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HHS plan for hospitals to stockpile pandemic flu antivirals draws fire

Cost and a host of consequences are cited

With a matching vaccine not expected to be available for at least five months if and when pandemic influenza hits, hospitals should stockpile flu antivirals to protect their health care workers, the U.S. Department of Health and Human Services (HHS) recommends in recently issued draft guidance.[1] Sounds straightforward enough, but the recommendations immediately drew strong reactions and raised thorny questions about health care worker willingness to take prolonged antiviral regimens, the potential for side effects and adverse reactions, and the cost and expiration dates of the products.

"We are very disappointed that the HHS hasn't placed more emphasis on personal protective equipment, covering coughs, hand hygiene, quarantine strategies, etc. — and less emphasis on antivirals," says **Susan Kraska**, RN, CIC, an ICP at Memorial Hospital of South Bend, IN. "In the end, wrapping your arms around an outbreak takes a lot more than the false sense of security prophylaxis offers. [Antiviral] stock rotation needs to occur, outdates and expirations need to be monitored, storage of stockpiles with temperature controls all take resources out of an already stressed health care system. This is not as simple as it may first appear."

The HHS calls for hospitals to provide antiviral regimens to health care workers during the duration of a pandemic outbreak in their community, which would typically translate to eight 10-dose regimens per worker over a 12-week period. The guidelines call for prophylaxis of hospital employees who are potentially exposed to patients, which HHS estimated to be about two-thirds of workers in any given facility. With the 10-dose regimens running in the $40-$50 range, the cost will not be inconsequential.

"The concept here is to protect people who are exposed to patients who may have influenza," says **Ben Schwartz**, MD, senior science adviser with the National Vaccine Program Office at the HHS. "We want to keep the people who are at high risk protected by giving them prophylaxis, and our estimate is that's about two-thirds of the population of health care workers."

The remaining one-third of workers should be considered for post-exposure prophylaxis (PEP) if they have close contact with an influenza patient, he tells *Hospital Infection Control.* "For those who are less likely to be exposed — who may never have an exposure or just have an infrequent exposure — PEP prophylaxis would be very effective," he says. "It also uses fewer antiviral drugs, so it is a more cost-effective approach."

The HHS draft recommendations make the assumption that there will not be a vaccine immediately available should a pandemic flu strain emerge, he adds, estimating 20 weeks from the appearance of a pandemic strain to creation of a matching vaccine. "Based on how quickly a pandemic may spread, we don't have confidence that a vaccine will be available at the beginning," Schwartz says. "Health care workers are recommended to be in the first group to receive vaccine once it is available; so by stockpiling antiviral drugs, it is in some ways a 'belt-and-suspenders' approach. It provides the confidence that hospitals will be able to protect their work force in a pandemic."

Whether it emerges via some mutation of avian influenza A H5N1, or some other strain, a fact not frequently noted is that even a perfectly matched vaccine will not provide immediate protection against a pandemic flu virus. "It takes two doses to stimulate immunity," he explains. "So after the health care worker gets the first dose, you need to wait either three or four weeks before giving the second dose, and then it may take another week or two before a good immune response develops. So even after the health care worker is vaccinated with that first dose, there is still a period of maybe five to six weeks in which they are vulnerable to getting infected. That is another reason that the antiviral drugs need to be available to protect these important workers."

Two FDA-approved influenza antiviral medications used in the United States are oseltamivir (Tamiflu®) and zanamivir (Relenza®). These neuraminidase inhibitors have activity against both influenza A and B viruses. While all bets are off if a pandemic flu strain emerges, advice distributed by the CDC during the 2007-2008 flu season underscores that using antivirals to stave off or lessen the severity of flu infections is not without risk. According to the CDC, "when considering use of influenza antiviral medications, clinicians must consider the patient's age, weight and renal function; presence of other medical conditions; indications for use (i.e., chemoprophylaxis or therapy); and the potential for interaction with other medications. The main side effects for oseltamivir are nausea or vomiting (10%). Rare cases of transient neuropsychiatric events (self-injury or delirium) have been reported during post-marketing surveillance among people taking oseltamivir, primarily in Japan. Zanamivir is not recommended for people with underlying airways disease (e.g., asthma or chronic obstructive pulmonary diseases)."[2] Thus, administering antivirals to large groups of health

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HHS antiviral plan: 100 million regimens in U.S. hospitals

Strategy includes prolonged prophylaxis, PEP

If hospitals nationwide followed draft recommendations to stockpile flu antivirals to protect health care workers against an influenza pandemic more than 100 million antiviral regimens would be required, according to the U.S. Department of Health and Human Services (HHS).[1] Key portions of the HHS recommendations are summarized as follows:

• **Antiviral drugs should be used as prophylaxis for the duration of community outbreaks for health care workers who have direct high-risk exposures to pandemic influenza patients and for frontline emergency services (e.g., law enforcement, fire, and emergency medical services personnel).** Workers in these occupational settings will be exposed to persons with pandemic illness and be at increased risk of acquiring infection. Moreover, burdens on health care and emergency services will be increased in a pandemic and prophylaxis will reduce absenteeism due to illness as well as from fear of becoming infected while at work. Because exposures would be frequent and prophylaxis before exposure is likely to be most effective in reducing illness and absenteeism, outbreak (pre-exposure) prophylaxis is recommended rather than post-exposure prophylaxis (PEP).

