2014 MERS-CoV Outbreak in Jeddah — A Link to Health Care Facilities

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A marked increase in the number of cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection occurred in Jeddah, Saudi Arabia, in early 2014. We evaluated patients with MERS-CoV infection in Jeddah to explore reasons for this increase and to assess the epidemiologic and clinical features of this disease.

We identified all cases of laboratory-confirmed MERS-CoV infection in Jeddah that were reported to the Saudi Arabian Ministry of Health from January 1 through May 16, 2014. We conducted telephonic interviews with symptomatic patients who were not health care personnel, and we reviewed hospital records. We identified patients who were reported as being asymptomatic and interviewed them regarding a history of symptoms in the month before testing. Descriptive analyses were performed.

Of 255 patients with laboratory-confirmed MERS-CoV infection, 93 died (case fatality rate, 36.5%). The median age of all patients was 45 years (interquartile range, 30–59), and 174 patients (68.2%) were male. A total of 64 patients (25.1%) were reported to be asymptomatic. Of the 191 symptomatic patients, 40 (20.9%) were health care personnel. Among the 151 symptomatic patients who were not health care personnel, 112 (74.2%) had data that could be assessed, and 109 (97.3%) of these patients had contact with a health care facility, a person with a confirmed case of MERS-CoV infection, or someone with severe respiratory illness in the 14 days before the onset of illness. The remaining 3 patients (2.7%) reported no such contacts. Of the 64 patients who were reported as asymptomatic, 33 (52%) were interviewed, and 26 of these 33 (79%) reported at least one symptom that was consistent with a viral respiratory illness.

The majority of patients in the Jeddah MERS-CoV outbreak had contact with a health care facility, other patients, or both. This highlights the role of health care–associated transmission.

Community-Acquired Pneumonia Requiring Hospitalization among US Children

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Incidence estimates that are based on the prospective data collection of hospitalizations for community-acquired pneumonia (CAP) among children in the United States are limited. Updated estimates of pneumonia that are confirmed radiographically and with the use of current laboratory diagnostic tests are needed.

Active population-based surveillance for CAP requiring hospitalization among children younger than 18 years of age in three hospitals in Memphis, Nashville, and Salt Lake City was conducted. Children with recent hospitalization or

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severe immunosuppression were excluded. Blood and respiratory specimens were systematically collected for pathogen detection with the use of multiple methods. Chest radiographs were reviewed independently by study radiologists.

From January 2010 through June 2012, we enrolled 2638 of 3803 eligible children (69%), 2358 of whom (89%) had radiographic evidence of pneumonia. The median age of the children was 2 years (interquartile range, 1–6); 497 of 2358 children (21%) required intensive care and 3 (<1%) died. Among 2222 children with radiographic evidence of pneumonia and with specimens available for bacterial and viral testing, a viral or bacterial pathogen was detected in 1802 (81%), one or more viruses in 1472 (66%), bacteria in 175 (8%), and both bacterial and viral pathogens in 155 (7%). The annual incidence of pneumonia was 15.7 cases per 10,000 children (95% confidence interval [CI], 14.9–16.5), with the highest rate among children younger than 2 years of age (62.2 cases per 10,000 children; 95% CI, 57.6–67.1). Respiratory syncytial virus was more common among children younger than 5 years of age than among older children (37% vs 8%), as were adenovirus (15% vs 3%) and human metapneumovirus (15% vs 8%). Mycoplasma pneumoniae was more common among children 5 years of age or older than among younger children (19% vs 3%).

The burden of hospitalization for children with CAP was highest among very young children, with respiratory viruses the most commonly detected causes of pneumonia.

Mass Treatment with Single-Dose Azithromycin for Yaws

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Mass treatment with azithromycin is a central component of the new World Health Organization strategy to eradicate yaws. Empirical data on the effectiveness of the strategy are required as a prerequisite for the worldwide implementation of the plan.

A repeated clinical surveys for active yaws, serologic surveys for latent yaws, and molecular analyses to determine the cause of skin ulcers and identify macrolide-resistant mutations before and 6 and 12 months after mass treatment with azithromycin on a Papua New Guinean island on which yaws was endemic was performed. Primary-outcome indicators were the prevalence of serologically confirmed active infectious yaws in the entire population and the prevalence of latent yaws with high-titer seroreactivity in a subgroup of children 1–15 years of age.

