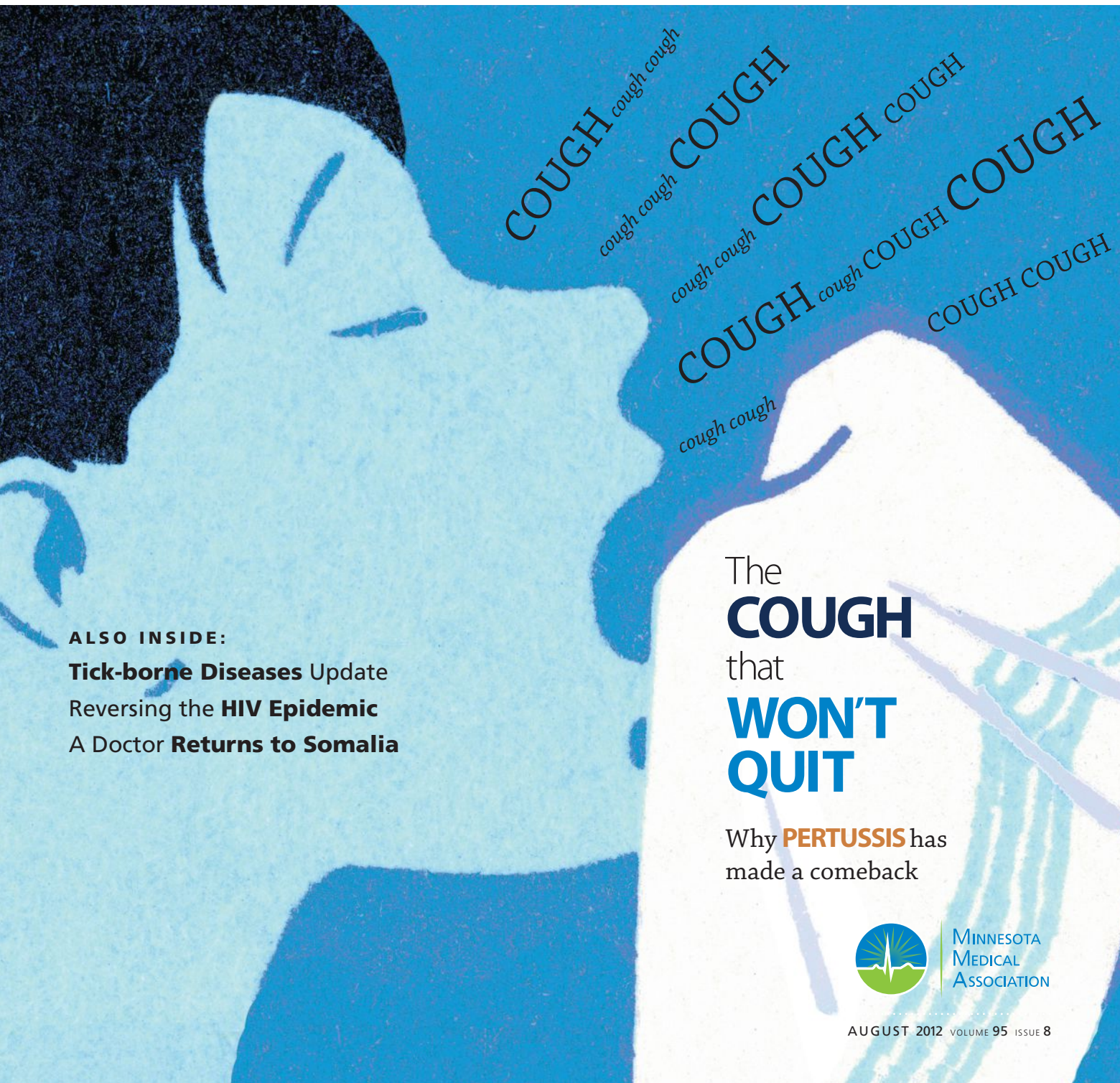


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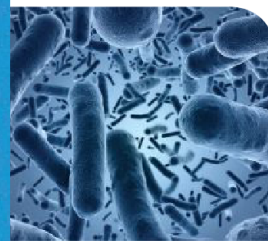
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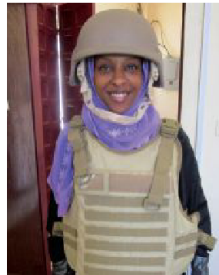
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Photo by Scott Walker

The advent of vancomycin-resistant *Enterococcus* and MRSA has demonstrated bacteria's dazzling ability to stay one step ahead of antibiotic development.

Will the bugs win?

Boris Reisberg was a crack infectious disease specialist at Northwestern University Medical School in the 1970s. With a dry, ironic wit he would engage medical students and residents in the obscurities of antibiotic sensitivities and the glories of new drugs that were vanquishing previously unconquerable organisms. Although he possessed encyclopedic medical knowledge, he remained approachable. And so, one day, a cocky resident decided to challenge him: “Dr. Reisberg, we now have aminoglycosides and next-generation penicillins and cephalosporins that can treat virtually every bacteria we encounter. Isn't your specialty really a dying specialty?” A thin grin glinted beneath Reisberg's bushy mustache as he answered, “Young man, medicine will always need infectious disease specialists. And even then, the bugs are going to win.”

Surveying the world of “bugs” in 2012, Reisberg seems quite prophetic. Old bugs such as the one that causes pertussis have stayed around and even resurged despite widespread vaccination and effective treatment. The old bugs have gotten tougher as the advent of vancomycin-resistant *Enterococcus* and MRSA has demonstrated bacteria's dazzling ability to stay one step ahead of antibiotic development and to expand into previously untouched, healthy populations. Since the '70s, new bugs have emerged and gotten tougher as well. *Clostridium difficile*, unheard of in Reisberg's time, surfaced as a by-product of heavy antibiotic use and now has changed its colors so that it afflicts even the healthy and antibiotic-naïve patient.

Other new bugs have radically altered the microbiological landscape. Lyme disease, characterized in the late 1970s, continues to stalk the forests and fields populated by the *Ixodes* tick. No sooner did the

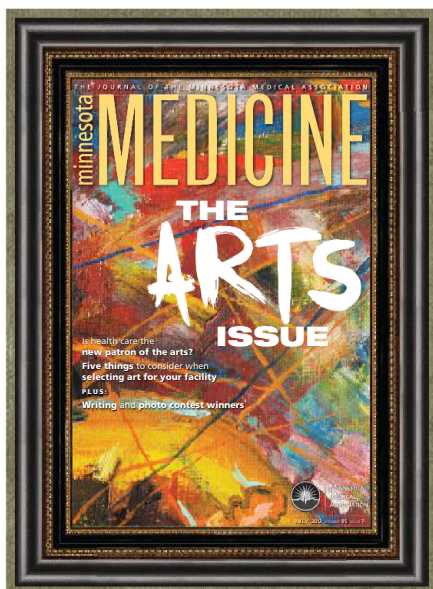
protean manifestations of Lyme disease get documented than new tick-borne illness such as anaplasmosis were identified. HIV appeared in the early 1980s and has accumulated quite a biography in just 30 years. And almost monthly another cancer tied to viral infection gets delineated. New infectious diseases alone are enough to keep future Reisbergs busy for generations, and perhaps tomorrow's infectious disease specialists will double as oncologists.

Each new infectious disease challenges not only microbiologists and pharmacologists to design therapeutic weapons but also carries ecological and social implications. Treating physicians don't just worry about antibiotic blood levels and sensitivities; they also need to think about the mechanics of prevention—mundane things such as mosquito netting, DEET insecticides, condoms and the influx of deer into urban environments. Even global climate change enters the realm of the infectious disease specialist as warming trends change the prevalence of diseases such as West Nile virus and dengue fever. Africa is moving to North America.

There's not much infectious disease gurus can do about global warming; but the gentle push to change physician antibiotic prescribing habits and animal antibiotic use has become a veritable raucous cause célèbre for many in the infectious disease community.

Will the bugs really “win” as Reisberg suggested? Such a statement certainly evokes improbable visions of late night sci fi with mammoth beetles overrunning Manhattan. An unlikely scenario. But any physician who has grappled with MRSA knows that the era of infectious disease is far from over.

.....
Charles Meyer can be reached at meyer073@umn.edu.



Arts issue inspires

Thank you for continuing the writing contest. Despite not submitting a story or poem this year, I enjoyed reading the winning entries and was inspired to put pen to paper to capture and express the

joys and heartaches of being a physician. When the arts issue lands on my desk each year, I immediately put it in my purse to take home to savor.

Last evening, while I was in the midst of dinner clean-up, I took a break and read “Better than This” by David Dvorak, M.D. (July p. 29). The story brought tears to my eyes. I am not sure how our country will solve its health care crisis; but this story exemplifies the problems. And it reminded me of how torn I feel. I want to provide excellent care to all families yet know this doesn’t always happen. Tests are foregone because of high deductibles, vaccines are delayed because of loss of insurance coverage, and treatments are altered, delayed or incomplete because of the cost.

The future of medicine is uncertain; but reading this edition of *Minnesota Medicine* each summer is something I look forward to. It reminds me of why I became a doctor in the first place.

Sarah Brandt, M.D.
Southdale Pediatrics



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The Centers for Disease Control and Prevention predicts half of the expected 1.5 million people in the United States living with HIV will be 50 years of age or older by 2015.

■ HIV/AIDS

New strategies for treating older people

Thanks to progress in treatment for HIV over the last three decades, many people with the virus now live long lives.

Two years ago, aware that older adults with HIV also have multiple other illnesses and that the physicians treating these patients typically are not equipped to handle their non-HIV-related problems, the American Academy of HIV Medicine, the American Geriatrics Society and the AIDS Community Research Initiative of America assembled a panel of experts to develop recommendations for managing older patients with HIV. The report on their efforts was published earlier this year.

The authors stress the recommendations are not guidelines but “treatment strategies” that will likely evolve, and they invite readers to participate in a forum to help shape care for this population in the future. The report, “The HIV and Aging Consensus Project: Recommended Treatment Strategies for Clinicians Managing Older Patients with HIV,” and ongoing forum are available at www.aahivm.org/hivandagingforum.

check this out

PTSD Coach is a mobile app for patients that features information on post-traumatic stress disorder (PTSD) and its treatment. Developed by the Department of Veterans Affairs, the app includes a questionnaire used in the VA system to screen for PTSD, tips for managing stress and links to resources. The app can be downloaded free from iTunes and Android Market.

Information about the app is available at www.ptsd.va.gov/public/pages/ptsdcoach.asp.



■ Texting

Reaching a new generation of parents

Public health officials in San Diego are exploring whether texting is a good way to deliver messages to parents about immunizing their 1-year-olds. In a study involving 600 parents, half will receive text message reminders about scheduling a visit for their child's 15- and 18-month immunizations. The other half will receive texts with general health information.



Can sending parents text reminders increase childhood immunization rates?

The project was prompted by the recent surge in pertussis cases seen across the country. Children receive their first three DTaP shots at 2, 4 and 6 months of age. The fourth shot is given between 15 and 18 months of age, and a fifth is given when a child enters school, at ages 4 through 6 years.

By the time their children are toddlers, busy parents may not be as vigilant about getting their child immunized as they were when the child was a newborn. According to the U.S. National Immunization Survey, only 67 percent of toddlers nationwide have had all the recommended vaccinations.

The texting project is an effort of the San Diego Beacon Community, one of 17 such communities nationwide that have received federal dollars to make innovative use of information technology to improve health.

Source: www.sandiegobeacon.org/news/201206/amid-us-pertussis-outbreak-san-diego-battling-%E2%80%98whooping-cough%E2%80%99-text-messages

■ Childhood immunizations

State immunization law under review

| BY KIM KISER

The Minnesota Department of Health is proposing changes to the state's child care and school immunization law to make it more consistent with federal recommendations.

The law was last revised in 2003. "Since then, new vaccines and schedule and timing changes for vaccines that are already in the law have come out based on scientific research," says Patricia Segal-Freeman, J.D., M.P.H., a policy analyst with the health department.

The changes would bring Minnesota's law in line with the standards set by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP).