• **PEP is recommended for exposed persons in the health care and emergency services sectors who do not have regular contact with ill persons and are not receiving outbreak prophylaxis.** Many workers in health care and emergency services are important to the delivery of those essential services but are not at high risk for exposure in the occupational setting. Examples might include kitchen and medical records staff at hospitals and 911 dispatchers for emergency response. PEP is recommended for these workers as this strategy requires fewer antiviral drug regimens compared with outbreak prophylaxis and is likely to provide sufficient protection for less exposed groups, the HHS states.

Of the approximate 13 million workers in the health care sector as defined by the Bureau of Labor Statistics, the HHS estimated that two-thirds of health care workers, or about 8.7 million, may have frequent high-risk exposures to pandemic flu. In addition, there are some 2 million people in the emergency services sectors, including medical services, fire service and law enforcement personnel. "The remaining 4.3 million health care sector workers would receive post-exposure prophylaxis when unprotected exposure occurs, estimated as four times during a 12-week community outbreak," the HHS calculated. "Based on these estimates, a total of 102.8 million antiviral regimens would be needed."

Other general recommendations in the guidelines include:

1. Use antiviral drugs from the Strategic National Stockpile to support a multifaceted international containment response, if feasible, to slow the introduction of pandemic influenza into the United States, and to respond to the first cases that are introduced, if warranted based on the epidemiological situation.

2. Recommended antiviral drug use strategies should be reconsidered at the time of a pandemic based on the epidemiology and impacts of the pandemic. Data collected during the pandemic may be critical for policy decisions. Preparation of protocols before a pandemic to facilitate rapid data collection would be useful. Data needs include:

A. Attack rate of pandemic illness, case fatality rates, and identification of groups at high risk for severe morbidity and mortality.

B. Susceptibility of the pandemic virus to antiviral drugs and monitoring data on the rate of antiviral resistance.

C. Estimates of the effectiveness of treatment in preventing severe morbidity and death.

D. Evaluation of increased treatment dose and/or duration, if appropriate, based on estimates of effectiveness of the standard regimen.

E. Adverse event surveillance to identify unanticipated adverse events following antiviral treatment and prophylaxis — especially if prophylaxis is continued for longer than FDA-approved indications. Current adverse event surveillance systems such as MedWatch should be supplemented with more active approaches.

3. If experience early during an influenza pandemic indicates that a treatment-focused strategy is not optimal because of biological (e.g., lower-than-anticipated antiviral treatment effectiveness), implementation (e.g., inability to deliver treatment early after illness onset), or behavioral (e.g., worker absenteeism due to fear of infection in the workplace) reasons, a mechanism needs to be in place to consider alternative strategies and provide national guidance. Advice from public health organizations, medical societies, and government advisory committees should be influential for decision making. ■

care workers would require some level of screening and follow-up.

"Health histories on employees will become an issue regarding staff ability to take the drugs," says **Katherine West**, RN, MSEd, CIC, a consultant with Infection Control/Emerging Concepts in Manassas, VA. "Side effects of the drugs are an issue as well. Lessons should have been learned from the anthrax episode in 2001 [with widespread administration of ciprofloxacin]. No questions were being asked about pregnancy, other current meds, medical history or allergies."

Will health care workers comply?

In addition — given the well-documented historical apathy of health care workers toward seasonal flu vaccination — it is not completely farfetched to ask whether they will comply with the antiviral recommendations even in the face of a pandemic. Kraska, who served on an Indiana state panel that looked at the role of antivirals in a pandemic, says the group came to a somewhat surprising conclusion.

"We looked at the issues surrounding mass prophylaxis and who should be included," she tells *HIC*. "Interestingly, we came to the conclusion that using antivirals for long periods wasn't acceptable to many health care workers. It is the uncertainty of how long? How effective? What is the impact on their health? To our knowledge, there are no studies that show the long-range effect of antivirals. Overall, we didn't feel it was more effective than preventing exposures in the first place [through barrier precautions and other infection control measures]."

The FDA has approved oseltamivir for a six-week prophylaxis course, Schwartz says, adding that ongoing studies may be able to extend the approved duration to 12 weeks. "In controlled trials with Tamiflu, there is some nausea and vomiting that may occur, but very rarely did someone receiving the drug need to stop taking it because of those side effects," he says. "In a pandemic, [health care workers] would recognize that they will be constantly exposed to patients with influenza. I think they would view this as an important way to protect themselves. Certainly, there would be noncompliance; people may forget to take it or stop taking it early. We see that with any drug in any population."

