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Elderly flu shots: No-brainer or no-gainer? Controversy, conflicting studies dog issue

New randomized clinical trial may be ethically off-limits

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Though recent conflicting studies and commentaries have thoroughly confused the issue, the take-home message for infection control professionals — which passes muster with all but the most strident critics — is that the elderly should be immunized against seasonal influenza. Period.

However, there has been considerable controversy about how much benefit the elderly gain by getting the annual shot, particularly whether it will help them mount a sufficient immune response to stave off fatal flu infections. It seems almost heresy to ask such a question in the infectious disease world, but what if the seasonal vaccine provides little benefit to the elderly, particularly those ages 70 and beyond?

“They should not feel totally protected on this vaccine if they are over 70,” says **Lone Simonsen**, PhD, MS, visiting professor and research director in the department of global health at the George Washington School of Public Health in Washington, DC.

One of the leading contrarians on the issue, Simonsen was among the first to point out that a substantial increase in elderly immunization rates in recent years has not translated to reductions in mortality.¹ Other researchers point to clear benefits in reduced hospitalizations and reduced mortality in the 50% range.² “Everybody is mighty confused,” Simonsen says of the public and press reaction to the conflicting findings and studies. “But immune senescence is a well-known phenomenon. If you ask an immunologist, they will tell you that the T-cells and B-cells — the whole immune system — is going down as you age.”

Still, it should be noted at the onset, that Simonsen is in favor of immunizing the elderly against seasonal flu to achieve whatever benefit can be gained. Though she has found fault with the methodology and perceived statistical biases of many vaccine efficacy studies, she endorses one study that found the immunized elderly had a 29% reduction in hospital admissions with laboratory-confirmed influenza.³

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"Maybe you can protect one-quarter to one-third of them," Simonsen says. "That is certainly worth doing, but what we are pointing out is that there is room for improvement here. We need better vaccines for seniors and in general better approaches on how to protect them indirectly and with antivirals."

Indeed, the issue also has raised questions about how the elderly will fare during a pandemic and what additional measures may be needed to protect them. The debate has opened up many lines of inquiry about additional ways to protect the elderly against flu through new

stronger vaccines, additional shots, antivirals, and other methods. (See related story, p. 4.)

Most flu deaths in elderly

Annual influenza typically infects 5%-20% of the U.S. population, resulting in some 300,000 flu-related hospital admissions and 36,000 deaths. Some 90% of those deaths occur in the elderly.^{4,5} The push to get seniors immunized has resulted in one of the best immunization rates in any age group, with those over 65 approaching a 70% seasonal influenza vaccination rate. However, the benefit of the shots — particularly in reducing mortality — is open to some question and controversy.

"Certainly the influenza vaccine is not as effective at preventing respiratory illness in the elderly and people with compromised immune systems as it is in healthier younger people," says **Carolyn Bridges**, MD, associate director of science at the Centers for Disease Control and Prevention. "The controversy really has been about the benefit of influenza vaccine in terms of preventing influenza-related hospitalizations and deaths."

Part of the controversy is criticism of the cohort studies and methodology of the research that has been done. "It is very difficult to precisely draw out what the true benefit of the vaccine itself is when you have a lot of biases in studies with people deciding on their own whether or not to get flu vaccine," she says. "It can be tough to tell the actual benefit of the vaccine. The controversy really is what are the best ways to assess influenza vaccine effectiveness outside of randomized clinical trials."

In that regard, a recent editorial in the British journal *Lancet* said the only way to resolve the issue is to face the "ultimate taboo" and conduct large, placebo-controlled randomized clinical trials — that is if "governments [are] courageous and honest enough to reassess their cherished policies."⁶ With flu immunization now a standard recommendation for the elderly, administering a placebo-controlled trial would set off ethical challenges. "We recognize that the use of placebo in such trials would be ethically unappealing, but head-to-head trials that test the currently used inactivated vaccine against other vaccine formulations may be feasible," Simonsen argues in a recent review article.⁷

The oft-cited clinical trial that was done on the issue was conducted in Holland in the early 1990s.⁸ "In the one decent randomized clinical trial in the elderly that looked at vaccinated vs.