The Department of Health has the authority to make modifications to the school immunization law through the rule-making process. Segal-Freeman says any revisions to the state's immunization and documentation requirements would take effect in the fall of 2013 at the earliest.

These changes are being considered:

- Requiring schools to submit their annual immunization status report to the Minnesota Department of Health rather than the Minnesota Department of Education;

- Applying the law to all school-based early childhood programs (currently, it only affects Early Childhood Special Education and certain child care settings);

- Changing the age for the first varicella immunization from 18 months to 15 months;

- Clarifying the documentation requirement for history of varicella;

- Changing the timing of the polio and DTaP vaccines so that the last dose is given on or after the child's fourth birthday;

- Requiring proof of hepatitis B, varicella and MMR vaccinations (or legal exemptions) for students in kindergarten through 12th grade (currently, the law only requires documentation for kindergarteners and seventh graders);

- Requiring hepatitis B vaccination for kids enrolling in child care or school-based early childhood programs, unless the parent or guardian takes a medical or conscientious exemption;

- Replacing the Td immunization required for seventh graders with Tdap;

- Requiring meningococcal vaccination for children starting in seventh grade, unless the parent or guardian takes a medical or conscientious exemption;

- Requiring a hepatitis A vaccination for children enrolling in child care or school-based early childhood programs unless the parent or guardian takes a medical or conscientious exemption.

To learn more and sign up for email updates, go to www.health.state.mn.us/divs/idepc/immunize/immrule/index.html.



International travel has been linked to an increase in measles cases in the United States.

■ Measles

Spotting a resurgence

By 2000, measles was considered almost a nonissue in the United States. And for the next 10 years, the nation saw only about 60 cases a year.

In 2011, however, officials reported 222 cases and 17 outbreaks (three or more cases linked in time or place). According to the Centers for Disease Control and Prevention, 200 of the cases were linked to international travel—U.S. residents traveling abroad or non-U.S. residents traveling to the United States. More important, 85 percent of the cases occurred in patients who were unvaccinated or had unknown vaccination status.

A dose of MMR vaccine is recommended for children between the ages of 12 and 15 months, with a second dose between ages 4 and 6 years. Adults who do not have immunity should receive at least one dose of the MMR vaccine. Two doses are recommended for health care workers, international travelers and college students.

Source: MMWR 2012;61:253-7.



More and more cases of diarrhea caused by *Clostridium difficile* are showing up outside of hospitals.

■ *C. difficile*

A menace moves into the community

Controlling the spread of Clostridium difficile is challenging. But some Minnesota researchers may be on to a solution. | BY TROUT LOWEN

Fifteen years ago, when referring to someone likely to become infected by *Clostridium difficile* (*C. difficile*), we would have described an elderly person who was or had recently been hospitalized and treated with antibiotics. But since then, *C. difficile* infection, which manifests as diarrhea, has been showing up in patients young and old and in the community as well as in the hospital.

Researchers at Mayo Clinic helped document that trend earlier this year. Their work, reported in the *American Journal of Gastroenterology*, showed a sharp increase in the number of community-acquired *C. difficile* cases in younger patients with no recent history of hospitalization or antibiotic use. “Basically, we found the infection is now spreading outside of the hospital and into the community, and people who were previously not at risk are now getting it,” says Sahil Khanna, M.B.B.S., of Mayo’s division of gastroenterology and hepatology, and lead author of the study.

Using the Rochester Epidemiology Project diagnostic index, the researchers tracked the incidence of community-acquired and hospital-acquired *C. difficile* infection in Olmsted County between 1991 and 2005. Of the 385 cases that met their criteria, a surprising 41 percent were community-acquired, that is, they occurred either within 48 hours of hospital admission or more than four weeks after discharge. Compared with patients with

They also found the *C. difficile* infection rate spiked during the last six years of the study.

Not only is *C. difficile* infection showing up in new places and more often, recurrence rates have increased and infections are more severe. *Clostridium difficile* is now the primary cause of antibiotic-associated infectious diarrhea. It affects millions of people worldwide each year and is responsible for more than 14,000 deaths in the United States annually, according to the Centers for Disease and Control and Prevention.

Alexander Khoruts, M.D., an associate professor of medicine in the University of Minnesota’s division of gastroenterology, hepatology and nutrition, says *C. difficile*, which is a normal constituent of the human gut, has evolved as antibiotic use has increased and become more toxicogenic and more prevalent. The emergence of more virulent antibiotic-resistant strains is making treatment even more difficult. “There’s an epidemic of *C. difficile* infection in this country, Canada and Europe,” Khoruts says. “It doubles every decade and causes more disease, more morbidity, and kills more people than it used to.”

Understanding the causes

Chief among the factors driving the trend is the overuse of antibiotics. Repeated use of antibiotics kills off normal bacteria in the intestine, creating an opportunity for *C. difficile* to take hold and spread.

In the Mayo children’s study, exposure to antibiotics occurred in 76 percent of cases. Those findings, and the data on who’s getting community-acquired *C. difficile*, should provide a wake-up call for physicians, Khanna says, both in terms of diagnosing and curbing the spread of *C. difficile*. Physicians should refrain from overprescribing antibiotics and test for *C. difficile* even in the absence of traditional risk factors such as age and exposure to antibiotics. “If you see patients who come into the clinic with diarrhea and there’s no other cause identified, even if those patients have not been

hospital-acquired infection, those with community-acquired infection were younger (median age 50 vs. 72 years), more likely to be female and less likely to have been exposed to antibiotics.

A follow-up study by Khanna and colleagues published in *AGA Abstracts* found 75 percent of cases of *C. difficile* in children younger than 18 years of age between 1991 and 2009 were community-acquired; the average age at symptom onset was 2.3 years.

admitted to a hospital or have not taken antibiotics, those patients should be tested for *C. difficile*,” he says.

A challenge to treat

Although antibiotics remain the first-line treatment for *C. difficile*, they are not effective in a significant number of cases. Between 20 and 30 percent of patients with *C. difficile* infection experience a relapse within 30 days, and the risk of recurrence doubles after two or more occurrences, as antibiotics such as metronidazole and vancomycin that are used to treat the infection kill off more healthy bacteria. “A fraction of patients just cycle in and out of the infection,” says Khoruts. “And anytime you treat it, you kill off more normal bacteria and perpetuate the cycle. So there’s a fraction of patients who just can’t get out of it.”

For recurrent cases, some physicians are trying alternative therapies. One of the most successful is fecal transplantation,

Clean, clean, clean

Better cleaning protocols and hand-washing are considered essential to stopping the spread of *C. difficile*. Alcohol-based hand cleaners don’t kill the spores, so thorough handwashing with soap and water is needed. Areas of clinics and hospitals where *C. difficile* is present should be cleaned with a bleach solution. In addition, patients with *C. difficile* should be isolated, and staff and visitors should wear gowns and gloves when entering those patients’ rooms. “When we implemented those things here at Mayo, we found that there was a very significant decrease in hospital transmission for *C. diff*,” says Sahil Khanna, M.B.B.S., of Mayo Clinic’s division of gastroenterology and hepatology.

Most hospitals in the United States need to do more than they currently are doing to combat the spread of *C. difficile*, says Alexander Khoruts, M.D., an associate professor of medicine in the University of Minnesota’s division of gastroenterology, hepatology and nutrition. Hospitals and clinics need to regularly launder physician coats and uniforms, remove soft fabric chairs that can’t be disinfected from hospital and waiting rooms and discourage physicians from wearing ties. “They’ve shown that doctors’ ties are probably the dirtiest piece of clothing they could possibly have,” he says.

Khoruts notes, however, that in the United Kingdom, where hospitals have instituted rigorous cleaning procedures, *C. difficile* infections have only fallen by 30 percent.—T.L.

“There’s an epidemic of *C. difficile* infection in this country, Canada and Europe.”

—Alexander Khoruts, M.D.

which involves repopulating the gut with microbes from a healthy donor.

Bacteriotherapy is not new. The first case reported in the medical literature was described in 1958 by Eiseman et al. in *Surgery*. It was pioneered in Minnesota for recurrent *C. difficile* infection by Johannes Aas, M.D., and colleagues in Duluth, who published their results with 16 patients in an article in the *Journal of Clinical Infectious Disease* in 2003. Interest has grown as understanding of the gut as a microbiome—a microbial community—has matured. But fecal transplantation isn’t often used because it’s challenging to perform, Khoruts notes.

One of the difficulties is finding a donor. Traditionally, physicians have asked patients to find their own, usually a family member or friend. Once a donor is found, that individual needs to be screened for infectious risk and other health concerns and the fecal material must be processed for transplantation. Those costs aren’t covered by insurance. The procedure is also aesthetically unpleasant, Khoruts says. “The odor and the aerosol that will be produced in your clinic space can drive patients and staff out of the building,” he adds.

Khoruts has been working with other university scientists to simplify the transplantation procedure. Their idea is to create a donor pool and prepare the material in a standardized way so that it can be frozen and stored for use when needed.

In an article published in the *American Journal of Gastroenterology* in January of this year, they outlined the results of their initial efforts to move preparation of the fecal material from the clinic to the lab and freeze it for later use. Khoruts and colleagues tested the modified material on 43 patients who had recurrent *C. difficile* infection. Eighty-six percent were free of infection after two months. Although the results are promising, more testing is needed, Khoruts says. The university’s Office of Technology Commercialization is working with CIPAC Limited, an Australian company, to conduct a multicenter clinical trial. In the future, Khoruts expects patients will be able to take a pill that ultimately will prevent the spread of *C. difficile*.

“I can see a broadening out to even preventing the first infection,” he says. **MM**

The Minnesota Department of Health is creating tools to help hospitals give patients the right antibiotic at the right time.

■ Antimicrobial stewardship

Wiser prescribing

Hospitals that make wise use of antibiotics are reducing drug-resistant infections, saving money and improving the quality of care. | BY HOWARD BELL



Every weekday at 11 a.m., infectious disease specialist Gary Kravitz, M.D., or one of his colleagues meets with clinical pharmacists at United Hospital in St. Paul to make antibiotic stewardship rounds. They retrieve from the electronic medical record a list of all patients receiving antibiotics, along with each patient's problem list, vital signs, lab, radiology and culture results. Kravitz and his team review all of it to determine if antibiotic treatment is indicated, and if a patient is receiving the right drug at the right dose and via the right route. "If we find, for example, that a patient admitted from the ED for shortness of breath was started on antibiotics for pneumonia, but the correct diagnosis is congestive heart failure, then we leave an electronic note for the attending physician recommending that the antibiotics be discontinued," Kravitz says. If that patient had fevers and multiple blood cultures growing methicillin-resistant *Staphylococcus aureus* (MRSA), they would recommend switching to a more effective antibiotic.

Antimicrobial stewardship is not a new idea. Efforts to monitor and promote the appropriate use of antimicrobials began prior to the Infectious Diseases Society of America's (IDSA) and the Society for Healthcare Epidemiology of America's (SHEA) issuing the first guidelines for developing hospital-based antimicrobial stewardship programs (ASPs) in 1997.

Lately, ASPs have become a focus of attention as the number of drug-resistant strains of pathogens has increased. Over the past three years, for example, the Minnesota Department of Health has documented increased numbers of carbapenem-resistant Enterobacteriaceae isolated from individuals in acute and long-term care facilities and the community. "These bacteria are

resistant to commonly used antibiotics," says Minnesota State Epidemiologist Ruth Lynfield, M.D. Agency for Healthcare Research and Quality data show hospital discharges with *Clostridium difficile* (*C. difficile*) increased 92 percent between 2001 and 2005 nationwide and, according to the Centers for Disease Control and Prevention (CDC), *C. difficile*-related deaths are at an all-time high, with the number being four times higher in 2007 than in 2000. Broad-spectrum antibiotics, in particular, set the stage for the emergence of resistant pathogens because they kill bacteria that keep their populations in check. "Misuse and overuse of antibiotics are key drivers of resistance," says Kravitz, an ASP expert with Infectious Disease Specialists of St. Paul. "We have nothing new in the pipeline to treat these infections."