Another question is how quickly antiviral resistance will appear once mass prophylaxis programs begin. "We also need to consider emerging resistance of influenza A to existing antivirals," says **Diana Carpal**, RN, CIC, a member of the Indiana antiviral panel and infection control and prevention coordinator at Saint Joseph Regional Medical Center in South Bend. "Inappropriate or mass use could 'push' this even faster, leaving our stockpiled supplies mostly ineffective."

Ultimately, the Indiana panel decided using antivirals for post-exposure prophylaxis (PEP) of health care workers would be more effective than starting them on regimens as soon as a pandemic strain appears in the community. The HHS guideline concedes that PEP could be an alternative strategy, but the effect essentially may be the same. "Because exposure to ill persons during a pandemic outbreak will be frequent for health care workers and emergency service personnel with direct patient contact, post-exposure prophylaxis would be essentially equivalent to outbreak prophylaxis — as soon as one 10-day course of PEP ended, another would likely begin," the draft guidelines states.

A modification of the PEP strategy may be to dispense PEP only when "unprotected" exposures occur. "Potential concerns with this approach for those with frequent high-risk exposures include whether it would be sufficient to reduce absenteeism that may occur due to fear of occupational infection, whether unprotected exposures could be accurately identified and how frequently they would occur in a heavily exposed population," the HHS states. "In addition, there is a lack of data on the effectiveness of personal protective equipment measures in preventing influenza transmission. A hybrid strategy that includes outbreak prophylaxis for workers with frequent high-risk exposures and post-exposure prophylaxis when unprotected exposure occurs for those who have less frequent or intensive patient contact tailors the intervention to the level of risk and is the preference of the [HHS] working group."

Hold back until pandemic is local

Antiviral medications are 70%-90% effective in preventing influenza, but the drugs must be taken each day for the duration of potential exposure to influenza or until immunity after vaccination develops. The HHS is advising that even if a pandemic begins elsewhere, antivirals should be held back until it hits your local area. "You want to wait until it is in your community," Schwartz says. "The trigger for hospitals is when they are notified by their public health officials that a pandemic virus is

in their area and an outbreak is beginning."

Though one certainly can argue that stocking antivirals is an investment in worker protection similar to the cost of vaccines for hepatitis B and other diseases, some hospitals may balk at such expenditure for a threat that is merely theoretical on the near horizon. A hospital with 2,400 employees, according to the HHS formula, would need to stockpile antivirals for 1,600 of them. At $400 per eight 10-pack doses, that translates to a $640,000 expenditure. With 7,000 employees, facilities such as the Marshfield (WI) Clinic are looking at much larger numbers. "For a system of our size, [this would require] a fairly significant outlay of cash," says **Bruce E. Cunha**, RN MS COHN-S, manager of employee health and safety at the clinic. "Given that the antivirals have expiration dates, I feel facilities are going to be reluctant to stockpile all that much."

The respective shelf-lives for Tamiflu and Relenza are seven years and five years if used in stockpiles, Schwartz says. "But the companies are continuing to test the potency of the drugs and they may in the future have longer [expiration dates] if it is FDA-approved," he adds.

In any case, hospitals should make the purchase to safeguard their workers, even if they have to make it again if the stockpile sits unused past the expiration period, Schwartz argues. "If a pandemic does not occur within the seven-year licensed shelf life, then they would need to repurchase their antiviral drugs — so this would represent a recurring cost," he says. "There is currently not a federal program that would purchase the drugs for prophylaxis of private sector health care workers."

The hospital stockpiles are not intended for treatment of infected patients, which would be covered by state and federal sources during a pandemic, Schwartz adds. Neither are the hospital stockpiles earmarked for family members of health care workers, though pandemic planners have warned that staff may not show up unless they believe their families are safe. "The [HHS guidelines] do not include a recommendation for family members, though a hospital could certainly choose to stockpile drugs for the family members as well as the health care workers," he says. "But given the burden and expense of protecting their health care work force, I think it's unlikely that hospitals would also choose to protect family members."

That said, health care workers receiving prophylaxis would pose no threat to their families, who would receive antivirals for treatment as needed from community sources, Schwartz emphasizes. "Recognizing that the way influenza is transmitted is by respiratory droplets, if you protect the health care worker then they would not be at risk to bring the infection home to their family," he says. "So one important thing to emphasize in the education that should be provided is that families of health care workers are not at increased risk compared to other families. That should reassure them they do not need special prophylaxis."

Indeed, the HHS draft guidelines argue essentially that prophylaxing health care workers may be the best strategy to get them to stay on the job. "The health care sector will face a massively increased burden while coping with a work force diminished by illness and possibly other causes of absenteeism — for example, caring for an ill family member or due to fear of becoming infected in the workplace," the guidelines state. ". . . [A]ntiviral prophylaxis may reduce absenteeism both by preventing illness and by improving perceptions of safety in the workplace."