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Editorial Questions

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placebo recipients in the Netherlands, vaccination prevented about 55% to 60% of laboratory-confirmed influenza cases. So it was not perfect," says **Kristin Nichol**, MD, MPH, MBA, core investigator in the center for chronic disease outcomes at the Minneapolis VA Medical Center.

Regarding that clinical trial, Simonsen is quick to point out that demonstration of vaccine benefit fell off at age 70. "It shows the vaccine works in younger seniors in their 60s, but when you get into your 70s, they saw a much lower apparent effectiveness," she tells *Hospital Infection Control*. "We don't know much about senior benefits because most of the studies are very biased and there is no gold standard clinical trial."

Mortality benefits challenged

In particular, Simonsen and other critics question flu vaccination studies in the elderly that claim reductions in mortality as much as 50%. "These studies have served to appease our minds in the sense that they have claimed astonishing benefits," she says. "They have basically claimed that you can prevent half of all winter deaths for any reason. That can't possibly be true."

In particular, Simonsen has a letter in press challenging the findings of Nichol's recently published paper in the *New England Journal of Medicine*, which showed flu vaccination in the elderly resulted in a 27% reduction in the risk of hospitalization and a 48% reduction in the risk of death.² "We have developed a framework to detect bias in studies like that and we apply it to the new data provided in that paper. We show profound bias in all of the four indicators that we looked at," Simonsen says.

Nichol is well aware of the controversy but stands by the findings. "Our study demonstrates significant benefit," she tells *HIC*. "We conducted a number of analyses specifically to explore for some of the concerns that all of us have as epidemiologists with regard to the possibility of potentially confounding [findings]. We think the findings are very robust."

In the study, data were pooled from 18 cohorts of community-dwelling elderly members of one health maintenance organization (HMO) for 1990-1991 through 1999-2000 and from two other HMOs for 1996-1997 through 1999-2000. Logistic regression was used to estimate the effectiveness of the vaccine for the prevention of hospitalization for pneumonia or influenza and death after adjustment for important covariates. Additional

analyses explored for evidence of bias and the potential effect of residual confounding. During 10 seasons, influenza vaccination was associated with significant reductions in the risk of hospitalization for pneumonia or influenza and in the risk of death among community-dwelling elderly people, the authors concluded.

"We included a sensitivity analysis that models the potential impact of an unmeasured confounder and still demonstrated significant benefit," Nichol says. "So from my perspective — particularly with regard to the question of mortality — even if there are unmeasured residual confounders in the studies, the suggestion is that there is still significant mortality benefit. Whether or not the exact number is known isn't as important as the conclusion that there appears to be some mortality benefit."

Even if the mortality issue is completely removed from the equation, the benefits of reduced hospitalizations would more than justify vaccinating the elderly against flu, she emphasizes.

"That is very relevant from the hospital perspective — the so-called controversy tends to focus on mortality — but our study shows significant benefit with regards to [fewer] hospitalizations," Nichol says. "Even if there was zero mortality benefit, just the hospitalization benefit would justify aggressive use of the vaccine."

Breakthrough flu in immunized

Still, the current reality is that the immunized elderly can still acquire influenza. In a study that primarily reported the benefits of using antivirals to reduce flu mortality, Canadian researchers found a high rate of vaccine failure in a prospectively identified cohort of patients with laboratory-confirmed influenza requiring hospital admission. Vaccinated patients hospitalized with flu included 186 (82%) of 227 patients more than 65 years old. "There was a significant burden of illness attributable to influenza in this highly vaccinated population," they noted. "... These data demonstrate that life-threatening influenza may still occur in highly vaccinated populations in years when the vaccine is well matched to the infecting strains."⁹

Despite the findings, the lead author of the study remains a strong proponent of flu vaccine in the elderly, reminding that it doesn't have to be very effective to be cost-effective. "You can't expect too much from [the vaccine], says **Allison McGeer**, MD, microbiologist and infectious disease consul-

tant at Mount Sinai Hospital in Toronto. "It is important to recognize that in elderly populations there are limits to any of the current vaccines we have."