Growing concern about antibiotic resistance led the IDSA and SHEA to release new guidelines for ASPs five years ago. Lynfield, who currently chairs the IDSA's antimicrobial resistance working group, is now championing an effort to get all Minnesota health care facilities to implement an ASP—starting with acute-care hospitals.

Despite the growing concern about antibiotic use, many Minnesota hospitals don't have an ASP, according to a 2011 Minnesota Department of Health survey. Reasons cited for not having one include lack of resources, lack of clinician support and never having heard of or considered an ASP.

"Many hospitals say they'd like to start a program but need help," Lynfield says. That fact has prompted the Department of Health to form an antimicrobial stewardship steering group to figure out how to help hospitals of all sizes create an ASP or improve what they already are doing. The group is developing protocols, order sets, educational materials, and strategies for overcoming IT challenges and getting administrative buy-in that

are expected to be available this fall. “We’re also developing a mentorship program,” Lynfield says, “so that those who’ve successfully launched an ASP can help those who want to start one.”

Lynfield says the group will eventually create similar materials for long-term care facilities and then for clinics. “It’s incredibly important for all health care facilities across the continuum of care to have ASPs to preserve the effectiveness of the antimicrobials we have.”

The right ingredients

Creating an ASP involves building a team that usually consists of an infectious disease physician, a doctoral-level pharmacist (Pharm.D.), and, if possible, a microbiologist, an infection preventionist and an information technology specialist. However, Lynfield says, “any physician knowledgeable about antimicrobial resistance and stewardship can lead an ASP.”

The ASP needs a physician leader—someone who has credibility with the medical staff and administration, Kravitz says. “Administration can be fearful that an ASP will alienate the hospital’s medical staff,” he explains, “but we haven’t found this to be a problem. Most physicians are very open to better stewardship.”

An effective program also includes use of formularies and a requirement for pre-authorization; a mechanism by which physicians can receive feedback about their prescribing habits; education about antibiotic dosing, duration and parenteral-to-oral conversion; and use of evidence-based guidelines for optimal prescribing. Electronic medical records can help in monitoring antibiotic use, according to Lynfield.

Having a restrictive formulary alone has little effect on antibiotic prescribing patterns, Kravitz says. “You also need to review medical records of all patients receiving antibiotics to verify their indication. Then if a change is needed, you need to give real-time feedback to the prescribing physician while the patient is in the hospital receiving antibiotics. You need to be aware of which antimicrobials work and [which ones] don’t work for specific bacteria in your facility.”

In addition to United Hospital, Kravitz and his colleagues provide such services for HealthEast’s hospitals in St. Paul, and they do electronic consults for Owatonna Hospital and St. Francis Regional Medical Center in Shakopee. In making

recommendations, they factor in practice guidelines, lab and radiology reports, sensitivity mismatch to see if a particular pathogen is sensitive to the prescribed antibiotic, and whether a lower-cost, equally effective medication is available. If Kravitz or his colleagues think a change is needed, they leave a note for the prescribing physician in the patient’s medical record. The note might suggest that the physician change to a different antibiotic, dose or route.

The antibiotic stewardship program at the Minneapolis VA Medical Center is essentially a decision-support system embedded in their EMR that helps physicians as they order antibiotics. The system, which is used for inpatients and outpatients in Minneapolis and at nine other VA facilities in the Upper Midwest, incorporates evidence gleaned from national guidelines and peer-reviewed literature and feedback from physicians and pharmacists at those facilities. It also is used to conduct ongoing analysis of susceptibility and resistance “for all the bugs we isolate,” says Gregory Filice, M.D., the VA’s infectious disease chief who helped create and manages the support system. “Unfor-

HOW TO START AN Antimicrobial stewardship program

In order to start an antimicrobial stewardship program, you need a champion, says Gary Kravitz, M.D., of Infectious Disease Specialists of St. Paul. That person can be an outside consultant like Kravitz or a physician who is employed by the hospital.

In addition, ASP teams usually include the following:

- A physician with expertise in infectious disease and antimicrobial stewardship
- A doctoral-level pharmacist (Pharm.D.)

And if possible:

- A microbiologist
- An infection preventionist
- An IT specialist

Effective programs also include:

- Formulary restrictions requiring pre-authorization
- Feedback to physicians
- Education
- Evidence-based guidelines for optimal dosing, duration of use and parenteral-to-oral conversion
- Electronic medical record systems

tunately,” he says, “we are finding that a number of bacteria we often see are less susceptible to commonly used antibiotics.”

Fifty percent of antibiotics prescribed are ordered through the decision-support system, which is voluntary, Filice says, in part because using it is more efficient than not using it. “About half the antibiotics on our formulary are restricted and require pre-approval from an infectious disease person,” he explains. “This usually requires paging someone, which takes time. Physicians ordering through the support system bypass this step so it’s quicker and easier.”

Filice says some VA physicians are reluctant to use what they consider “cookbook” medicine, even though it’s really evidence-based. Despite that, he says “we’ve had almost no negative feedback, and surveys show our medical staff overwhelmingly values the decision-support system.”

What the research shows

The cost of starting an ASP can be an obstacle to getting buy-in from hospital leaders, however. “If you can show that an ASP saves money, the administration will more likely support it,” Kravitz notes. He says studies have shown that antibiotic stewardship can, on average, save a 300-bed hospital between \$300,000 and \$400,000 per year, often with improved patient outcomes. “Hospitals with ASPs cut their antibiotic prescription costs by 20 percent and the cost of treating *C. difficile* infection by 20 percent—and many have done much better.”

A randomized controlled study at a Pennsylvania teaching hospital showed savings of \$600 per hospitalized patient as a result of having an ASP. The biggest cost savings came from shorter ICU stays. A 2005 Cochrane Review showed that reducing antibiotic use by 22 to 36 percent saves \$200,000 to \$900,000 per year, depending on the size of the hospital. In addition, Kravitz says hospitals that discontinued their ASP because of staff cuts saw significant increases in antibiotic costs, driven mostly by increased prescribing of broad-spectrum and high-dose antimicrobials.

How well ASPs slow the emergence of drug-resistant bacteria is harder to measure. “Probably the best evidence they do is the decreased incidence of *Clostridium difficile*,” Kravitz says. He says some studies show Gram-negative bacilli, especially Enterobacteriaceae, are less resistant as a result. Others have shown decreased incidence of vancomycin-resistant *Enterococcus* as well as fewer drug-resistant infections in patients with hospital-acquired pneumonia, including ventilator-associated pneumonia. A study of an

“If you can show that an ASP saves money, the administration will more likely support it.”

—Gary Kravitz, M.D.

antimicrobial program in a VA hospital published in the July 2003 *American Journal of Health System Pharmacy* showed that restricting use of third-generation cephalosporins, vancomycin and clindamycin significantly reduced drug-resistant infections.

The Minneapolis VA is still analyzing how much its decision-support system improves patient outcomes and reduces drug-resistant infection rates. “What we do know,” Filice says, “is that the antibiotic courses ordered through the decision-support system are 33 percent more likely to have the right drugs, route, dose and duration. It’s hard to say how much worse resistance and infection rates would be if we weren’t doing something.”

To most, ASPs make sense from a cost and quality standpoint. “When you consider,” Kravitz says, “that 30 percent of a hospital’s pharmacy budget is spent on antibiotics and 40 to 50 percent of antibiotic use is inappropriate or unnecessary, there’s a lot of room for improvement.” **MM**

ANTIMICROBIAL STEWARDSHIP resources

The Minnesota Department of Health is developing tools specifically for Minnesota health care facilities. In the meantime, there’s much to read online.

- The CDC’s resources include tools and techniques for implementing ASPs—www.cdc.gov/getsmart/healthcare/learn-from-others/CME/antimicrobial-stewardship.html
- The Greater New York Hospital Association’s experience with ASPs—www.gnyha.org/6652/Default.aspx
- The Infectious Diseases Society of America’s resources including Practice Guidelines for Antimicrobial Agents—www.idsociety.org/Antimicrobial_Agents/
- Johns Hopkins’ experience with antimicrobial stewardship—www.hopkinsmedicine.org/amp
- An article from the *Journal of Managed Care Pharmacy* on how to start an ASP—www.amcp.org/data/jmcp/S18-S23.pdf

Some clinics in Minnesota have considered discontinuing their vaccination program because of the cost.

■ Vaccine costs

A poke in the pocketbook

Vaccinating children may be the right thing to do, but rising costs and marginal reimbursements are making it a challenge for clinics. | BY KIM KISER

When Robert Jacobson, M.D., was finishing his pediatric residency in New Haven, Connecticut, in 1987, vaccinating infants was simple: a dose of oral polio vaccine followed by a single shot of diphtheria, tetanus and pertussis (DTP) vaccine at 2, 4 and 6 months of age. The cost of the DTP shot: about \$10. Today, the babies he sees in his practice at Mayo Clinic get a combination of diphtheria, tetanus and acellular pertussis, polio and *Haemophilus influenzae* type B (Hib) in one shot in addition to immunizations for rotavirus and hepatitis B at those ages. The cost of the combination vaccine alone: about \$80.

“We’ve seen a dramatic increase in the number of vaccines and the expense,” says Jacobson, a professor of pediatrics at Mayo and chair of the Minnesota Chapter of the American Academy of Pediatrics’ (MN AAP) immunization work group. In the meantime, reimbursement from payers hasn’t kept pace with the cost of procuring and administering vaccines. “Most physicians are happy if they can break even with vaccination programs,” Jacobson says.

New combined formulations are one factor affecting physicians’ bottom lines. David Estrin, M.D., a pediatrician with South Lake Pediatrics in the Twin Cities, recalls how his clinic was affected when it started using Pentacel, the combination DTaP, polio and Hib vaccine that was approved for use in 2008. “We made the decision to use it because it eliminated two pokes to the patient. However, there was a



significant hit of many tens of thousands of dollars to the practice because insurers paid for one poke rather than three," he recalls.

The economics of providing vaccinations is now being examined. In one study, researchers from the University of Michigan looked at financial information from private payers in that state, California, Georgia, New York and Texas and found mean reimbursement for the vaccine itself ranged from 80 percent to 123 percent of the average purchase price. Reimbursement for administration averaged \$16 for the first dose and \$11 for subsequent doses. The results were published in *Pediatrics* in 2009.

In 2011, the MN AAP surveyed pediatrics and multispecialty primary care clinics with at least one pediatrician regarding vaccine financing. Of the 17 responses from pediatrics-only groups (representing 31 clinic sites), 81 percent said net revenue from vaccinating children and adolescents has decreased in the last three years; 45 percent of the 28 multispecialty groups (representing 108 sites) indicated the same. Of the responding pediatrics groups, 17 percent noted that they have increased referrals to public health clinics, where kids can get shots for free, and 18 percent said they have considered getting out of the vaccine business altogether. Of the multispecialty respondents, 16 percent said they have increased public health referrals and 7 percent said they have considered eliminating vaccines for children and adolescents.

The price of a dose

Determining the true cost of vaccinating children is complicated. For one thing, the price of the vaccine itself can vary wildly from practice to practice. "We see small providers in greater Minnesota having to pay a lot more per dose than large health systems that have buying power," says Margaret Roddy, immunization program manager for the Minnesota Department of Health. Clinics that vaccinate children who are eligible for the Minnesota Vaccines for Children program, a federally funded initiative that

has provided free vaccine for children on Medicaid, who are American Indian, or who are uninsured or underinsured, pay nothing for those doses.

In addition, Roddy says, the price of vaccine hasn't held steady. "From last year to this year, there was a 4 percent increase across the board in vaccine costs," she says. Because clinics must maintain inventory, vaccines represent a significant investment—one that can tie up tens of thousands of dollars.

In addition to the cost of the vaccine itself, private clinics also have the expense of paying staff to order and monitor their stock; then there is the cost of properly storing them. Vaccines must be stored at specific temperatures, which requires special equipment and back up systems. "Poor storage could ruin your inventory," Jacobson says. "You might be sitting on \$20,000 to \$30,000 worth of vaccine that could be lost in an electrical failure."

Waste also complicates the cost equation. Sometimes vaccines are drawn and parents decide at the last minute not to

go through with the immunization or the child may be too uncooperative to vaccinate. In such cases, the dose is lost, and clinics must eat the cost. According to the American Academy of Pediatrics, about 5 percent of inventory is lost to waste.