Uncharted territory

The HHS guidelines concede the health benefits of this ambitious prophylactic strategy cannot be easily quantified. Several studies suggest that health care workers who have patient exposure have increased rates of seasonal influenza infections, the guidelines note.[3,4] In addition to the direct effect of reducing pandemic influenza illness and its consequences, prophylaxis also would reduce the risk of transmission to family members, co-workers, and to patients, the guidelines state. Influenza prevention by vaccination of health care workers has been shown to reduce nosocomial infection in acute care hospitals and mortality in long-term care facilities for the elderly.[5,6]

Nevertheless, given the litany of concerns, the HHS may face formidable opposition to its guidelines and compliance problems if they are finalized as drafted. Ultimately, the specter of pandemic flu may stand as its own best argument for preparation. It is oft described as something that must be faced eventually, a "when-not-if" biological disaster that could all but shut down the health system. And H5N1 is conceivably but a few fateful mutations away from becoming easily transmissible among humans.

"Part of the planning for hospitals is acquiring the materials, whether it be masks or respirators or antiviral drugs that will protect their health care workers and maintain operations during a pandemic," Schwartz says. "One cannot predict

whether H5N1 is going to ever cause a pandemic. It certainly is the greatest pandemic threat that is out there. The continued circulation of this virus in poultry and the occasional infection of people certainly raise the risk that such a mutation could occur. Whether it does or not is totally unpredictable."

(Editor's note: The HHS issued a notice regarding the guidelines and a comment period in the June 3, 2008, Federal Register. *The guidelines are posted at http://aspe.hhs.gov/panflu/antiviral-n-masks.htm. The comment period ends July 3, 2008*.)

References

1. Department of Health and Human Services. Proposed Guidance on Antiviral Drug Use during an Influenza Pandemic, 2008. Available at: http://aspe.hhs.gov/panflu/antiviral-n-masks.htm.
2. Centers for Disease Control and Prevention. Influenza Antiviral Medications: Summary for Clinicians, 2007. Available at: www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm.
3. Elder AG, O'Donnell B, McCruden EAB, et al. Incidence and recall of influenza in a cohort of Glasgow healthcare workers during the 1993-4 epidemic: Results of serum testing and questionnaire. *BMJ* 1996; 313:1,241-1,242.
4. Kawana A, Teruya K, Kirikae T, et al. Syndromic surveillance within a hospital for the early detection of a nosocomial outbreak of acute respiratory illness. *Jpn J Infect Dis* 2006; 59:377-379.
5. Salgado CD, Giannetta ET, Hayden FG, et al. Preventing nosocomial influenza by improving the vaccine acceptance rate of clinicians. *Inf Cont Hosp Epidemiol* 2004; 25:923-928.
6. Carman WF, Elder AG, Wallace LA, et al. Effects of influenza vaccination of healthcare workers on mortality of elderly people in long-term care: A randomized controlled trial. *Lancet* 2000; 355:93-97. ■

CDC mulled other theories in Vegas HCV outbreak

77 more HCV cases now being investigated

Centers for Disease Control and Prevention investigators considered several other theories before concluding that improper needle practices and reuse of single-dose vials of propofol likely caused a recent HCV outbreak among patients at a Las Vegas endoscopy clinic. The outbreak led to the largest "look-back" notification in history, as some 40,000 patients were advised to be tested for hepatitis C and B, as well as HIV.

The CDC officially has confirmed six cases, citing "inappropriate reuse of syringes [and] . . . use of medication vials intended for single-person use on multiple persons" as the most likely source of transmission.[1] **(See special report in *Hospital Infection Control*, April 2008.)**

Since the initial report, the Southern Nevada Health District had identified 77 additional HCV-infected patients that are "potentially linked" to the Endoscopy Center of Southern Nevada. Health investigators also reported a separate HCV case that appears to involve transmission at another Las Vegas clinic, the Desert Shadow Endoscopy Center. "While it has been determined this acute case is linked to the center there is not sufficient information at this time to determine the likely source of disease transmission," the state health officials reported.

Concerning the original investigation into the practices at the Endoscopy Center of Southern Nevada, a May 15, 2008, "trip report" by CDC investigators reveals the agency looked at transmission via endoscopy equipment and considered the possibility that an infected clinician was raiding the drug supply. The latter theory fell down the list rather quickly because no HCV-positive clinic worker was identified. "Transmission of HCV from infected staff has occasionally been reported zand typically involved diversion of narcotics such as fentanyl," the CDC investigators reported. "This route of transmission appears unlikely in the clinic setting given that no staff members have tested positive for HCV infection and propofol is not a commonly abused medication."

Observation of anesthesia administration practices indicated that some staff routinely reused syringes during individual procedures to withdraw anesthesia from single-use propofol vials that were inappropriately used to provide medication for multiple patients, the CDC reported. "Similar practices have previously been implicated in the transmission of bloodborne pathogens," investigators noted. Another possible route that was considered was inadequate endoscope reprocessing.