Those limits were dramatically driven home a few years ago when McGeer saw three nursing home residents with laboratory-confirmed infections with the exact same flu strain (A/Sydney) in successive years. "So even a previous infection was not enough to protect these people," she emphasizes. "If you can't protect with a previous infection, then what you can do with a vaccine is going to be limited."

That said, she finds the whole controversy somewhat puzzling given the aforementioned publication of a randomized clinical trial showing vaccine benefit.

"In most things in life when you have a randomized controlled trial, particularly in the setting of a lot of other evidence, it is a given [benefit]," she says. "For people to look at the data to say [the research] overestimates the effect, to my mind, is silly. A randomized control trial says it works and there is no place in medicine where we should be trying to second-guess that. [But] there is still a huge burden left despite vaccine and we need to worry about that."

An important caveat about McGeer's findings, Nichol notes, is that the study looked at patients hospitalized with influenza and then determined vaccination rates. That is very different from saying there will be a similarly high percentage of vaccine failure in community-dwelling elderly people, she says.

"We started with an entire population, looking at vaccinated and unvaccinated people, and then looking at how many were hospitalized or died," Nichol says. "But it is true even in our study, vaccinated people were hospitalized and vaccinated people died. It's not like it goes to zero. It's just that their risk — after taking into account age and comorbidities — is substantially lower."

That means influenza should not be ruled out in patients coming in to hospitals with flu-like symptoms and a history of vaccination, she notes. "There will be vaccine failures, so from the perspective of [immunized] people coming in to the hospital you should still think about influenza," Nichol says. "They might have it and you should still consider antiviral treatment if it is within the appropriate time frame."

In addition, hospitalized elderly patients should be offered flu vaccine if they have no history of immunization, Bridges adds. "It varies by

hospital in terms of when they would do that — at the beginning or ending of a hospitalization," she says. "People who have been hospitalized within the last year also are a high priority for getting vaccine. The inactivated vaccine is the only one available for people 50 and older. It has been out there 60 years. It has a very strong safety profile, and there is certainly no reason why it can't be offered to hospitalized patients. In general, you want to give it to people when they are most likely to have the best immune response, but it is better to give it than to have a missed opportunity."

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Pandemic, vaccine debate spur ideas to save elders

Antivirals, new vaccines, higher doses

Regardless of the current controversy regarding the efficacy of seasonal influenza vaccination in the elderly, it seems a given that seniors will fare much worse should a pandemic strain arise that eludes an immune response in all ages.

But under closer scrutiny, that logic does not hold.

The fate of the elderly in the next flu pandemic will be in part determined by the genetic shuffle and mutation of the virus that eventually emerges, whether it be avian influenza A (H5N1) or another novel virus. Surprisingly, the elderly were relatively unscathed by the legendary 1918 pandemic, which strangely targeted young healthy people. However, the 1957 and 1968 pandemics conformed to more traditional expectations, causing the most mortality in the elderly, infants, and those with underlying health conditions.

“The 1918 pandemic is our current scenario for pandemic planning, but infants and seniors were just not really at risk in that one,” says **Lone Simonsen**, PhD, MS, visiting professor and research director in the department of global health at the George Washington School of Public Health in Washington, DC. “The problem is we don’t know what’s coming. If it is more like ‘57 or ‘68, then the seniors will be the most at risk and they should be the ones protected by vaccination. The pandemic plan has just changed the opinion about the high-risk groups. [The elderly] used to be absolutely on top and now they have pregnant women, infants, and toddlers [above them].”

38 million at high risk

The CDC pandemic plan includes among its groups “at high-risk of severe complications” the approximately 38 million people in the U.S. age 65 years or older. Although, as Simonsen noted, on the plan posted on the HHS web site as this issue were to press, the elderly group was listed only one notch above healthy adults ages 19 to 64, who unless designated by occupation or some other factor would be of lowest priority to receive vaccine. (Available at <http://www.pandemicflu.gov/index.html>.)

Planners are looking at all possibilities for a flu pandemic and are well aware that various populations could be affected differently dependent on the stain that emerges, says **Carolyn Bridges**, MD, associate director of science at the Centers for Disease Control and Prevention. “The impact on all age groups is being looked at based on historical data from the previous three pandemics,” she says. “In the 1918 pandemic deaths, the number of excess deaths — the number of deaths above expected — was really highest in the less-than-2-years-olds and young adult age groups. The other two pandemics, the excess

deaths were really under 4 years old and then 65 and older.”

