and was admitted the same day. The Florida hospital is using the CDC recommended standard, contact and airborne isolation precautions, meaning health care workers entering the patient's room should be donning N95 respirators. "Public health and hospital officials are investigating and responding to the situation by reviewing appropriate infection control measures taken by the hospital, interviewing the healthcare staff and family members and others who had very close contact with the patient to obtain detailed information on their exposures," Schuchat said.

Orlando Health's Phillips Hospital is also contacting any emergency room staff and patients who may have been exposed to the MERS case before he was placed in isolation. In an unusual twist, the MERS patient had recently "accompanied [another] patient undergoing a medical procedure at Orlando Regional Medical Center," Phillips hospital stated. The hospitals are apparently affiliated, as both issued the same press release. Staff, patients and other contacts of the patient at both hospitals are being advised to take precautions that include voluntary quarantine and reporting to an emergency room at the first sign of symptoms.

Reference

1. World Health Organization: WHO concludes MERS-CoV mission in Saudi Arabia. May 7, 2014: http://bit.ly/1fP2kF6 ■

Infectious Disease [ALERT]

Updates

By Carol A. Kemper, MD, FACP

Time for a sea change in infection control

Palmore TN and Henderson DK. Carbapenem-resistant enterobacteriaceae: A call for cultural change. Ann Intern Med 2014; 160(8): 567-569.

This excellent article nicely summarizes the current threat of multi-drug resistant organisms to health care in the United States, detailing the catastrophic effects, both in terms of lives lost, human effort, and dollars spent, because of a single outbreak of carbapenem-resistant infection at the NIH. Only through the use of rigorously applied infection control practices and the use of newer molecular techniques, which could more rapidly drill down on the "gaps" in surveillance and controls, was the outbreak stemmed. As the authors state, the ability to identify these gaps "while the trail is still warm" was essential in stemming the outbreak. Hospitals elsewhere in the U.S. without access to these newer technologies may not be so fortunate.

At our hospital, in an effort to improve compliance with hand cleansing and personal protective gear, there is an ongoing debate with employee and medical staff about the merits of both practices (especially with some of our surgical staff, who not only walk on water, but walk right past towers of gowns and gloves, signage, alcohol dispensers and sinks, without seeing them). The infection control staff has been puzzling through this problem. Agreed, part of the art of medicine is the human touch — the laying of hands, the feel of a hot brow or a tense belly. And through that touch, we hope to heal. Is the experience or impact of that healing touch significantly diminished when wearing gloves ?

One of the problems is that newer surveillance practices are identifying patients who are simply colonized with resistant organisms — they're not symptomatic from the MRSA in their nares or the ESBL or CRE in their stool, at least not yet. (And their bed, bedside tray table, and sink area are definitely not symptomatic !) One physician recently argued that he used gloves when touching a patient

"symptomatic" with *C. difficile*, saying he needed to protect himself, but completely missing the point. .

There needs to be a sea change in how nursing and physician staff think about patient flora and common contact, with "complete vigilance and scrupulous consistency in adhering to infection prevention principles." Hospitals all over the U.S. are under "siege" from organisms being brought in through their doors, often by patients simply colonized with the newer multi-drug resistant "flora." As much as direct patient contact may be essential to healing, we touch patients all the time who may unknowingly harbor organisms potentially dangerous to others, not just patients with recognized infections or even identified colonization thru enhanced surveillance. Hence, the need to be vigilant all the time with good hand cleansing practices. Even the hands putting on gloves should be cleansed. We can no longer assume that because a patient appears healthy or lacks specific symptoms, they do not harbor multi-drug resistant gram negatives or even C. difficile. Hospital acquired infections do not occur until someone spreads them in hospital.

Does Herpes zoster increase stroke risk?

Langana Sinead M, et al. Risk of stroke following Herpes Zoster: A self-controlled case-series study. Clin Infect Dis 2014; doi 10.1093/cid/ciu098. First published online April 2, 2014.

Using the UK Clinical Practice Database, which includes longitudinal data for nearly 8% of the population of the UK, these authors examined whether a diagnosis of Herpes zoster increased the risk of stroke. Clinical data have suggested an increased risk for stroke within a year following an episode of zoster. Zoster infection may result in invasion of arteries and vasculopathy and even frank vasculitis; certainly the number of patients who exhibit positive CSF PCRs for VZV during episodes of zoster speaks to the ready invasion of the central nervous system. Zoster may also result in a systemic inflammatory response, which could lead to plaque rupture and thrombotic events. One can also imagine the sheer stress and discomfort associated with zoster might result in a hypertensive event.