"Occasionally, patient-to-patient HCV transmission has been attributed to inadequate cleaning or disinfection of patient equipment, but we consider this mechanism less likely in the context of our investigation," the investigators reported.

In the clinic, endoscope reprocessing procedures were generally followed, except that enzymatic cleaning solution was used on more than one endoscope. Manual cleaning with brushes to remove biofilms and high-level disinfection, which are considered most important for reducing potential

bloodborne pathogen transmission, were judged adequate, the report notes. "However, because recordkeeping was lacking in some respects, we could not determine whether endoscopes had been processed at the same time or by the same machine (this was not recorded in the charts)," the investigators concluded.

On Sept. 21, 2007, — the day five of the six confirmed HCV cases were at the clinic — patient records indicated that two of the case-patients had procedures performed with one particular endoscope. However, the "clinic staff attributed this to a clerical error," the CDC reported. "In addition, in [previous outbreaks], endoscopic biopsies were found to be an independent risk factor for HCV infection, (though deficiencies in the handling of parenteral medications were also noted)," the report concludes. "In our investigation, only three of six clinic-associated case-patients had a biopsy done, and the needle used was reported to be a single-use disposable item."

Reference

1. Centers for Disease Control and Prevention. Acute hepatitis C virus infections attributed to unsafe injection practices at an endoscopy clinic — Nevada, 2007. *MMWR* 2008; 57; 513-517. ■

Rust never sleeps: Staph eats away at vanc efficacy

FDA lowers vancomycin breakpoints

The much-feared widespread emergence of vancomycin-resistant *Staphylococcus aureus* has not occurred, with true VRSA still a rare phenomenon. But perhaps the path to this milestone toward a post-antibiotic era will occur in more incremental steps.

Researchers are finding that vancomycin is "losing potency" against methicillin-resistant *S. aureus* (MRSA) infections, meaning the time honored antimicrobial may yield to drug resistance in a very different way than originally imagined.[1]

Vancomycin use has increased dramatically worldwide since the mid-1980s, largely as a result of empirical and directed therapy against burgeoning MRSA infections. With limited choices, clinicians have traditionally relied on vancomycin alone in the management of serious MRSA infections and have enjoyed a significant period free of vancomycin resistance in *S. aureus*. Even now, five decades after its introduction, vancomycin resistance among *S. aureus* strains, as currently defined microbiologically, remains rare. "Yet it is becoming clear that vancomycin is losing potency against *S. aureus,* including MRSA," the authors conclude. "Serious infections due to MRSA defined as susceptible in the laboratory are not responding well to vancomycin. This is demonstrated by increased mortality seen in patients with MRSA infection and markedly attenuated vancomycin efficacy caused by vancomycin heteroresistance in *S. aureus.* Therefore, it appears that our definition of vancomycin susceptibility requires further scrutiny as applied to serious MRSA infections, such as bacteremia and pneumonia."

As a result of such findings, the Food and Drug Administration recently lowered the vancomycin "breakpoints" for staph infections. The Infectious Disease Society of America reported on its web site that FDA made the move in an updated package insert for a vancomycin injection product; the first of what will apparently be new cut-point labeling for all vancomycin meds. The minimum inhibitory concentration (MIC) (µg/mL) has been lowered from ≤ 4 to ≤ 2 for susceptible; from 8-16 to 4-8 for intermediate; and ≥ 32 to ≥ 16 for resistant. The change follows mounting evidence that patients infected with *S. aureus* strains with MIC of 4 µg/mL were failing therapy. **Robert C. Moellering Jr**., MD, FIDSA, past president of IDSA and lead author of the aforementioned paper, explained the situation to *Hospital Infection Control.*

"The old breakpoints were set at a time when there was no resistance [to vancomycin] and there were no failures," said Moellering, physician-in-chief and chairman of the department of medicine at the Beth Israel Deaconess Medical Center in Boston. "People began noticing a lot of things that were occurring. [For example], the old breakpoints had 8 and 16 MIC as being intermediate, when it was clear that organisms were essentially resistant and then [patients] failed therapy."

Cases of vancomycin-intermediate *S. aureus* (VISA) began occurring in the United States in the mid-1990s after first being reported in Japan. In 2002, a sci-fi scenario researchers had long feared occurred when vancomycin-resistant genetic material from a coinfecting enterococci strain to *S. aureus* within a patient, creating the first clinical strain of a much-anticipated superbug: VRSA. These strains continue to be reported sporadically, but did not emerge and flourish as feared — all the while though vancomycin was losing efficacy at the

lower end of the scale.

"There were a bunch of strains they began calling hetero-VISA strains, which MICs that were susceptible but when you tested them in the laboratory they had numerous small colonies, subpopulations for which the MIC was a lot higher," Moellering says. "They also were beginning to fail therapy. There has also been what is called 'vancomycin creep,' that is that the minimal inhibitory concentration of vancomycin as far as the strains in the susceptible range have been going up imperceptibly. As those MICs go up, more and more of those become heteroresistant as well."