Was it the cytokine storm?

A prevailing theory about the 1918 pandemic — which occurred before a flu vaccine or antibiotics were available — is that it prompted a hyperimmune response, the famously described “cytokine storm.” In the ongoing research with the reconstructed 1918 strain, CDC researchers are finding that it replicates deep within mice lungs, prompting a similar immune system hyperreaction. Cytokines are proteins in the immune system that send out messages as part of the body’s response to an invading pathogen. A cytokine storm is a term used to describe an extremely powerful cytokine reaction — an over-reaction, if you will — that may do more harm than good. That could possibly explain why the 1918 pandemic caused such devastating mortality in young and healthy people who usually survive disease epidemics. Provoking a hyperimmune response — something that would be much less likely in elderly people with weakened immune systems — may be the key to the 1918 strain’s legendary virulence.

On the other hand, the elderly would be in serious peril if a pandemic virus essentially mimicked a seasonal strain, which causes the majority of fatal infections in those 65 years and older. But they would not be defenseless. One promising line of research in developing a pandemic vaccine — which experts say could take as much as five months after a pandemic strain emerges — is the use of immune boosters called adjuvants. For example, aluminum salts or “alum” can boost the immune system by prompting immune-system cells to secrete key proteins and enhance B-cell response to the vaccine. “The good news for pandemic vaccine [development] is that they are working with adjuvant vaccines, which is another way to augment protection for seniors,” Simonsen says. “There have been several studies showing that with adjuvant flu vaccines, you actually get a better antibody response and a longer duration of it.”

Other measures needed

With an effective vaccine not likely to be available during the beginning of a pandemic, community mitigation measures such as shutting down schools and public gatherings may limit

transmission and protect the elderly. Another key weapon against pandemic influenza in the elderly would be the use of antiviral drugs such as oseltamivir (Tamiflu®) and zanamivir (Relenza®). These antiviral medications can be used as a prophylaxis to prevent flu or to lessen the severity of illness if administered within a few days of infection. “The goal of the federal government in planning is to have enough antiviral medication to treat 25% of the population with the hope that would decrease complications,” Bridges says. “For example, in a nursing home, even if a vaccine was available you might not see good immune response in that population. Another strategy might be doing very good surveillance in nursing homes, looking for influenza. Then when you find it, you give everyone an antiviral.”

Antivirals, herd immunity

In a recent study, a prospectively identified cohort of patients with laboratory-confirmed influenza requiring hospital admission, treatment of adults with oseltamivir was associated with a clinically significant reduction in mortality within 15 days, the authors found.¹

“The evidence that it helps seriously ill people with seasonal flu supports the argument that it is likely to be of some benefit in a pandemic,” says lead author **Allison McGeer**, MD, microbiologist and infectious disease consultant at Mount Sinai Hospital in Toronto. “I don’t think anyone should be relaxing about pandemic flu or thinking that [antivirals are] going to make a huge difference, but it does give me hope that it could make some difference.”

While seniors may not achieve an immune response after vaccination — and thus remain vulnerable to flu infection — antivirals work independently to kill circulating virus. “It acts directly against the virus, so you are not expecting a contribution from the immune system,” she says. “When using a vaccine, you are dependent on the host immune system for its function. When you are [using] an antiviral, as long as [the elderly] absorb as well as the next person, there should be no difference between them.”

In addition to pandemic discussions, the controversy over the efficacy of the flu vaccine in the elderly has actually invigorated research and discussion, she says. “I think the good thing is that people are talking about better vaccines for the elderly with some of the adjuvant work that is

happening with H5N1 vaccines,” she says. “People are talking about double doses and different delivery systems to try and get the elderly to respond a little better.”