At baseline, 13,302 of 16,092 residents (82.7%) received one oral dose of azithromycin. The prevalence of active infectious yaws was reduced from 2.4% before mass treatment to 0.3% at 12 months (P<0.001). The prevalence of high-titer latent yaws among children was reduced from 18.3% to 6.5% (P<0.001) with a near-absence of high-titer seroreactivity in children 1–5 years of age. Adverse events identified within 1 week after administration of the medication occurred in approximately 17% of the participants, including nausea, diarrhea, and vomiting, and were mild in severity. No evidence of emergence of resistance to macrolides against Treponema pallidum subspecies pertenue was seen.

The prevalence of active and latent yaws infection fell rapidly and substantially 12 months after high-coverage mass treatment with azithromycin, with the reduction perhaps aided by subsequent activities to identify and treat new cases of yaws.

Less-Tight versus Tight Control of Hypertension in Pregnancy

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The effects of less-tight versus tight control of hypertension on pregnancy complications are unclear.

An open, international, multicenter trial involving women at 14 weeks 0 days to 33 weeks 6 days of gestation who had nonproteinuric preexisting or gestational hypertension, office diastolic blood pressure of 90–105 mm Hg (or 85–105 mm Hg if the woman was taking antihypertensive medications), and a live fetus were included. Women were randomly assigned to less-tight control (target diastolic blood pressure, 100 mm Hg) or tight control (target diastolic blood pressure, 85 mm Hg). The composite primary outcome was pregnancy loss or high-level neonatal care for more than 48 hours during the first 28 postnatal days. The secondary outcome was serious maternal complications occurring up to 6 weeks post partum or until hospital discharge, whichever was later.

The analysis of 987 women were included (74.6% had preexisting hypertension). The primary outcome rates were similar among 493 women assigned to less-tight control and 488 women assigned to tight control (31.4% and 30.7%, respectively) and the rates of serious maternal complications were 3.7% and 2.0%, respectively despite a mean diastolic blood pressure thatwas higher in the less-tight-control group by 4.6 mm Hg. Severe hypertension (≥160/110 mm Hg) developed in 40.6% of the women in the less-tight-control group and 27.5% of the women in the tight-control group ($P<0.001$).

No significant between-group differences in the risk of pregnancy loss, high-level neonatal care, or overall maternal complications were shown, although less-tight control was associated with a significantly higher frequency of severe maternal hypertension.

Age of Transfused Blood in Critically Ill Adults

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Fresh red cells may improve outcomes in critically ill patients by enhancing oxygen delivery while minimizing the risks of toxic effects from cellular changes and the accumulation of bioactive materials in blood components during prolonged storage.

In this multicenter, randomized, blinded trial, the authors assigned critically ill adults to receive either red cells that had been stored for less than 8 days or standard-issue red cells (the oldest compatible units available in the blood bank). The primary outcome measure was 90-day mortality.

Between March 2009 and May 2014, at 64 centers in Canada and Europe, 1211 patients were assigned to receive fresh red cells (fresh-blood group) and 1219 patients were assigned to receive standard-issue red cells (standard-blood group). Red cells were stored for a mean (±SD) of 6.1±4.9 days in the fresh-blood group as compared with 22.0±8.4 days in the standard-blood group ($P<0.001$). At 90 days, 448 patients (37.0%) in the fresh-blood group and 430 patients (35.3%) in the standard-blood group had died. In the survival analysis, the hazard ratio for death in the fresh-blood group, as compared with the standard-blood group, was 1.1. There were no significant between-group differences in any of the secondary outcomes (major illnesses; duration of respiratory, hemodynamic, or renal support; length of stay in the hospital; and transfusion reactions) or in the subgroup analyses.

The transfusion of fresh red cells, as compared with standard-issue red cells, did not decrease the 90-day mortality among critically ill adults.

Antibiotic Treatment Strategies for CAP in Adults

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The choice of empirical antibiotic treatment for patients with clinically suspected CAP who are admitted to non–intensive care unit (ICU) hospital wards is complicated by the limited availability of evidence. Strategies of empirical treatment (allowing deviations for medical reasons) with beta-lactam monotherapy, beta-lactam–macrolide combination therapy, or fluoroquinolone monotherapy were compared.

In a cluster-randomized, crossover trial with strategies rotated in 4-month periods, the noninferiority of the beta-lactam strategy to the beta-lactam–macrolide and fluoroquinolone strategies were tested with respect to 90-day mortality in an intention-to-treat analysis.