The upshot of the revised breakpoints is "that vancomycin should no longer be used to treat organisms that have a MIC of 4," he adds. "Now it turns out there are not a huge amount of MRSA strains floating around that that have vancomycin MICs of 4. So changing the breakpoints doesn't have a gigantic impact, but people are re-looking at it now because there is even a question of whether they ought to drop it one more set of dilutions, i.e., down to 2. When you start getting strains with MICs as high as 2, there are a lot of them that are heteroresistant that don't show it by standard testing in the clinical lab, but for which vancomycin is clinically less effective."

There are other drug alternatives, but gradually losing the old mainstay against MRSA is none the less discomforting. "Right now because testing for heteroresistance in particular is so difficult, many clinicians haven't really caught on to the fact vancomycin is losing its efficacy up front," Moellering says.

The incremental resistance is occurring through a number of genetic changes in staph strains. "It is not one simple mutation," he says. "Some of them lead to cell wall thickening, some may allow the organism to become tolerant to vancomycin, so it inhibits but doesn't kill it. Some of these changes actually lead to decreased virulence in these organisms, which is why you see patients who have prolonged vancomycin-resistant staph or MRSA and don't die."

Reference

1. Sakoulas G, Moellering RC. Increasing antibiotic resistance among methicillin-resistant *Staphylococcus aureus* strains. *Clin Infect Dis* 2008; 46: S360-S367. ■

C. diff hospitalizations, deaths nearly double

Toxic strain, aging population likely factors

An aging population and the emergence of a hypervirulent strain are combining to make *Clostridium difficile* disease a killer. Hospitalizations and deaths from *C. diff*-associated disease (CDAD) are on the rise in the United States.

The incidence of adult CDAD hospitalizations doubled from 5.5 cases per 10,000 population in 2000 to 11.2 in 2005, and the CDAD-related age-adjusted case-fatality rate rose from 1.2% in 2000 to 2.2% in 2004, researchers found.[1] In addition to a near doubling of deaths, their analysis detected a 23% annual increase in CDAD hospitalizations in the six-year period from 2000 through 2005. One factor is likely increased virulence of the organism, specifically the emergence of a highly virulent strain (NAP1) that is 20 times more toxic than typical *C. diff.* The study appears to reflect the consequences of NAP1 emergence in terms of hospitalizations and deaths, but another factor may be the aging of the population, the lead author tells *Hospital Infection Control*.

"There are other reports of this hypervirulent strain and that may be responsible for what we are seeing — at least partially," says **Marya Zilberberg**, MD, founder and president of EviMed Research Group LLC in Springfield, MA. "My own personal sense is that our population [also] is getting older and sicker; there is a lot more chronic disease then there used to be. That predisposes you to *C. diff* disease," she adds.

Whatever the reasons, increasing hospitalizations and mortality trends make preventing *C. diff* transmission all the more important. As a start, infection control professionals should establish surveillance systems for the pathogen and verify their local situation.

"All hospitals should really consider surveillance of some kind," Zilberberg says. "No. 2, obviously cleaning isolation of cases, barrier precautions, those are all things that can prevent the spread of *C. diff* from person to person. But it is very important to understand where you stand currently as an institution. If you don't quantify things, A: you don't recognize them as a problem; and B: you can't fix them. Every institution really needs to ask the question how much *C. diff* do we have?"

The researchers identified CDAD-related hospitalizations for 2000-2005 from the National Inpatient Sample data, available on the Healthcare

Costs and Utilization Project Net web site, administered by the Agency for Healthcare Research and Quality. The National Inpatient Sample is a stratified 20% sample of U.S. community hospitals, and the data are weighted to provide national estimates. CDAD was identified by the presence of the International Classification of Diseases, 9th revision; Clinical Modification (ICD-9-CM); diagnosis code 8.45 (intestinal infection with *Clostridium difficile),* and the numbers of discharges per year were age-stratified.

Reference

1. Zilberberg MD, Shorr AF, Kollef MH. Increase in adult *Clostridium difficile*-related hospitalizations and case-fatality rate, United States, 2000-2005. *Emerg Infect Dis* [serial on the Internet] 2008. Available at http://www.cdc.gov//EID/content/14/6/929.htm. ■

OSHA proposes a formula for pandemic stockpiles

480 N95s or one elastomeric needed per HCW

For the first time, a newly proposed guidance puts a number and a cost to the respirators needed to protect health care workers during an influenza pandemic: 480 respirators at a cost of about $240 to protect a single employee, or a single reusable elastomeric respirator with three filters at a cost of $40 per employee.