Then there are the costs associated with administration—evaluating whether a patient is eligible for a vaccine, determining whether there are contraindications, counseling parents who may be hesitant to vaccinate their child or who may have misinformation about vaccines, obtaining parents' informed consent, and documenting that a patient has been immunized. "It's very hard to get sufficient reimbursement for that," Jacobson says.

Recouping costs

Getting paid for all this presents its own set of challenges. One of the problems has been timing. Payers set their reimbursements at a certain time of the year and if manufacturers raise their prices afterward, there's no recouping the dif-

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ference until reimbursements are revisited. In addition, payers are sometimes slow to cover new vaccines. “We’ve had in the past several instances of insurance companies either not covering them or covering them at less than the cost of purchasing them,” Estrin says.

The reimbursement situation may be improving. For one thing, payers and manufacturers have done a better job of coordinating increases in price and payment schedules, Estrin says.



Medicaid pays less than half of what Medicare does for vaccine administration. “Yet everyone would recognize that the cost involved with administering vaccine to a baby is much more than administering one to an adult.”

—Robert Jacobson, M.D.

In addition, a recent coding change increased the payment for combination vaccines. According to Estrin, they used to be paid per injection; they are now being paid per vaccine component. “So now, giving three separate shots doesn’t net you any more than giving one with three,” he says. “That was a big improvement because otherwise it was another barrier to immunization—the number of pokes a child had to endure.”

Medicaid reimbursement remains problematic, however. Although the Vaccines for Children program made free vaccine available to clinics that immunized children who were on Medicaid, are uninsured or are underinsured, “the administration fee remains insufficient,” Jacobson says. He adds that Medicaid pays less than half of what Medicare does for vaccine administration. “Yet everyone would recognize that the cost involved with administering vaccine to a baby is much more than administering one to an adult.”

From better to worse?

The Minnesota Vaccines for Children Program has helped offset the low Medicaid administration payments by covering the cost of the vaccine. But as of July 1, the program stopped providing private clinics with free vaccine for children who are underinsured—whose health plans don’t cover the cost of vaccines or who have high deductible health plans that don’t include first-dollar coverage for preventive care.

According to Roddy, the federal funding the state received to offset the purchase price of vaccine for underinsured children was cut by 25 percent last year. “And we’re looking at an additional 20 percent cut for this next year,” she says. “At the same time, the federal contract price for purchasing vaccines went up. The combination of those two things made it impossible to cover the funding needed to serve this population in private clinics.”

Estimates vary as to the number of children who may be affected by the change. Roddy says Department of Health data indicate 150 private clinics saw one or more underinsured children last year. Jacobson says approximately 3 percent of Mayo Clinic patients are considered underinsured; and he notes that through his work with MN AAP, he has heard of clinics with up to 10 percent of their pediatric patients underinsured.

Those children will still be able to receive free vaccinations, but they will have to go to a public health clinic to get them—and that concerns physicians like Estrin. “I think it will discourage parents,” he says. “And as a result, not everyone is going to get their immunizations and children will remain susceptible to disease.”

Roddy explains that a provision in the federal Affordable Care Act (ACA) is likely to meet the needs of these children—but not until all health plans comply with the requirements. The law mandated first-dollar coverage for preventive services including immunization starting in September 2010. But a clause allows insurers to continue their existing benefit set, which may not include such services, until they make major changes to the ben-

efits being offered. Roddy says the health department has seen the number of underinsured kids drop since the law took effect and expects that trend to continue.

In the meantime, the Department of Health has convened a work group that is looking at increasing underinsured children's access to free immunizations. The Department of Health will ask the CDC for permission for private clinics to serve underinsured children in areas that have few public clinics. CDC approval is expected to take several months, and only a small number of sites are expected to be approved. They're also looking at creating a vaccine purchasing pool, an idea that has been explored in Maine, Washington, New Hampshire and a number of other states. "These models have been found to be successful," says Jacobson, who along with Estrin, is involved in the state work group. In addition, a provision in the ACA will raise reimbursement for vaccine administration to Medicare levels for patients enrolled in Medicaid starting in 2013. He says this will help the bottom line of clinics that serve children on Medicaid.

Until changes happen, however, clinics that provide vaccinations to children will continue to do so, even if it means losing money. "We are going to continue providing vaccines to them," Jacobson says of underinsured children. "We'll take it on as a loss. We don't want to send them away, and we don't want to leave parents with an expense they can't afford." **MM**



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The COUGH that WON'T QUIT

Why **PERTUSSIS** has
made a comeback

By Jeanne Mettner

In 2010, health care workers at Children's Hospitals and Clinics of Minnesota started noticing as many as three to five children per week coming to the emergency department with uncontrollable coughing. In some cases, the children had coughed so hard that they had vomited or passed out; some of the infants were dehydrated and had difficulty feeding. The patients' parents, who in many cases, had already brought their child to a primary care provider or to urgent care, were worried because the cough was just not improving. Lab tests showed the young patients did not have a novel disease. They had pertussis.

The surprised parents were among the first in the state to learn that an illness that doctors have struggled to treat and patients struggled to survive for generations was back. "I often explain to parents that there is a symbol in the Chinese language for this illness, which translates roughly as 'the hundred-day cough,'" says Robert Sicoli, M.D., co-medical director of the emergency department at Children's Hospitals and Clinics of Minnesota, "so its chronicity has been known for a very long time and across cultures." Indeed, old pertussis has made a comeback.

During the next two years, reports of cases of the disease, also known as whooping cough, started coming out of school districts and health departments. Now 2012 is shaping up to be a record year for pertussis.

Since 2007, the incidence of pertussis has been increasing steadily in the United States. In California, for example, a 2010 outbreak resulted in more than 9,000 cases and 10 infant deaths, prompting the state to declare the century's first epidemic of pertussis in the United States. Earlier this year, Washington State

COUGH cough COUGH

Countering the **ANTIVACCINE ADVOCATES**

Perhaps the biggest reason for the falling immunization rate in Minnesota and elsewhere in the United States is the antivaccine movement. According to an article published in *Pediatrics* in October 2012, one in 10 parents do not follow the recommended immunization schedule for their children. An analysis by the Associated Press in 2011 found that the exemption rate for childhood vaccinations in Minnesota was 6.5 percent—close behind Alaska and Colorado, which have the highest opt-out rates (9 percent and 7 percent, respectively) in the nation.

In the article “The Age-Old Struggle against the Antivaccinationists,” which was published in the *New England Journal of Medicine* in 2011, Mayo Clinic’s Greg Poland, M.D., and Robert Jacobson, M.D., outline a strategy for expediting “the funeral of antivaccination campaigns.” They recommend 1) continuing to publish and fund high-quality, evidence-based studies on vaccinations; 2) maintaining and/or improving the Vaccine Adverse Events Reporting System (VAERS) and the Clinical Immunization Safety Assessment Network; 3) teaching clinicians, patients and parents how to counter antivaccinationists’ “false and injurious claims;” and 4) “enhancing public education and public persuasion.” Poland says the key to doing this is “increasing scientific literacy at all levels of education.”

Patsy Stinchfield, a pediatric nurse practitioner who serves as director of infectious disease services and of infection prevention and control at Children’s Hospitals and Clinics of Minnesota, says it’s up to physicians and other providers to speak up if we are to dispel misinformation about vaccines. “We need to say ‘We are not going to let movie stars and the media tell us what should be done with immunizations.’ This is a fundamental health care intervention that saves lives, and we need to speak strongly about that fact.”—J.M.

declared it had an epidemic of pertussis, with more than 3,000 cases reported through mid-July. Although Wisconsin has not yet declared an epidemic, the state had seen more than 3,100 reported cases as of mid-July. Minnesota is not far behind. As of June 30, 1,758 known cases had been reported; more than 400 of those were reported in July.

“For years, we just did not see that many cases, and now Minnesota is averaging 1,300 diagnosed cases a year,” says Linda Van Etta, M.D., an infectious disease specialist for St. Luke’s Infectious Disease Associates in Duluth. “It’s definitely been making a resurgence.”

An opportunist

The most recent uptick in cases didn’t surprise health officials or infectious disease specialists. According to Patsy Stinchfield, a pediatric nurse practitioner who serves as director of infectious disease services and of infection prevention and control at Children’s, pertussis is endemic in Minnesota and periodically appears and reappears. “It is a cyclical disease that tends to re-emerge and be problematic in three-year waves,” she says. “And it is the one vaccine-preventable disease that despite our best efforts we are not yet on top of.”

A number of factors have contributed to the recent rise in the number of cases. For one thing, vaccine rates are not where health officials want them to be in large part because of the antivaccine movement (see “Countering the Antivaccine Advocates”). Data from the CDC’s National Immunization Survey indicated that in 2010 87.8 percent of children 19 to 35 months of age received the appropriate course of the diphtheria/tetanus/acellular pertussis (DTaP) vaccine. In Minnesota, the rate fell from 87.2 percent in 2008 to 85.4 percent in 2009. According to a report by Children’s, for every percentage point drop in the immunization rate, 4,230 kids are exposed to vaccine-preventable disease. “Pertussis is one of the most contagious diseases and without immunization rates greater than 95 percent of the population, pockets of the unimmunized can add to the spread of disease in communities,” Stinchfield says.

Second, we’ve learned immunity from the childhood pertussis vaccine, which is given at 2, 4 and 6 months of age and then again between 15 and 18 months and 4 to 6 years, erodes over time. “The durability of immunity afforded by a pertussis vaccine is about five to 12 years, considerably shorter than the length of immunity following natural infection, which can be up to 30 years,” says Greg Poland, M.D., who leads Mayo Clinic’s Vaccine Research Group. “By the time they reach age 10 or 11, many of these kids no longer have immunity.” In fact, according to health officials, many of the cases have occurred among middle and junior high school students. Lakewood Elementary School in Duluth, Shakopee Junior High School in Shakopee and Wayzata East Middle School in Wayzata are among the schools that reported cases during the 2012 school year.

A third reason for the increase may be that physicians don’t always think “pertussis,” especially when they see an adult patient

with a persistent cough. “Physicians in the nonpediatric specialties do not tend to include pertussis as part of the differential diagnosis perhaps because they keep thinking of it as a childhood disease,” notes Poland, who often gives talks on vaccine-preventable diseases to physicians and other health care professionals. “And the average adult certainly doesn’t come in and say, ‘Doctor, I think I have pertussis’—if they come in at all because of their cough.” Besides, if they were vaccinated as children, they assume they are protected.

A twist on transmission

Poland notes that with many childhood diseases and illnesses, children are the reservoirs, carrying the disease to adult populations. With pertussis, it’s the other way around: Adults and adolescents who have lost immunity from their childhood vaccinations are transmitting it to younger populations. Van Etta notes that about half of the cases of pertussis in Minnesota occur among kids 8 to 18 years of age and 25 percent are in adults. Newborns and infants are especially vulnerable. Children do not develop full immunity until they have had five doses of the vaccine. With this in mind, it is not surprising that in Minnesota, 95 percent of the hospitalizations for pertussis are for babies up to 3 months of age. Stinchfield says Children’s is admitting approximately one very young baby with whooping cough each month.

At any age, pertussis is not pleasant. Relentless jags of coughing can lead to vomiting, broken ribs and even passing out. But for infants, the consequences can be dire. To know the effect it has on them requires some understanding of the disease itself.

When a human breathes in the *Bordetella pertussis* bacteria, it lands on the cilia and paralyzes the little hairs that normally sweep and move bacteria and mucus in the airway. What results is a buildup of bacteria and mucus, which the body attempts to forcibly remove through intense muscular spasms—coughing. In infants, pertussis can lead to pneumonia, hypoxia, encephalitis, even death. “I have taken care of many children in my 30-year career, and it is very scary to be helping an infant who is turning blue and gasping,” Stinchfield says, adding that beyond antibiotics, the treatment in these cases is supportive care such as oxygen and IV fluids. “If their condition is so serious that they cannot breathe on their own, they need ventilator support and occasionally extracorporeal membrane oxygen until the infection resolves.”