Adults > 18 years of age with first ever zoster and first ever stroke occurring within a 12-month period between 1987 and 2012 were identified, revealing a total of 11,997 cases. Of these, 6,584 met inclusion criteria for the study. Patients could have no prior history of zoster or stroke; and individuals with a history of TIA, subarachnoid hemorrhage or cerebral aneurysm were excluded. The median age was 77 years, 57% were women, and the median period of observation was 12.5 years. Most cases of zoster did not specify a site of involvement; but 6% specifically indicated zoster opthalmicus and 0.5% had trigeminal nerve involvement. Systemic antiviral therapy was administered to 55%.

The rates of stroke were determined for the period of "exposure", starting the day after the zoster diagnosis and extending to a period of 12 months, divided into 4 time intervals (1-4 weeks, 5-12 weeks, 13-26 weeks, and 27-52 weeks). Overall, compared with baseline, rates of stroke were significantly increased post zoster-event at 1-4 weeks (incidence ratio [IR], 1.63) and at 5-12 weeks (IR, 1.23), and then gradually subsided by 6 months post-diagnosis. A lack of systemic antiviral therapy nearly doubled the observed risk of stroke at 1-4 weeks post-event (IR 2.14) compared with those receiving antivirals. For those receiving antivirals, the risk of stroke, compared with baseline, was significantly increased at 5-12 weeks (IR 1.28) but not for the other time intervals. And, surprisingly, a diagnosis of zoster opthalmicus was strongly associated with an increased risk of stroke at weeks 5-12 post-zoster (IR 3.38). The greatest risk of stroke was observed for persons with zoster opthalmicus who did not receive antivirals, who had > 5–fold risk of stroke at 5-12 weeks (IR 5.47). Similar results were observed when combining individuals with ocular and trigeminal involvement.

Examining a large longitudinal population database, an episode of zoster significantly increases the risk of stroke within 6 months, especially when antiviral therapy is not received, or the site of zoster involvement is either ocular or trigeminal. Interestingly, these data suggest a somewhat delayed onset of risk, approximately 5-12 weeks following a diagnosis, which would suggest some kind of delayed affect of viral infection, rather than a direct result of viral replication or invasion of virus into vessels during acute infection. Decreasing the viral load — either in tissues or in the CSF — with antiviral therapy appears important in reducing risk of stroke, even if a delayed risk. Maximizing the use of shingles vaccines, and quickly initiating antiviral therapy are important clinical goals.

CME INSTRUCTIONS

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

1. Read and study the activity, using the provided references for further research.
2. Scan the QR code to the right or log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

CME QUESTIONS

1. Which of the following is correct with regard to MERS-CoV infection?

A. It has been detected in camels.
B. Human-to-human transmission after close contact has been observed.
C. The outer limit of its incubation period is believed to be 14 days.
D. All of the above.

2. Healthcare-associated pertussis in Arizona was associated with:

A. delayed diagnosis of symptomatic patients

B. under-immunization of healthcare providers

C. lack of enforcement of leave policies for ill healthcare providers

D. blocked access to sinks

E. all of the above

3. What would be a difference in coronary status between HIV-infected and non infected homosexual and bisexual men?

A. Calcified coronary plaques

B. Non-calcified coronary plaques

C. Myocardial infarction

D. Presence of coronary artery stenosis of >70%

CME OBJECTIVES

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

- discuss the diagnosis of infectious diseases;
- explain current data regarding the use of new antibiotics for commonly diagnosed diseases and new uses for traditional drugs;
- discuss the latent information regarding risks, benefits, and cost-effectiveness of new and traditional diagnostic tests; and
- discuss new information regarding how infectious diseases are transmitted and how such information can lead to the development of new therapies

TIPPING POINT

"Humanity shares a common ancestry with all living things on Earth. We often share especially close intimacies with the microbial world. In fact, only a small percentage of the cells in the human body are human at all. We are vastly outnumbered, even within our bodies, by microbial life …This is also an essential relationship, because humanity could not survive without an array of microflora that both nourish us and that provide needed enzymes for life processes. Yet, the common biology and biochemistry that unites us also makes us susceptible to contracting and transmitting infectious disease."

Brenda Wilmoth Lerner, Infectious Diseases: In Context