The U.S. Occupational Safety and Health Administration issued the proposed guidance to help employers determine how many respirators and facemasks to stockpile for pandemic preparedness (www.osha.gov/dsg/guidance/stockpiling-facemasks-respirators.html). It requested comments on the guidance through July 8. **(See editor's note for more information, p. 83.)**

OSHA is encouraging employers to stockpile respirators because "manufacturing capacity at the time of an outbreak would not meet the expected demand for respiratory protection devices during the pandemic," the agency said. "It is also important to note that respirators and facemasks are just one element of a multilayered approach to pandemic preparedness. There are many other protective measures that can and should be elements of a comprehensive pandemic preparedness plan."

"When you put all this together, we believe there will be substantial ability to protect critical work forces and the population in general," says **Ben Schwartz**, MD, senior science adviser with the National Vaccine Program Office at the U.S. Department of Health and Human Services, who helped OSHA draft the respirator guidance.

Until now, hospitals and health systems have had to make their own assumptions and estimates to determine how many respirators to stockpile, says **Lewis J. Radonovich**, MD, director of Biosecurity Programs for the Office of Program Development at the North Florida/South Georgia Veterans Health System in Gainesville, FL.

"I think it's very valuable for the individual health care center or system to have this type of guidance available to them," says Radonovich, who has been involved in research on respiratory protection and pandemic preparedness. "Without this, we're all left to our own devices to make these decisions."

Hospitals are expected to adapt the guidance to their own particular circumstances. For example, in its proposed guidance, OSHA assumes that a third of hospital employees will be at high risk due to direct patient contact. The actual number, however, will vary based on the nature of the pandemic and personnel decisions.

If a disproportionate number of the pandemic influenza patients are children, then pediatric hospitals may be especially hard-hit and a higher proportion of their employees may be at risk.

The Cost of Stockpiling

These cost estimates were developed by OSHA for a single employee at high risk of exposure:

- **Option 1** — Using disposable N95 respirators:
  — 480 N95s @ $0.50/respirator = $240 per employee protected
- **Option 2** — Using reusable elastomeric respirators:
  — 1 respirator @ $25 + 3 sets of filters @ $5 set = $40 per employee protected
- **Option 3** — Using 1 PAPRs shared by 4 employees on shift work:
  — 1 PAPR @ $800 + 1 spare battery @$160 + 3 extra hoods @ $90 each + 3 sets of filters @ $30 set = $1,320 / 4 employees = $330 per employee protected

(Note: Hooded PAPRs do not need to be fit-tested, which can result in other programmatic cost savings.)

Conversely, hospitals may reduce the number of employees at risk by cohorting patients and limiting the number of nonclinical personnel who come onto the floor, says Schwartz.

The proposed guidance also estimates that each health care worker will use four disposable N95 respirators per shift. Employees would wear the respirators continuously and dispose of them after each of two breaks, at lunch and at the end of the day, he reports.

It isn't prudent to expect health care workers to reuse the respirator during the day, Schwartz says. "After several hours (of continuous use), it may become saturated with secretions and make the workers breathing a little more difficulty," he says, adding, "There is some risk of contamination by doffing and donning the contaminated respirator."

Hospitals also shouldn't count on extending the use of N95 respirators by asking employees to wear a surgical mask over the respirator to protect it from contamination, Schwartz notes.

"We have to be equally concerned about a shortage of face masks. Given the [OSHA] recommendations for use of face masks not only in health care but in other sectors as well, the estimated requirements [for face masks during a pandemic] are in the tens of billions," Schwartz says.

OSHA recommends face masks for employees who have "high-frequency, close contact (within 6 feet) of the general population." That would include store clerks, bank tellers, waiters, and numerous other service workers.

A pandemic can range from mild to severe, but in its proposed guidance, OSHA assumes that "community mitigation," such as closing schools and cancelling public gatherings, would reduce illness to about 15% of the population. The guidance is based on a pattern of two waves striking a community, each lasting 12 weeks. With a five-day workweek, that would equal 120 days of protection needed for employees.

Before deciding how many respirators to stockpile, hospitals should consider the types of respirators that would best suit their needs. Based on the cost comparison, elastomeric respirators would be the cheapest alternative.

VISN 8, the Veterans Health Administration health care network that encompasses Florida, southern Georgia, Puerto Rico, and the U.S. Virgin Islands, has purchased some elastomeric respirators in addition to N95s, says Radonovich.

Reusable respirators offer a clear advantage during a pandemic, he says. "We anticipate, based on warnings, that the manufacturers won't be able to produce enough disposable N95s during a pandemic to meet the demand. We needed another option," he says.

CNE/CME *questions*

1. The HHS plan projects what proportion of health care workers should receive prophylaxis during a pandemic?

A. One-third
B. Two-thirds
C. Three-fourths
D. All workers

2. The HHS guideline said that post-exposure prophylaxis of flu-exposed workers could be an alternative strategy to "outbreak prophylaxis" but the effect essentially may be the same in a pandemic. Why is that?