Whipping the whoop

Diagnosing whooping cough early is critical to whipping it. And doing so means physicians need to place it further up on the differential diagnosis. When a patient is in the beginning stage of the illness, clinicians may attribute the cough to a viral or

bacterial upper airway or lower respiratory tract infection, delaying diagnosis and treatment and allowing more time for the patient to infect others. Although the classic “whoop,” which is caused by the gasping that occurs at the end of the coughing fit, is often present in young children, it is not a signature symptom in adults or adolescents. Thus, physicians should consider pertussis for any cough that persists more than two to three weeks.

Diagnosis requires sending a nasopharyngeal or aspirate sample for polymerase chain reaction (PCR) testing, which can be done by the Department of Health. The PCR test has optimal sensitivity during the first three weeks of coughing. (The CDC has information on the technique for obtaining a nasopharyngeal swab sample at www.cdc.gov/pertussis/clinical/diagnostic-testing/specimen-collection.html.) Because test results often do not come back for several days, the patient should be prescribed an antibiotic, usually azithromycin, immediately. (Clarithromycin and erythromycin also can be used, but they require a longer course—seven days and 14 days, respectively.) “Once you test, don’t wait for the results to treat the patient with azithromycin,” Van Etta says.

In some cases, azithromycin may be given to healthy family members and others who are in close contact with the patient to prevent transmission. Pertussis is most easily transmitted during the first stage, the catarrhal stage, which can last up to two weeks—often long before the patient is diagnosed. “If one person comes down with it in a household, 80 percent of the members in that household will become ill,” Van Etta says. According

Pertussis VACCINE CAMPAIGNS

In addition to the Minnesota Department of Health’s efforts, the Minnesota Academy of Family Physicians Foundation has developed a vaccination campaign designed to increase immunization rates among family physicians and health care staff. Clinics that achieve 100 percent pertussis immunization rates among eligible family physicians receive a certificate and are entered in a random drawing for a gift card. A number of health care systems also have campaigns in place. At St. Luke’s Hospital in Duluth, health care workers’ pertussis vaccination rates went from 12 percent to 80 percent thanks to their two-week long “Whip the Whoop” campaign. The hospital continues to offer the vaccine to all new hires and any employee who comes in for their annual influenza vaccine. Children’s Hospitals and Clinics of Minnesota also offers the vaccine to its employees.

to the CDC, prophylactic treatment should only be provided to those who are younger than 12 months of age, who are vulnerable to the complications of pertussis, and who work in health care settings and come in close contact with high-risk individuals. The Minnesota Department of Health advises prophylactic antibiotics when exposure to a patient with a laboratory-confirmed case has occurred within the previous 21 days.

Vaccinating people is also key to beating whooping cough. In 2005 the Tdap booster was released. Currently, the CDC's Advisory Committee on Immunization Practices (ACIP) recommends that the Tdap booster be given to kids beginning at age 12, women at or beyond their 20th week of pregnancy, and any adult who has not previously received the acellular pertussis booster. "Many health systems are doing a good job of implementing adult vaccine schedules through standing orders," Poland notes. "In those that have standing orders, no matter what hospital or clinic you walk into, boom, you are given a list of vaccines you should have at your age, and if you haven't had a vaccine, you are given the opportunity to get it right then and there." Although the booster has been shown to increase immunity against pertussis and is effective at preventing pertussis in the short term, experts note that it is too early to determine its longer-term effect on incidence rates.

To increase overall vaccination rates in Minnesota, the Department of Health is working to change the state's school and child care immunization laws so that they more closely align with the CDC's recommendations, says Kris Ehresmann, director of Infectious Disease Epidemiology, Prevention and Control Division of the Minnesota Department of Health. With regard to pertussis, the health department is proposing that the DTaP vaccine be given after the child's fourth birthday, rather than between the ages of 4 and 6 years, and that the current tetanus booster requirement for seventh graders be replaced with a requirement for Tdap. "Until an immunization guideline is part of the school law, many nonpediatric clinicians—internal medicine, family practice—will not be thinking about pertussis and other vaccine-preventable diseases as much as they could," Ehresmann says.

Addressing the antivaccine attitudes of some parents is tricky but essential to staving off pertussis, says Stinchfield. She notes that keeping at-risk populations protected requires everyone in the community maintaining their vaccines. And promoting

herd immunity requires providers to be more proactive. Says Stinchfield: "As clinicians, we get short on time, and we may feel like we are not going to make headway with parents who are vaccine-hesitant or against vaccines; but the fact of the matter is that we are the experts, we are the ones who have to speak much more strongly and confidently. Our job is to protect that child, and if we let them leave without being vaccinated, we've failed that child as well as the community."

Here to stay?

Even if all of the recommendations and strategies for preventing and controlling pertussis are implemented, it remains to be seen whether the disease can be eradicated in the United States. One reason for the uncertainty is that Tdap is not yet recommended for 8- to 10-year-olds, who comprise 25 to 30 percent of total pertussis cases. "As we see more cases nationally within that age bracket, there will need to be discussions about whether it would be appropriate to start vaccinating younger," Ehresmann notes.

Another factor adding to the uncertainty is the formulation of the vaccines themselves. The first vaccines against pertussis were whole-cell vaccines, suspensions of whole bacterial cells that had been killed. Today, most pertussis vaccines, including the new Tdap booster, include only components of bacterial cells. "The newer acellular vaccines produce fewer adverse reactions, but the question is whether that purification has changed the effectiveness," Ehresmann says. "We don't know if there are other things in the whole-cell vaccine that provided some sort of unforeseeable protection; only time will tell." (The ACIP is discussing the need for a second Tdap booster.)

Despite school being out for summer, pertussis cases have continued to rise across the nation. Cases have been reported in Florida, Kansas, Iowa and New York, and experts are warning that the illness could continue to spread through such venues as day care centers and summer camps. As school reconvenes, pertussis is likely to gain steam. Stinchfield advises clinicians to continue doing what they can to reduce transmission: get vaccinated themselves, recommend the Tdap vaccine for their patients, and insist that coughing patients wear masks and get roomed promptly and that health care workers with coughs wear masks, practice good hand-hygiene and stay home if they are sick. "Pertussis may be here to stay for a while, but that doesn't mean we are powerless," she says. "The best thing we can do at this point is be cognizant of the role that clinicians can play in preventing further pertussis cases." **MM**

Jeanne Mettner is a frequent contributor to *Minnesota Medicine*.

RESOURCES

The Immunization Action Coalition has resources for physicians including standing orders for vaccine (www.immunize.org/catg.d/p3073.pdf) and a Q&A with Centers for Disease Control and Prevention experts (www.immunize.org/askexperts/experts_per.asp).

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Tracie Newman and her daughter, Autumn, who contracted chickenpox at 9 months of age. Today, Autumn is a thriving 2-year-old.



Photos courtesy of Tracie Newman

The N of 1

Stories, rather than studies, can have an overwhelming impact on parents who are making decisions about whether to vaccinate their child.

By Tracie Newman, M.D., M.P.H.

As a mother of three young children, a pediatrician and an advocate of public health, immunizations and the misinformation surrounding them have been on my mind for many years. It is difficult for me to understand why we as a community, as a nation, have become so polarized about something that to me seems so straightforward and beneficial.

I think one reason is that as society has become more complex, conscientious young parents have felt pressured to become experts on just about everything. Breast or bottle? Cloth or disposable? Organic or nonorganic? Make my own baby food or feed my child store-bought? Co-sleeping? Circumcision? Private or public school? The list goes on and on. Somewhere along the way, the “choice” of whether to immunize their children gets thrown in.

But many times, parents are making this crucial (and potentially life-or-death) decision based on little more than a conversation with a neighbor. I have learned that an “N of 1” can be

overwhelmingly powerful. In statistics, N represents the number of subjects in a study. It’s your sample size. Generally, the larger the sample size (N), the higher the power of a test.

Precise steps have been taken in thousands of studies proving the safety and efficacy of immunizations. But none of this can compete with anecdotal evidence from a friend or relative. All it takes is to hear of a sister’s friend’s neighbor’s child having what may be a reaction four days after getting a vaccine and that’s it. That N of 1 has more power than any evidence I or any physician could ever present in the clinic or that any public health campaign could convey. I get it. It is human nature to be more affected by those close to us than the distant unknown “Ns” in clinical trials. But does that truly make anecdotes more valid? Since they seem to be the way to convince people these days, I will set aside the studies for a moment and share with you my own personal story.

The N is Autumn, my 2-year-old daughter. When she was 9 months old, too young to receive the varicella vaccine, she contracted chickenpox. This was the direct result of exposure to an intentionally unvaccinated older child in her Early Childhood Family Education class. Chickenpox is highly contagious; you need only to be in the same room with someone who is infected to contract it. It also has a fairly long incubation period ranging from 10 to 21 days, and people are infective 48 hours prior to the appearance of a rash.

My typically happy, thriving baby was covered in lesions. Her fits of screaming told me she was in pain. It was difficult for her to nurse or take a bottle because the ulcers had invaded the inside of her mouth. We almost had to hospitalize her for IV fluids to ensure her hydration. Today, Autumn has permanent scars from the chickenpox, one of which is on her face.

I think we belittle varicella infections. We weren't vaccinated against this infection and everything turned out just fine, right? That might have been the case for some of us. But chickenpox can have very serious sequelae: secondary skin infections such as cellulitis, myositis and necrotizing fasciitis; toxic shock syndrome; pneumonia; hepatitis; encephalitis; dehydration; and neurologic complications such as Reye syndrome, transient focal deficits, aseptic meningitis, vasculitis, acute cerebellar ataxia, transverse myelitis, hemiplegia, delirium and seizures. In one study, encephalitis accounted for 20 percent of complications in patients hospitalized with varicella infections. There is a 10 percent mortality rate associated with encephalitis. Still want to have your pox party?

Autumn was an unknowing victim of someone else's selfish decision. And I watched her suffer needlessly for weeks. The ripple effect of that person's choice was that my husband and I both had to take time off work to care for her. We essentially were forced to quarantine Autumn in our home in order not to expose

others. Nannies, grandparents, siblings, aunts, uncles and friends were all affected in some way. Yet the impact could have been greater. What if a child or sibling of a child in that ECFE class had been on chemotherapy or was otherwise immunosuppressed? Chickenpox can be a death sentence in such instances.


And what about the unvaccinated child? He or she has missed an important window for receiving vaccinations. An estimated one in five children worldwide lacks access to routine vaccinations, which means diseases such as chickenpox, measles and pertussis are still out there, placing adults and children who are unvaccinated at risk if they leave areas of herd immunity.

When parents choose not to vaccinate their child, they are making a decision that can be life-altering. And the child never gets a say in the matter. I once had a young man present to my clinic to "finally get the shots my parents were against" now that he was an adult. He

returned week after week to gain immunity to as many diseases as he could. We do not fully know what the consequences will be for the next generation; but with recent reports that cases of measles are at a 15-year high and of the increasing number of pertussis outbreaks around the country, I am concerned.

I would like to propose that parents allow themselves the luxury of having one job: simply being Mom or Dad. Speaking from experience, this is a tireless yet gratifying job in and of itself. And I also propose they let the experts who have devoted many years of their lives to study and training and who have the best interest of children at heart make the decisions regarding vaccinations. It is often said that a little knowledge is a dangerous thing. But when it comes to a child, is a little really enough? **MM**

Tracie Newman is a pediatrician with Sanford Health, a clinical assistant professor of medicine at the University of North Dakota and a mother of three.



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The surgical team at Banadir Hospital in Mogadishu. The author is third from the left.

Photos courtesy of Hani Ahmed

Going home

A young physician who fled Somalia as a child returns to offer help.

By Hani Ahmed, M.D.

At the age of 5, my father took us out of Somalia as political unrest engulfed the country. It was the late 1980s—a time when the popular feeling was one of optimism that the growing crisis would soon blow over. With \$4,000—his life savings—stuffed in a suitcase, he packed his six children up and fled the tumultuous nation against the wishes of his family. We could not foresee that this act would shield us from the ensuing 20 years of war and anarchy that befell the country.