Ongoing studies in administering the elderly a seasonal vaccine with large quantities of antigen are showing some promise, Bridges adds. There are 15 mcg of antigen per dose of inactivated flu vaccine. In one study, researchers have found that elderly volunteers were able to muster 44% to 79% higher levels of antibody after being given high-dose shots that contained 60 mcg of antigen.² Moreover, the vaccine was well tolerated at all dosage levels. “There have also been a number of studies that have been done over the years looking at the benefit of giving an extra dose during the year to elderly people,” Bridges says. “There is general agreement that we need a better vaccine for the elderly — a more immunogenic vaccine. As people age and have high-risk conditions, their immune response is diminished.”

Another common sense strategy is vaccinating all health care workers, while promoting herd immunity by immunizing children and family members who may be in contact with the elderly. “There is no doubt that the most cost-effective way to prevent influenza is to extend vaccination programs,” McGeer says. “If we actually got 80% of the population vaccinated, including most kids, the herd immunity effect might be big enough that it wouldn’t have to worry so much about elderly people.”

Benefits of health care worker vaccination in reducing mortality in the elderly have been clearly shown, but it is too early to tell the whether the more recent push to immunize children will translate to benefits for their elders.

“The [push to vaccinate children] was really made because of new and more specific evidence that kids in those young age groups were at high risk of influenza [complications], not to promote herd immunity,” Bridges says. “What kind of vaccination rate would you really need to obtain to see indirect benefit for the elderly? I don’t know what that is, but I don’t think we have seen it yet.”

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Time is right to make 'business case' for IC

Decreasing LOS may be a good approach

All the planets appear to be lining up to make a persuasive "business case" for infection control. In addition to slated federal reimbursement cutbacks, awareness and activism from consumers, patients and legislators have increased exponentially. The unprecedented level of activity and concern about health care-associated infections should have administrators and hospital boards eager to listen and support infection control efforts to solve the problem.

"I think the administrators and hospital boards are very aware of all that," says **Eli N. Perencevich**, MD, MS, an associate professor of epidemiology and preventive medicine at the University of Maryland School of Medicine in Baltimore, "Now is a unique time. The more we work with them now, the better off we will be in the long run."

Still, infection control professionals may wonder why it's necessary to make the business case for infection prevention, to convince administrators they will save money by funding efforts that ultimately save lives. Moreover, when such business cases are made the findings are often framed in terms of "cost savings" to the facility; as if it wouldn't have been worth it if they had to pay to prevent infections.

Perencevich addresses this issue in a recently published paper, which has been issued as a guideline by the Society for Healthcare Epidemiology of America. (SHEA)¹ "Because U.S. national health expenditures were estimated to be \$2.08 trillion in 2006, or 16% of the gross domestic product, there is no inherent reason that infection control interventions must save society money," he wrote. "Ideally, society should be willing to spend money to prevent either a myocardial infarction or a surgical-site infection."

ICPs and health care epidemiologists often fall into this mindset when they present their research, he notes. "They only say it is cost-effective if it is cost-saving," Perencevich tells *Hospital Infection Control*. "We feel like this is because they believe it is only effective if it is cost-saving. If you believe it and you talk that way, then we will never get people to realize that they actually can pay money to prevent [infections]. We are willing to spend \$40,000 on a kidney transplant but not willing to spend \$10

to prevent that person from getting an infection."

While society would benefit from a reduced incidence of nosocomial infections, there is currently no direct reimbursement to hospitals for the purpose of infection control, which forces health care institutions to make economic decisions about funding infection control activities, he notes in the paper. Therefore, demonstrating value to administrators is an increasingly important function of ICPs and hospital epidemiologist because health care executives are faced with many demands and shrinking budgets, he concedes.

Show attributable costs

While making the business case, it's important not to overstate the benefit by simply saying preventing infection "Y" will save the hospital "X" dollars. From the hospital's financial perspective, a certain percentage of these costs currently are reimbursed by third-party payers, Perencevich reminds. Therefore, the emphasis in a business-case analysis should be on the attributable costs and attributable complications. An attributable cost or complication is one that would not have occurred during a hospital stay that is identical to the one being analyzed except for the complication or infection of interest, he points out in the guideline.