A total of 656 patients were included during the beta-lactam strategy periods, 739 during the beta-lactam–macrolide strategy periods, and 888 during the fluoroquinolone strategy periods, with rates of adherence to the strategy of 93.0%, 88.0%, and 92.7%, respectively. The median age of the patients was 70 years. The crude 90-day mortality was 9.0% (59 patients), 11.1% (82 patients), and 8.8% (78 patients), respectively, during these strategy periods. In the intention-to-treat analysis, the risk of death was higher by 1.9% points with the beta-lactam–macrolide strategy than with the beta-lactam strategy and lower by 0.6% points with the fluoroquinolone strategy than with the beta-lactam strategy. These results indicated noninferiority of the beta-lactam strategy. The median length of the hospital stay was 6 days for all strategies, and the median time to starting oral treatment was 3 days.

Among patients with clinically suspected CAP admitted to non-ICU wards, a strategy of preferred empirical treatment with beta-lactam monotherapy was noninferior to strategies with a beta-lactam–macrolide combination or fluoroquinolone monotherapy with regard to 90-day mortality.

Effects of Red-Cell Storage Duration on Patients Undergoing Cardiac Surgery

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Some observational studies have reported that transfusion of red-cell units that have been stored for more than 2–3 weeks is associated with serious, even fatal, adverse events. Patients undergoing cardiac surgery may be especially vulnerable to the adverse effects of transfusion.

Therefore, a randomized trial at multiple sites from 2010 to 2014 was conducted. Participants 12 years of age or older who were undergoing complex cardiac surgery and were likely to undergo transfusion of red cells were randomly assigned to receive leukocyte-reduced red cells stored for 10 days or less (shorter-term storage group) or for 21 days or more (longer-term storage group) for all intraoperative and postoperative transfusions. The primary outcome was the change in multiple organ dysfunction score (MODS; range, 0–24, with higher scores indicating more severe organ dysfunction) from the preoperative score to the highest composite score through day 7 or the time of death or discharge.

The median storage time of red-cell units provided to the 1098 participants who received red-cell transfusion was 7 days in the shorter-term storage group and 28 days in the longer-term storage group. The mean change in MODS was an increase of 8.5 and 8.7 points, respectively. The 7-day mortality was 2.8% in the shorter-term storage group and 2.0% in the longer-term storage group (P=0.43); 28-day mortality was 4.4% and 5.3%, respectively (P=0.57). Adverse events did not differ significantly between groups except that hyperbilirubinemia was more common in the longer-term storage group.

The duration of red-cell storage was not associated with significant differences in the change in MODS. It was conducted that the transfusion of red cells stored for 10 days or less was not superior to the transfusion of red cells stored for 21 days or more among patients 12 years of age or older who were undergoing complex cardiac surgery.

Anesthetic Neurotoxicity – Clinical Implications of Animal Models

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Some anesthetics and sedatives have been shown to cause neurotoxic effects in labaratory animals. The Food and Drug Administration collaboration Smart Tots recommends undertaking large-scale clinical studies and avoiding nonurgent surgical procedures requiring anesthesia in chidren younger than 3 years of age.

New studies have confirmed that commonly used anesthetics and sedatives that either increase inhibitory g-aminobutyric acid receptor activity (e.g., propofal, etomidate, sevoflurone, desflurane, and isoflurane) or block excitatory glutamate receptors (e.g., ketamine) produce profound neurotoxic effects in laboratory animals. The infectable anesthetic propofol, most commanly used to induce a rapid loss of consiousness, causes apoptosis of neurons and oligodendrocytes in the brains of fetal and neonantal macaque monkeys

Similarly, the commenly used inhaled anesthetic isoflurane induces widespread apaptosis in the neonatal primate brain. The glutamate receptor antagonist ketamine, when administred as a single dose over a prolanged period (24 hours) during a sensitive phase of brain development, causes long-lasting deficits of memory and attention in primates. Studies involving species ranging from nematodes to nonhuman primates have revealed histologic changes and, in some cases imparied performance on behavioral test. Factors that influence the extent of injury include the age at the time of drug exposure and cumulative anesthetic dose. Histologic changes include widespread apoptosis and cell death, a reduction in the number of synapses, changes in neuronal morphology, and impaired neurogenesis in the hippocampus.

Although there are insufficient clinical trials to support, these animal experiments can be reduced school performance and learning in children. Well-designed clinical trials are needed to answer many important fundamental questions. For example, are pediatric patient populations at higher risk? Does the extent of anesthetic-induced neurotoxic effects depend on the cumulative dose? Do underlying diseases or inflammatory processes increase the risk of brain injury?

While we await clinical studies that can definitively determine whether anesthetics cause injury in humans, surgeon, anesthesiologist, and parents should consider carefully how urgently surgery is needed, particularly in children under 3 years of age.