Twenty-three years later and a resident at Hennepin County Medical Center in Minneapolis, I found myself headed back to Somalia with the help of the American Refugee Committee to volunteer for a month. Excited and not knowing what to expect, I flew halfway around the world to see and treat the most vulnerable patients in a prestigious Mogadishu hospital called Banadir. A center of excellence in its early days, Banadir now carried the stains of war, and its corridors swelled with refugees from the famine-stricken regions of the south. Although lacking supplies and in disrepair, the hospital remains one of the few in the region, and people trek long distances to its doors. Arriving in the city, I felt a mix of emotions—an overwhelming sense of homecoming fused with sorrow at what had become of my childhood home.

The 40-bed internal medicine ward at Banadir was the newest addition to the facility, as well as the most neglected. The hospital was extremely short-handed, and because medical education was among the casualties of the war, the physician and nursing staff tended to be inexperienced. Our team consisted of one newly graduated intern, a nurse and several support staff. It didn't take long before I realized I was the most senior member of the small team, rendering me solely responsible for my patients' lives. As a resident who is used to supervision, I felt out of my element.

Moments after introductions, I was taken to the bedside of a patient, a cachectic-looking young man lying on a thin mattress surrounded by his worried family. He had a mass in his epigastrium and an intestinal obstruction. There were circular burn marks on his abdomen where a homeopathic healer had attempted to relieve his condition. Further history revealed that he had been coughing up blood-tinged sputum for months and his chest X-ray confirmed the apical cavities of TB. Because the surgeons would not explore his abdomen without a tissue diagnosis, we quickly put funds together and arranged for him to be taken the following morning to the only pathologist in the city for an FNA of his mass. Later that night, he began to

cough terribly, his breathing becoming more strained. Our only oxygen machine was already in use, so we asked to use the one in the operating room. This was not a small request, as a needier patient could be brought in at any moment. The next morning, when I returned to work, I was informed that the man had coughed up a lot of blood and died. This news hit me hard, and I had to convince myself that there was nothing we could have done—that his TB was so advanced that even if we started treatment before testing his sputum, it would not have changed his fate.

The many patients at the hospital who were infected with TB illustrated what a terrible killer it is. The disease seemed to consume their bodies. More alarming was the emerging surveillance data showing a rapidly increasing number of cases of multidrug-resistant disease, no doubt a consequence of the dismantled health programs in the precarious region.

Urosepsis complicating obstructive kidney stones was another surprisingly common affliction. The water in Somalia is chock full of minerals, which quickly crystallize in the urinary tract. Patients frequently arrived in shock, some after several days of being unable to urinate. I recall the frustration I felt when I asked for antibiotics and fluids only to find them locked away in cabinets. One time, a nurse inadvertently left with the key, and after unsuccessful attempts to reach her, I broke open the locks. I learned that medicine was always kept guarded because of its potential to be sold on the black market, a common practice in the Third World and a concept I had never imagined.

Also surprising was the prevalence of peptic ulcer disease. The acid-loving *H. pylori* was not only ubiquitous, it also was deadly. Upper GI bleeding was common among young patients. The one whom I will never forget was a woman about my age who was also a new mother. She had had gnawing epigastric pain for months when she started vomiting blood. While taking her history, she suddenly jumped from her bed and had a bowel movement the color and consistency of cranberry juice. I felt a sudden dread; my heart began to race. She continued to rapidly lose blood and became unconscious within minutes. I desperately inserted an 18-gauge into her femoral vein for a makeshift central line. We pushed fluids and whatever blood we had. There were no intravenous PPIs anywhere in the hospital, so I gave her what I had: ranitidine, vitamin K and epinephrine. The hospital



TOP: A typical ward in the hospital's pediatric wing. BOTTOM: The area outside the surgical ward. This area was always crowded with victims of war-related injuries.

had no endoscope, and when the surgeons arrived, they quickly realized that she could not survive an emergency laparotomy. When she passed away, her family turned to me and thanked me for doing my best. I wept openly with them. I thought about the young woman often after that. I thought about how rarely patients died from bleeding ulcers back home.

On the plane back to the United States, I reflected on my father's decision to leave Somalia all those years ago and how it changed the course of my life. I went back to Somalia to put my medical skills to use to help people escaping the famine and the consequences of war. I managed to save lives and provide comfort. But there, I learned to practice a different kind of medicine—to do what you can with what you have. In the end, it made me a better doctor, and for that I am grateful. **MM**

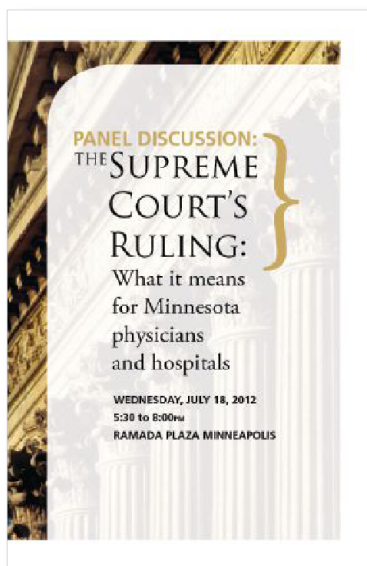
Hani Ahmed is a second-year internal medicine resident at Hennepin County Medical Center in Minneapolis.



MINNESOTA
MEDICAL
ASSOCIATION

THE PHYSICIAN ADVOCATE

The MMA's monthly report on policy, people and politics



AS THE DUST SETTLES

Panel discussion delves into details of Supreme Court's ACA ruling

It may take years to figure out the implications of the Patient Protection and Affordable Care Act (ACA); but in the meantime, health care reform keeps moving forward in Minnesota—at least for officials in the state's Health, Human Services and Commerce departments. This became clear in mid-July at a panel discussion hosted by the

MMA and Minnesota Hospital Association.

More than 160 physicians and hospital administrators gathered in Minneapolis to hear state leaders, a former U.S. senator, an independent orthopedic surgeon, a Mayo Clinic executive and a small-town hospital CEO discuss the ramifications of the Supreme Court's ruling and how it will affect the delivery of care in the North Star state. The following summarizes some of the discussion at the event.

Health insurance exchange

Depending on whom you ask, Minnesota may or may not have a state-run health insurance exchange in its future. A Senate bill to create an exchange petered out in the Legislature in late March, likely because the lawmakers who opposed it anticipated that the Supreme Court would find the ACA unconstitutional.

When that didn't happen, opponents still resisted. In June, Sen. David Hann, chair of the Senate Health and Human Services committee, told the St. Paul *Pioneer Press*: "People do not want this law." He pointed out that because the Legislature won't reconvene until 2013, "there's no possible way we can pass a health exchange between now and January."

State leaders are moving forward nonetheless. In July, the Commerce, Health and Human Services departments hired Virginia-based Maximus Inc. to develop an online exchange that will include a consumer-friendly Orbitz-like tool to help Minnesotans shop for health insurance and/or sign up for Medicaid.

According to the ACA, citizens either need to have access to a state-run online insurance exchange or to one run by the federal government. "We don't want the feds to do things for us," said Manny Munson-Regala, J.D., deputy exchange director for the Minnesota Department of Commerce, one of the panelists at the July event. He estimates that 1.2 million Minnesotans are expected to use the online tool.

Over the next several months, Commerce officials will put many of the pieces in place so that the state can meet the federal government's next deadline—November 2012, the date by which states must file their intent to run their own exchange. The website must be ready to handle open enrollment starting January 1, 2014.



1



2



3

1. Former U.S. Sen. David Durenberger moderates a panel of state leaders.
 2. More than 160 physicians and hospital administrators attended the event.
 3. Health Commissioner Edward Ehlinger, M.D. shares a laugh with a guest.

Medicaid expansion

When the Supreme Court ruled the ACA's individual mandate constitutional as a tax, it also determined that the federal government can't force states to expand Medicaid. Consequently, states need to determine whether they want to expand the program. As of mid-July, seven governors had already said they will not expand Medicaid; and many more are leaning in that direction. Gov. Mark Dayton has said he wants Minnesota to participate in the expanded program.

For those participating, the federal government will provide 100 percent of the funding for three years (and 90 percent thereafter) to move individuals with incomes less than 133 percent of poverty into the Medicaid program.

"Do we take up the government's offer to cover these single adults?" Human Services Commissioner Lucinda Jesson, J.D., asked during the discussion. Minnesota is already providing coverage for many of these individuals through the MinnesotaCare program, which is paid for almost exclusively with state funding that includes revenue from the provider tax.

The state will also need to decide what to do with adults whose incomes fall between 133 percent and 250 percent of poverty and are currently enrolled in MinnesotaCare. Jesson suggested that the state could move enrollees to the exchange to access federal subsidies—with or without additional state financial support and benefits—or use the federal funds available for this population to create a "basic health plan" operated by the state.

"This will be a big issue in the state Legislature," Jesson said.

What lies ahead

A lot of heavy lifting awaits physicians and administrators. Panelists encouraged the physicians and hospital administrators in attendance to think hard about how they approach

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the future.

Physicians need to be mindful of the business side of health care, said Nicholas Meyer, M.D., an orthopedic surgeon in independent practice at St. Croix Orthopaedics. “What comes first? Your business or your patients?” he asked. “From a philosophical, humanitarian point of view, we all want to say our patients,” he said. “But when you think about it, if you don’t protect your business, and your business goes under, you’re not there to care for your patients.”

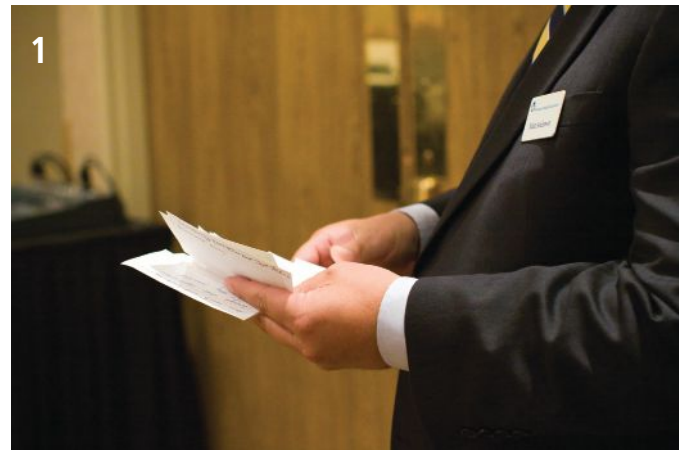
Robert Nesse, M.D., CEO of Mayo Clinic Health System, agreed that significant change lies ahead. He outlined five essentials for achieving accountable care: a network of providers; an integrated and aligned care model (not necessarily common ownership); coordination of care among these entities; a financial model that rewards value, not volume; and the need for practice and data analytics, which will require significant new collaborations.

“At Mayo Clinic, we very clearly understand that unless the health system changes significantly, we do not have a sustainable business model for the future,” Nesse said. “And my guess is that if Mayo Clinic doesn’t think it has a sustainable business model, you’re probably thinking the same thing, or ought to be.”

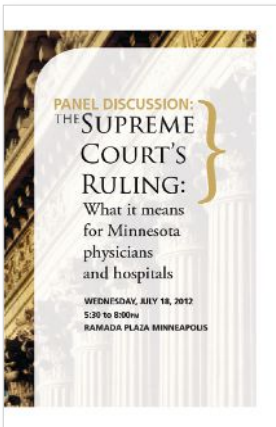
A few expressed doubts about whether the ACA will be implemented. One member of the audience asked about the ramifications to the state if the ACA is repealed in November, following the 2012 election. Commissions Ehlinger and Jesson said they don’t see that happening. Even if it were to happen, the effects in Minnesota could be minimal.

“Minnesota has been working on health reform for a long time,” Ehlinger said, noting that the state has been examining many of the items covered in the ACA: population health, improving access, looking at quality and value, searching for efficiencies and examining various levels of coverage.

“We can’t stop,” Ehlinger said. “We can’t say we’re going to go back to how we’ve been doing things the past 30 years. We need to move forward. I think people are going to recognize that this is a good step forward. It needs to be tweaked. It’s going to be modified over the years, but it is a good start.”