"If you are going to make a business case for say, eliminating catheter-related bloodstream infections (CR-BSI) [by saying] it will save the hospital such-and-such amount of money, [remember] the only money that it will save is directly related to the CR-BSI that you prevent," he says. "You should look at attributable costs, which are only a portion of the whole hospitals costs. We should be careful about only looking at the costs associated with the actual infection."

Another business case approach that may be easier to prove is focusing on fixed costs instead on cost savings. Researchers have shown that one of the best ways to justify an infection prevention program is to show increased hospital profits via reductions in lengths of stay.² For example, say an ICP could show that an effort to reduce surgical site infections decreased overall length of stay in the hospital by 234 days. If the mean length of stay in the hospital is four days, then 59 new patients could be admitted, he notes.

"I think it's easier to convince hospital administration if you can show what you are doing will decrease length of stay — that the [hospital] can admit more patients to those same beds," he says.

"It's basically increasing the utilization of the fixed costs as a way to show a benefit. A lot of people don't have access to cost accounting systems to determine the cost of infections, but everyone has length of stay [data]."

Communicating with administration and finding out the best way to justify your program is the key, he says. "They are on your side," Perencevich says. "You realize there aren't infinite dollars for anything let alone infection control. But given a fixed amount of dollars you want to spend them the best way you can. You want to work with them to develop the best practices and strategies for your unique institution to decrease infection and improve quality."

Nine key steps

The SHEA guideline on making a business case for infection prevention lists the following nine key steps:

Step 1: Frame the problem and develop a

hypothesis about potential solutions.

Step 2: Meet with key administrators.

Step 3: Determine the annual cost.

Step 4: Determine what costs can be avoided through reduced infection rates.

Step 5: Determine the costs associated with the infection of interest at your hospital.

Step 6: Calculate the financial impact.

Step 7: Include the additional financial or health benefits.

Step 8: Make the case for your business case.

Step 9: Prospectively collect cost and outcome data once the program is in effect.

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MRSA hospitalizations double from 1999 to 2005

'This is an clearly an epidemic phenomenon'

Hospitalizations related to methicillin-resistant *Staphylococcus aureus* (MRSA) infections more than doubled, from 127,000 to nearly 280,000, between 1999 and 2005, according to a new study.¹ During that same period, hospitalizations of patients with general staph infections increased 62% across the country.

The study found that such infections are now "endemic, and in some cases epidemic," in many U.S. hospitals, long-term care facilities, and communities. The researchers concluded that control of MRSA should be made a national priority.

"I would argue that MRSA has been an endemic disease and it's in the population all the time," says one of the authors, **David Smith**, PhD, associate professor of emerging pathogens and zoology at the University of Florida in Gainesville. "But a doubling is out of proportion to the normal variance you would see in a population where you are staying steady. We are above the baseline, the 'steady state' for MRSA since 1999. This is clearly an epidemic phenomenon."

Though the study was insufficiently powered to prove the point, Smith thinks the increase is

being driven by the rise of community-acquired (CA) MRSA. "Anecdotally, it all points to the increase mainly being community-acquired," he says. "If you look at the increases by cause of infection, you see that cellulitis and abscesses are the ones that have just shot up."

A steady but less dramatic increase was seen over the period for traditional health care-associated infections associated with devices or surgery, he notes. "Just anecdotally talking to emergency room physicians what you are really seeing is a lot of people coming in with [wounds] that have not healed and then it turns out to be MRSA," Smith says. "A lot of those are easily treated, but they can turn into severe infections. I think basically we are seeing a big change in community-acquired MRSA that has been reflected in hospitalizations."

Of interest, the researchers used more stringent mortality criteria and ended up with 11,000 estimated MRSA deaths annually, well below the 18,650 deaths reported in another recent study.² "We limited deaths to MRSA that we attributed to records where it was listed as one of the first two causes," he explains. "If MRSA was one of the first two primary diagnoses and the patient died, then we called it a MRSA death. They included any death associated with MRSA. In earlier drafts, we considered any deaths associated with MRSA and our number was almost identical to theirs." The estimated incidence of

S. aureus was based on hospitalizations with *S. aureus*-related discharge diagnoses from the National Hospital Discharge Survey (NHDS).