A. Because roughly the same number of workers will refuse.
B. Exposures will be so frequent that PEP will be ongoing.
C. A mutating flu virus will require both prophylaxis and PEP.
D. All of the above

3. The HHS emphasized that pandemic flu is expected to spread rapidly, so as soon as the first case appears in the United States all hospitals should begin administering antivirals to workers.

A. True
B. False

4. Which factors were cited by researchers as possible contributors to an increase in hospitalizations and mortality from *Clostridium difficile*-associated disease (CDAD)?

A. Emergence of a hypervirulent strain.
B. Lack of effective drugs.
C. Aging of the population.
D. A and C

CNE/CME instructions

Physicians and nurses participate in this CE/CME program by reading the issue, using the provided references for further research, and studying the questions. Participants should select what they believe to be the correct answers, then refer to answer key to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing the semester's activity, you must complete the evaluation form that will be provided and return it in the reply envelope to receive a credit letter. ■

Yet elastomeric respirators pose issues as well. They must be fit-tested, just as N95s are. The facepiece may make it harder to communicate with patients. And they aren't comfortable to wear for long periods of time, says **William Buchta**, MD, MPH, medical director of the Employee Occupational Health Service at the Mayo Clinic in Rochester, MN.

Mayo has purchased 200,000 N95 respirators and 300,000 face masks for a pandemic stockpile. "We want to be able to last for a 2½-month period," he says. Mayo also has powered air-purifying respirators (PAPRs), which do not require fit-testing and, in some cases are recommended for high-risk procedures such as bronchoscopy.

The Marshfield (WI) Clinic has a warehouse full of N95 respirators, gloves, and gowns for a potential pandemic. Elastomerics sound like a good idea but have some drawbacks, says **Bruce Cunha**, RN, MS, COHN-S, manager of employee health and safety. "People just do not understand how uncomfortable it is to wear a [half-face] respirator for any length of time," he says. "You have a rubbery substance against your skin and you're breathing 98.6° air. The inside of those things get very warm, very quickly."

The reusables also need proper handling and cleaning. "You're going to have to train employees how to clean them properly, or you're going to have to have someone who cleans them on a daily basis," he says.

Schwartz urges health care employers at least to consider the elastomeric respirators — perhaps by trialing them at the hospital. The key is to have respirators that will be available in an emergency situation — and reusable respirators have an obvious advantage.

"While elastomerics may not be a solution for routine health care, I think it's important for planners to realize the primacy for maintaining services during an emergency," he says.

(Editor's note: For more information, go to www.osha.gov/dsg/guidance/stockpiling-facemasks-respirators.html. Comments on the OSHA guidance can be made through July 8.) ■

Flu and MRSA make a deadly combo

Initial therapy did not cover MRSA in some cases

A disturbing number of cases of pneumonia caused by staph infections resulted in death among young, otherwise healthy patients during the 2006-2007 flu season, with more than three-quarters caused by methicillin-resistant *Staphylococcus aureus* (MRSA), researchers found.[1]

"Staph-caused pneumonia in the nonhospitalized population is rare to begin with, especially in otherwise healthy, young people, but the amount caused by MRSA was particularly striking," says lead study author **Alexander J. Kallen**, MD, a medical epidemiologist at the Centers for Disease Control and Prevention. "More than three-quarters (79%) of the staph-caused pneumonia patients were infected with MRSA. Many of the MRSA patients were not treated up front for MRSA, which suggests that doctors did not initially suspect this organism in these patients."

In early 2007, federal and state public health officials began to receive reports from health departments of severe staph-caused pneumonia. Many appeared to involve MRSA and were fatal. Of the 47 staph-caused pneumonia patients for whom researchers had a complete record, 24

CNE/CME objectives

After reading each issue of *Hospital Infection Control*, the infection control professional will be able to do the following:

- identify the particular clinical, legal, or educational issue related to epidemiology;
- describe how the issue affects nurses, hospitals, or the health care industry in general;
- cite solutions to the problems associated with those issues, based on guidelines from the federal Centers for Disease Control and Prevention or other authorities, and/or based on independent recommendations from clinicians at individual institutions. ■

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died. Thirteen of the 24 were 18 years old or younger and 44% had no known pertinent medical history. Patients who had had the flu were about twice as likely to die from the staph-caused pneumonia as those who had not. The average time between symptom onset and death was four days. "The important public health message is twofold: Anyone who wants to decrease their chances of getting the flu and its complications like staph pneumonia should get a flu vaccine, and physicians should be alert to the possibility of MRSA causing severe pneumonia in outpatients and treat it accordingly," Kallen says.

The 2007-2008 flu season is undergoing a similar study.

Reference

1. Kallen AK. Brunkard J, Moore Z, et al. *Staphylococcus aureus* community-acquired pneumonia during the 2006 to 2007 Influenza Season. *Ann Emerg Med* (published online) 05 June 2008, at: www.annemergmed.com/article/S0196-0644(08)00773-7/abstract. ■

CNE/CME answers

1. B; 2. B; 3. B; 4. D.