1. Attendees wrote down their questions for the panelists.
2. Manny Munson-Regala, J.D., deputy exchange director for the Department of Commerce, discusses the state’s recent efforts on the exchange.
3. Guests listen intently to a panel made up of two physicians and one hospital administrator.
4. MMA Board member Carl Burkland, M.D., and MMA Past-President Patricia Lindholm, M.D., (second from right) discuss health care before the event.



THEY SAID IT

Quotes from the panel discussion

“This is a time that had to come.”
– Former U.S. Sen. David Durenberger

“From my perspective, [accepting the federal money for Medicaid expansion] is a good deal for taxpayers because we are already paying for a lot of this with state dollars. It’s a good deal for people because they are getting a better benefit set. And it is very helpful to providers as well.”

– Lucinda Jesson, J.D.

Commissioner, Department of Human Services



“You don’t need to be owned, but you do need to understand what it takes to be aligned.... Accountable care is a very, very iterative thing. Maybe defined market by market.”

– Robert Nesse, M.D.

CEO Mayo Clinic Health System



“My job is to make sure we have the best medical care system in the world, the most efficient medical care system in the world, the highest quality medical care system in the world, and try and make it so nobody ever needs it. I’m trying to put [physicians] out of business, but I don’t think you have to worry about that.”

– Edward Ehlinger, M.D.

Commissioner
Department of Health

“We need to involve the patient in the decision-making process, and we need to educate patients in regard to the costs. I think the best way to educate them, unfortunately, is for them to feel it as well. And I think [physicians] need to remain flexible and ready to adapt.”

– Nicholas Meyer, M.D.
St. Croix Orthopaedics

“[With an exchange] we are providing an environment where the dialogue about eligibility is taken for granted. We are moving from an environment about whether or not you are eligible to an environment where we figure out what you are eligible for.”

– Manny Munson-Regala, J.D.

Deputy exchange director, Department of Commerce



FOCUSED for SUCCESS



Creating an indispensable MMA

The MMA is putting finishing touches on its *Focused for Success* plan, which addresses issues that member-physicians say are most important to them.

Focused for Success is a comprehensive roadmap for the MMA's work over the next three to five years. It focuses the association's efforts and resources on three primary goals:

- Helping Minnesotans become the healthiest in the nation;
- Making Minnesota the best place to practice medicine; and
- Advancing professionalism in medicine.

"Our efforts will touch the practice and professional life of every physician in Minnesota," says Dave Thorson, M.D., chair of the MMA Board of Trustees. "I'm confident that our efforts will reduce the time physicians spend on administrative activities, will improve patient health and will increase professional satisfaction."

He notes that the plan emerged as a response to physicians' needs. "We listened to physicians through surveys, focus groups and individual conversations, then used this information to develop our goals and create work plans that will help make the MMA indispensable for all doctors," he says.

Here is a look at issues the MMA will tackle as part of *Focused for Success*.

HEALTHIEST in the NATION



Helping Minnesotans become the healthiest in the nation

Minnesota has long been recognized as one of the healthiest states in the nation, but there's room for improvement. The MMA has targeted improving the quality of clinical care as well as increasing access to physicians as two of its priorities. In particular, the MMA will focus on the following:

Improving the quality of care for patients with chronic illness, especially where there are disparities between the care certain groups receive and what the rest of the population receives. The MMA will also lead efforts to influence and define Minnesota's quality improvement agenda by ensuring physicians have a stronger voice in developing and implementing performance measures and by holding forums for physicians to discuss and shape a relevant measurement agenda. In addition, the MMA will partner with Minnesota Alliance for Patient Safety to expand safety efforts in clinics.

Increase the primary care physician workforce. The MMA will partner with medical schools, training sites and state leaders to accelerate the commitment to increase the number of primary care physicians in the state. The MMA also will work to improve the practice environment by promoting the adoption of the health care home model.

BEST PLACE to PRACTICE



Making Minnesota the best place to practice medicine

Medicine has undergone significant changes in the past 20 years that have had a profound effect on physicians. The MMA is committed to improving the practice climate so that physicians can focus their time and talent on the care of patients, rather than on administrative tasks. To do that, the MMA will work to:

Reduce the hassles associated with prior authorization of pharmaceutical prescriptions by bringing representatives from health plans and other interested stakeholders together to develop a standardized process.

Promote new and innovative payment and delivery models. The MMA will help physicians navigate the many complex and evolving options for delivering high-quality care at a lower cost.

Advancing PROFESSIONALISM



Advancing professionalism in medicine

In order to strengthen the ties that bind all physicians, the MMA will strive to:

Protect the core values of the medical profession by ensuring continued competency and training of physicians and strengthening the physician-patient relationship.

Foster an improved culture of professionalism that promotes collegiality among physicians.

Complete information about the MMA's *Focused for Success* is available on the MMA website at www.mnmed.org/FocusedPlan.

VITAL SIGNS

MMA NEWS IN REVIEW

CME Available to Physicians Attending Annual Meeting

Continuing Medical Education credit is available for three break-out sessions at this year's MMA Annual Meeting at the Marriott City Center in Minneapolis on September 14 and 15.

The first session, which takes place Friday, September 14, from 5 to 6 p.m., includes a presentation on "Engaging Patients: Moving from Consumers to Partners in Healthcare" featuring **Gary Oftedahl**, M.D., chief knowledge officer for the Institute for Clinical Systems Improvement. A non-CME session will take place concurrently: "From One Physician to Another: Financial Planning Skills for a Lifetime," by **Joel Greenwald**, M.D., a certified financial planner. Both sessions are free to MMA members and nonmembers.

On Saturday, September 15, from 9:15 to 10:15 a.m., both members and nonmembers are invited to hear keynote speaker **Joseph Bujak**, M.D., discuss "Bringing Physicians Together, a Journey from I to We to Us." The talk will be followed by a discussion (from 10:30 to 11:45 a.m.). This session is free to MMA members; \$40 for nonmembers.

The Minnesota Medical Association is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Minnesota Medical Association designates this live activity for a maximum of 3.25 *AMA PRA Category 1 Credits*[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Register at www.mnmned.org/annualmeeting.



Ncha Xiong,
M.D.



Elizabeth
Goelz, M.D.

Young Physicians Receive Urban Loan Forgiveness

A program designed to encourage young physicians to go into primary care practice in underserved communities recently presented awards to two recipients.

In July, **Ncha Xiong**, M.D., and **Elizabeth Goelz**, M.D., received grants to pay down their educational debt from the Urban Physician Loan Forgiveness program, which is funded in part by the MMA Foundation (MMAF).

Through the program, which is managed by the Minnesota Department of Health's Office of Rural Health and Primary Care, recipients can receive up to \$100,000 over four years. The MMAF provided \$100,000 to match the state's funding and create the two positions.

Xiong will begin her employment at the Northpoint Health and Wellness Center in Minneapolis in September. Goelz is already employed at Hennepin County Medical Center's General Internal Medicine Clinic.

The MMAF is funded by contributions from individuals and organizations including the Blue Cross and Blue Shield of Minnesota Foundation, HealthPartners and UCare.

Need to Conduct a CG-CAHPS Satisfaction Survey? Here are Some Resources

All Minnesota clinics that serve patients 18 years of age and older, except for behavioral health and pediatric/adolescent medicine clinics, are required to conduct a patient satisfaction survey between September and November of this year using the CG-CAHPS (Clinics and Groups, Consumer Assessment of Healthcare Providers and Systems) survey instrument.

The MMA and Minnesota Medical Group Management Association (MMGMA) have compiled a list of survey vendors that can help your clinic fully comply with this new state requirement.

Clinics have the option of using a MN Community Measurement-selected vendor or contracting with one of several CMS-approved vendors, who will conduct the survey and submit data to MN Community Measurement. Find more information at www.mncm.org.

Following is a list of CMS-approved vendors. Survey administration fees are negotiated between the vendor and the clinic.

AVATAR INTERNATIONAL

Contact: Jennifer Beecher at jbeecher@avatar-intl.com or call 800-282-8274 x108.

INFORMED DECISIONS, INC.

Contact: Jim Theuer at jim@strategy.com or call 651-335-9498.

MINNESOTA RURAL HEALTH COOPERATIVE

Contact: Lou Wischer at lwischer@mrhc.net or call 507-423-5300 x 214.

PRESS GANEY

Contact: Ryan Brubeck at rbrubeck@pressganey.com or 888-234-5145 or 312-805-3957.

Members Making a Difference

MMA members **Linda Van Etta**, M.D., FACP, ABIM, and **Terry Cahill**, M.D., will represent the MMA on a group that will examine the state's Medi-

cal Practice Act to ensure that it “effectively protects the safety and well-being” of Minnesota citizens.

MMA member **Peter Gloviczki**, M.D., was elected 2012-2013 president of the Society for Vascular Surgery. Gloviczki is the Joe M. and Ruth Roberts Professor of Surgery at the Mayo Clinic and chair of the Division of Vascular Surgery. He also served as director of the Gonda Vascular Center at Mayo Clinic.

The Minnesota Chapter of the American Academy of Pediatrics has added these three MMA members to its board: **Damon Dixon**, M.D., a University of

Minnesota pediatric cardiology fellow; **Angela Mattke**, M.D., Mayo Clinic; and **Stephen Sundberg**, M.D., Gillette Children’s Specialty Healthcare. In addition, MMA members **Robert Jacobson**, M.D., Mayo Clinic, will take over as president and **Sue Berry**, M.D., the University of Minnesota, will serve as president-elect.

MMA member **Ronald Petersen**, M.D. was among four physicians honored by the Alzheimer’s Association for extraordinary contributions to Alzheimer’s disease research at the Alzheimer’s Association International Conference in Vancouver, B.C., in mid-July.

MMA Provides RAC Recommendations to DHS

In late June, the MMA sent a list of recommendations to the Minnesota Department of Human Services for consideration as it works to implement a Recovery Audit Contractors (RAC) program for the state’s Medicaid program.

In September 2011, the Centers for Medicare and Medicaid Services issued a rule that requires each state to enter into contracts with one or more eligible Medicaid RACs in order to detect and correct improper overpayments and underpayments in the Medicaid program. Minne-

Seven Key Actions from AMA Annual Meeting

At the AMA Annual Meeting in Chicago in June, the MMA delegation, which included 10 delegates, two alternates and three staff members, helped create new AMA policy, inaugurate a new president and elect a president-elect.

Here are seven notable actions from the meeting:

ADOPTED An MMA-backed resolution calling for increased transparency in the marketing techniques used to recruit young physicians finishing residencies and fellowships. **Maya Babu**, M.D., MMA delegate, presented the resolution.

ADOPTED A 2010 MMA-backed resolution that made its way through the Council on Medical Education calling for the AMA to review the current secured testing methods for recertifying specialty physicians and replace them with measures that test the competency of physicians while taking into account the needs of adult learners. **John van Etta**, M.D., MMA delegate, acted as lead physician for this resolution.

RECOMMENDED FOR FURTHER STUDY An MMA-backed resolution asking the AMA to examine the current training environment and make it a high priority for residents to perform an adequate number of procedures to master the skills of their specialty. **Stephen Darrow**, M.D., MMA alternate delegate,

presented the resolution.

LITIGATION CENTER CASES Every year, the AMA’s Litigation Center presents the most important cases in which it has participated. This year, two Minnesota cases were presented to the assembly. Medical Staff President **Steve Meister**, M.D., presented the Avera-Marshall case and a representative of Mayo Clinic presented the Prometheus patent case. The MMA supported each case and worked with the Litigation Center in the development of amicus briefs.

AMA MINORITY AFFAIRS SECTION MMA member **Dionne Hart**, M.D., became the first Minority Affairs Section delegate seated in the House of Delegates. This was the first year the Minority Affairs Section had a representative in the house. Hart is chair of the MMA Minority and Cross-Cultural Affairs Committee.

RECERTIFIED MMA member **Eric Tangalos**, M.D., worked with the American Medical Directors Association to increase membership and have the section recertified for its seat in the House of Delegates.

RESIDENT/FELLOW SPEAKER OF THE HOUSE After serving one term as Speaker of the House for the Resident/Fellow section, **Stephen Darrow**, M.D., was unsuccessful in his bid for a second term.