Widespread implications

The indication that community-associated MRSA is spreading rapidly into hospitals has widespread implications, including empirical treatment for infections, the authors warn. In hospitals, hand-washing practices must be improved, they said, echoing the sentiments of many an ICP. "Hand washing really does work, but people really don't wash their hands," Smith says. "They don't see the negative consequences for the patients immediately and they don't see a reward for it if they do it themselves. It's not surprising that they are lax about it."

Ultimately, some system of incentives and accountability may need to be developed to improve the cardinal principle of infection control, he notes. Meanwhile, the increase in skin and soft-tissue infections means standard precautions — including use of gloves — are likely warranted when dealing with all skin and soft tissue infections in outpatient clinics and acute care facilities, the authors recommend. Contact precautions, including use of gowns and gloves, should be implemented for all wound care in acute care facilities, and institutional programs to enhance antimicrobial drug stewardship should be implemented, they conclude. "Clinicians should be aware of the magnitude of the issue and consider MRSA a highly likely cause of skin and soft-skin tissue infections, even in areas where the prevalence of MRSA is believed to be low," they warn.

In addition, the rising incidence of MRSA will likely increase demand for vancomycin, creating more pressure for drug resistance to emerge. The researchers recommend national surveillance or reporting requirements for the infections. "It's a shame that we had to wait this long to get numbers like this," Smith says. "It would have [been better] to have detected and noticed this change and gotten real good numbers on it much earlier than we have."

Hospitals can't do it all

The authors called for more research to explore the interaction between community- and hospital-associated infection, stepped-up efforts to control hospital infection, and increased investment in the development of a staph vaccine. The latter

will be particularly important if resistant staph continues to emerge in the community, where prevention efforts are problematic. "Hospitals can certainly play their part, but if this thing is raging in the community it's hard to imagine how hospital infection control is going to do anything," Smith says. "If this is something you get playing football, sitting on a bench where someone else has sat or touching a doorknob, it is not going to go away because hospitals are doing their part."

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2. Klevens RM, Morrison MA, Nadle J. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. 2007; 298:1,763-1,771. ■

Deaths, severe reactions after treatment for TB

No HCWs reported, but CDC beefing up tracking

Alarmed by continuing deaths and severe adverse reactions after treatment for latent tuberculosis, the Centers for Disease Control and Prevention is seeking funding approval for a national surveillance system to track the events.

Between October 2000 and October 2007, 79 patients receiving treatment for latent TB infection (LTBI) were reported to the CDC for severe adverse events related to medications. "None of them were health care workers, which is a good thing," says **Lilia Mangan**, RN, MPH, epidemiologist in the CDC division of TB elimination.

However, the findings have implications for health care workers, who may receive treatment after a TB skin test conversion resulting from an occupational exposure.

"We do not think that being a health care worker poses a greater risk of developing severe adverse events related to [treatment] than other patients being treated for LTBI," she says. "There is no change in the recommendation for treatment of health care workers exposed to TB. Isoniazid right now is the preferred treatment."

A severe adverse event is defined as a drug-related reaction resulting in hospitalization or

death of a person receiving treatment for LTBI. "Severe adverse events to LTBI treatment are rare, but recently recognized as a catastrophic medical phenomenon," she says. "It is essential to find out who is affected, how often this occurs, and, whether there are personal risk factors that contribute to severity of adverse reactions."

Deaths reported among people treated for LTBI included two of 50 people who were on the then-recommended two-month regimen of rifampin and pyrazinamide (RZ). "As a result of those investigations, we don't recommend RZ anymore for treatment for latent TB infection," Mangan says. "The preferred treatment right now is nine months of isoniazid [alone]."

Indeed, RZ regimens were found to be associated with elevated rates of liver injury, hospitalization, and death, in one study.¹ However, adverse events continue to be reported, including nine deaths in 22 severe adverse reactions in people treated with isoniazid. Two of three patients on other regimens (e.g., pyrazinamide and ethambutol) also died.

"Since we stopped recommending RZ, the ones that we are getting now are isoniazid-related severe adverse events," she says.

The purpose of the surveillance system is to determine the annual number of the events, reveal trends, and identify any common characteristics of the patients affected. The Food and

Drug Administration collects data on adverse events related to drugs through its MedWatch Program, but it does not include the disease context and risk factors that are essential for revising

CNE/CME questions

1. Of the estimated annual seasonal flu death toll for seasonal influenza, what percentage of mortality is in people ages 65 years and older?
 - A. 5%
 - B. 20%
 - C. 60%
 - D. 90%
2. Even if the mortality issue is completely removed from the equation, advocates of flu immunization in the elderly say reduced hospitalizations would clearly justify widespread vaccination.
 - A. True
 - B. False
3. Among the additional measures being discussed and studied to increase the immune response to flu vaccine in the elderly are:
 - A. using vaccine with immune boosters called adjuvants.
 - B. administering vaccine with large quantities of antigen.
 - C. giving an additional flu shot.
 - D. All of the above
4. A recommended business case approach to infection control that may help ICPs justify their programs is showing reduced:
 - A. length of stay.
 - B. admissions.
 - C. deaths.
 - D. All of the above

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CNE/CME instructions

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treatment options for LTBI, she says. Reporting will be conducted through telephone, e-mail, or during CDC site visits. "We want this surveillance system so that we can systematically collect data from these reports to find out why and when these adverse events are occurring," Mangan says. "We are also including pediatric cases because we have had [reactions in children] that received isoniazid. Our case definition for them is less stringent."

The case definitions that will be used in the surveillance system are as follows:

- **Adult Case Definition:** A person who is 15 or more years of age who developed a severe adverse event that resulted to an admission to a health care facility (e.g., acute care hospital, urgent care center, jail infirmary) or death as a result of taking at least one dose of drug therapy for the treatment of LTBI.

- **Pediatric Case Definition:** A person who is less than 15 years of age who developed an adverse event that resulted to a visit to a health care facility (e.g., emergency room, doctor's clinic, hospital, urgent care clinic, jail infirmary) as a result of taking at least one dose of drug therapy for the treatment of LTBI.

Reference

1. McElroy PD, Ijaz K, Lambert LA, et. al. National Survey to Measure Rates of Liver Injury, Hospitalization, and Death Associated with Rifampin and Pyrazinamide for Latent Tuberculosis Infection. *Clin Infect Dis* 2005; 41:1,125-1,133. ■

CDC cautions about report of rise in new HIV infections

Washington Post: *Annual estimates may double*

The Centers for Disease Control and Prevention is responding to a recent *Washington Post* report that CDC estimates of new HIV infections in Americans annually may be 50% higher than previously believed.¹ A statement released by

Kevin Fenton, MD, director of the CDC National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, included the following points:

"Recent media reports have speculated about CDC's pending estimates of new HIV infections in the United States. CDC emphasizes that the new estimates are not yet final. In recent years, CDC has worked to develop an innovative system designed to estimate the number of new HIV infections in a given year. As a result of new technology that can distinguish recent from long-standing infections, the new system will provide the clearest picture to date of new HIV infections in the United States. Given the importance of the new estimates in guiding HIV prevention policy and programs, CDC's public health responsibility is to ensure accurate information. The estimates have been submitted for further analysis and rigorous scientific review to ensure the accuracy of the complex new methods and of the estimates themselves. The new estimates utilize complex methods based on a number of statistical assumptions. Any modification to those assumptions during the scientific review process will affect the

CNE/CME answers

1. D; 2. A; 3. D; 4. A.

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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■ Joint Commission moving on MDROs?

■ Patient consent laws for HIV source testing

■ Zero heroes: Success stories from infection rate flatliners

■ HIV increase: Surveillance artifact?

■ New antibiotic provides alternative to vancomycin

final estimates. It would not be responsible for CDC to discuss specific data before we are certain that the new estimates are reliable."

Citing anonymous sources, the *Post* reported that the estimated number of new HIV infections each year will be moved from 40,000 to the 55,000-60,000 range. The higher estimate is the product of a new method of testing blood samples that can identify those who were infected within the previous five months. The higher estimate is based on data from 19 states and large cities that have been extrapolated to the nation as a whole, the newspaper reported.

Reference

1. Brown D. Estimate of AIDS Cases in U.S. Rises. *The Washington Post*. Dec. 1, 2007. ■

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