Stephen Darrow, M.D.



Steve Meister, M.D.

If you are interested in being part of the 2013 AMA Annual Meeting, please contact Dave Renner at 612-362-1875.

For more information on the 2012 AMA Annual meeting, go to www.ama-assn.org/ama/pub/meeting/index.shtml.

sota has had an RAC program in place for Medicare claims since October 2008.

The MMA recommended that:

- The RACs hire a full-time medical director who has an M.D. or a D.O. degree. The MMA explained that physician medical directors are able to understand diverse medical diagnoses, treatments and claims that others on the RAC team may not be able to understand.
- RACs should have a three-year look-back period for claim reviews, which is consistent with the Medicare RAC program and has proven to be a sufficient length of time to detect improper payments.
- The number of medical record requests by RACs should be limited to no more than three medical records within a 45-day period per individual practitioner, and physicians should be granted a reasonable amount of time to comply with the requests. Medicare RACs allow 45 days.

In order to reduce improper coding and billing errors, physicians and others should be educated about the purpose of the RAC, audit policies and protocols including the process used to identify overpayments, how providers can avoid RAC audits, what a demand letter looks like and what a physician should do upon receipt of one, the appeals process and how the RAC will coordinate with other auditing entities.

Because RACs are paid a contingency fee for overpayments identified and recovered, the RAC should receive its compensation after all appeals have been fully exhausted or the time frame for filing an appeal has lapsed. This will reduce the need for the state's Medicaid program to identify and collect fees already paid to RACs for claims that were subsequently overturned on appeal. It will also reduce any incentive for RACs to identify claims that will likely be overturned on appeal.

The fees paid to Medicaid RACs for identifying underpayments should be set at a rate equal to those for detecting overpayments. This will ensure that RACs have incentive to identify them.

MMA IN ACTION

Happenings around the state



Eric Dick

Eric Dick, MMA manager of state legislative affairs, provided an overview of the 2012 legislative session and its impact on physicians at a meeting of the University of Minnesota's neurosurgery department in late June. In addition to answering questions related to physician workforce and scope-of-practice issues, Dick shared thoughts about what the 2013 legislative session might

include. **Katie Snow**, a project coordinator for the Twin Cities Medical Society, joined Dick at the meeting. She discussed the work of Honoring Choices Minnesota, a TCMS-led effort to highlight the importance of advance care planning.

In early June, **Karolyn Stirewalt**, J.D., MMA policy counsel, attended the HealthPartners Physician Wellbeing Symposium. Later in the month, she attended the American Society of Medical Association Counsel annual meeting in Chicago. And in mid-July, she represented the MMA at the Board of Medical Practice's board meeting.



Karolyn Stirewalt

The MMA and the Minnesota Academy of Family Physicians Foundation co-hosted a session on effectively working with medical interpreters in late May for the University of Minnesota Department of Physical Medicine and Rehabilitation Residency Program. **Brian Strub**, MMA manager of physician outreach, attended the session. Strub also represented the MMA in early June at the 2012 Minnesota Cancer Alliance Summit in Brooklyn Center and attended a June meeting of the University of Minnesota Medical School's student council to talk about the MMA's Medical Student Section and ways medical students can become involved in organized medicine.

In late June and early July, **Mandy Rubenstein**, MMA manager of physician outreach, represented the MMA at three University of Minnesota medical residency orientation sessions.



Mandy Rubenstein

Vaccinations

A Public Health Triumph and a Public Relations Tragedy

By Robert M. Jacobson, M.D., F.A.A.P.

■ Routine vaccination has been hailed as one of the top public health achievements of the last century. However, despite the reduced number of cases of and deaths from vaccine-preventable diseases such as pertussis and measles, outbreaks continue to occur as more parents fail to adequately vaccinate their children because of misinformation about immunizations. This article describes the challenges of making sure all children in the United States are fully immunized and what physicians need to know to effectively work with parents who may be hesitant to vaccinate their children.

In 1999, the Centers for Disease Control and Prevention (CDC) identified routine vaccination as one of the top 10 public health achievements of the century.¹ In their acknowledgment, CDC officials referred specifically to the impact of vaccines universally recommended for children.² In 1900, a year typical of the time before vaccination against smallpox became routine in the United States, more than 21,000 children contracted the disease and nearly 900 of them died from it. Since 1974, as a result of the routine use of the smallpox vaccine, that disease has been eradicated worldwide. In the 20th century, 21 more vaccines were developed or licensed, and 11 became universally recommended. Administration of these vaccines has led to dramatic reductions in the number of cases of as well as deaths from smallpox, polio, diphtheria, pertussis, measles, mumps and other preventable diseases (Tables 1 and 2).³

Safety Concerns

Vaccinations should be considered a public health triumph. However, successful suppression of disease has led to a tremendous amount of recklessness on the part of parents. Most in this country have never seen a case of smallpox, diphtheria, measles, mumps or rubella. Our current generation of parents does not know what physicians or nurses mean when they talk about *Haemophilus influenzae* type b. Even when outbreaks of vaccine-preventable diseases do occur, they fail to capture the public's attention for long. Thus people are more likely to read or hear about claims of vaccine-induced adverse events than reports about the diseases the vaccines prevent. As a result, some parents succumb to fear about vaccine-related adverse events and fail to have their children vaccinated on time or at all.

But what is the reality with regard to adverse events associated with vaccines? In the United States, we not only conduct prelicensure tests of vaccines (before a vaccine is licensed by the Food and Drug Administration [FDA]), but we also do postlicensure monitoring. Modern prelicensure studies of vaccines engage tens of thousands of research subjects, far more than the number in clinical trials of pharmaceuticals. For example, the prelicensure studies of the human papillomavirus vaccine involved more than 20,000 individuals. Postlicensure, we have two major systems for detecting vaccine-safety problems—the Vaccine Adverse Events Reporting System (VAERS) and the Vaccine Safety Datalink program.

If we look at VAERS data from the years 1991 to 2001, over which time 1.9 billion doses of vaccine were given in the United States, we get a sense of the infrequency of adverse events.⁴ During those 11 years, 129,000 reports were made to VAERS, which averages out to be 12,000 reports a year and 68 reports per million doses of vaccine given. Of those, 26% were for fever, 16% for injection site hypersensitivity and 11% for rash. These are transient local and systematic effects that we might anticipate from exposure to a foreign substance such as a vaccine. With modern manufacturing of vaccines, the severity of these effects has been dramatically reduced; nonetheless, they exist and are common.

As for serious adverse events, the rates are very low. Of the 68 reports per million doses given each year, only 14% are for serious adverse events.⁴ And of those, 2% involve life-threatening illness, 10% hospitalization, 1% the prolongation of hospitalization, 3% permanent disability and 2% death. In addition, the association between these events and vaccines is not causal. When the FDA and the Institute of Medicine

TABLE 1

Vaccine-Preventable **Disease** in the United States: Pre-Vaccine Era versus Post-Vaccine Era

VACCINE-PREVENTABLE DISEASE	PRE-VACCINE		VACCINE ERA	
	YEAR	CASES	YEAR	CASES
SMALLPOX	1921	102,791	2009	0
DIPHTHERIA	1921	206,000	2009	0
PERTUSSIS	1943	175,000	2009	16,858
TETANUS	1948	600	2009	18
POLIO	1952	29,000	2009	0
MEASLES	1962	503,000	2009	71
MUMPS	1964	212,000	2009	1,991
RUBELLA	1969	57,686	2009	3
CONGENITAL RUBELLA	1970	70	2009	2
HIB	1980	20,000	2009	38

Sources: Centers for Disease Control and Prevention. Impact of vaccines universally recommended for children--United States, 1990-1998, MMWR Morb Mortal Wkly Rep. 1999;48(12):243-8. Summary of Notifiable Diseases: United States, 2009. MMWR Morb Mortal Wkly Rep. 2011; 58(53):1-100. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/mm5853a1.htm. Accessed July 19, 2012.

(IOM) reviewed the 206 VAERS-reported deaths that occurred between 1990 and 1991,⁵ they found that only one of those deaths clearly resulted from vaccination. This was the case of a 28-year-old woman acquiring Guillain-Barre syndrome after tetanus vaccination. Approximately 350 million doses of vaccine were given during that period.

Despite the rarity of actual serious adverse events from vaccinations, claims about adverse events have generated media coverage and led to litigation. Litigation associated with the older, whole-cell pertussis vaccine, included in DTP vaccine, nearly shut down the U.S. vaccine industry. This older form of the vaccine, which is no longer used in this country, was well-known for its reactivity. In our experience at Mayo Clinic, 80% of infants receiving the older form suffered fever or irritability or both—effects that were transient but nonetheless real. Despite scientific evidence to the contrary, during the 1980s the U.S. public was inundated with claims that vaccines caused major neurologic disorders, permanent disability and even death. These claims were followed by lawsuits, the number of which peaked at 255 in 1986.

Over a 10-year period, most vaccine manufacturers abandoned production in the United States, and DTP prices rose dramatically from \$0.45 per dose to \$10.10 per dose. In response, Congress passed the National Childhood Vaccine Injury Act in 1986. This resulted in major changes in how the courts handled vaccine litigation. It also created the National Vaccine Injury Compensation Program, which helps pay for the care of those seriously injured from vaccines while removing the adjudication of claims of serious adverse events associated with vaccines from the civil courts and from trials by jury. Vaccine manufacturing has since resumed, resulting in increased production and innovation.

TABLE 2

Vaccine-Preventable **Deaths** in the United States: Pre-Vaccine Era versus Post-Vaccine Era

VACCINE-PREVENTABLE DISEASE	PRE-VACCINE		VACCINE ERA	
	YEAR	DEATHS	YEAR	DEATHS
SMALLPOX	1921	495	2007	0
DIPHTHERIA	1921	15,000	2007	0
PERTUSSIS	1943	9,269	2007	9
TETANUS	1948	120	2007	5
POLIO	1952	2,175	2007	0
MEASLES	1962	900	2007	0
MUMPS	1964	11	2007	0
RUBELLA	1969	29	2007	1
CONGENITAL RUBELLA	1970	700	2007	3
HIB	1980	495	2007	0

.....
Delivery Challenges

Although the threat of litigation has been successfully addressed by the National Childhood Vaccine Injury Act, physicians, nurse practitioners and public health officials still struggle to deliver vaccines to patients. One reason is the sheer number of immunizations that children should receive. Thirteen vaccines are routinely recommended for children. This translates to 24 injected doses and two to three oral doses of vaccine by 2 years of age. Each child should receive eight more vaccine doses for five more diseases by age 6 and 12 more influenza vaccine doses over the next 12 years; in addition, teens are supposed to receive three more vaccines, six doses in all.

This is not to imply that we have been falling behind in our efforts to keep children up to date with their immunizations. The vaccines are designed so that a number of them can be given at once. Combination vaccines reduce the number of injections needed at a single visit; in most cases, these are preferred over separate injections. In the last decade, our up-to-date immunization rate for children 19 to 35 months of age for more established vaccines has held steady at 70% to 80%. That rate often falls when we add new vaccines. Generally, though, it moves up into the 70% to 80% range after a few years (Figure). Of course, we want the up-to-date rate to approach 100%.

Much of the problem with achieving this in the past has been the affordability and availability of vaccine. To address this, in 1993 the federal government created the Vaccines for Children program, which today serves 45% of U.S. children. Before Vaccines for Children, private practitioners would routinely refer uninsured or underinsured children to public health clinics for their vaccinations. The discontinuity of care often resulted in undervaccinated children. The Vaccines for Children program offers providers in private practices free vaccine so they can vaccinate qualifying children.

Another major obstacle to getting our up-to-date rate to

100% has been confusion over which vaccines are recommended and when they should be given. Starting in the 1990s, the Advisory Committee on Immunization Practices (ACIP) began addressing the problem of conflicting recommendations. Now, ACIP childhood immunization recommendations represent not only those of the federal government but also those of the American Academy of Pediatrics and the American Academy of Family Physicians. These are updated at least annually. It should be emphasized that these are not requirements but recommendations; individual states determine school and day care immunization requirements.

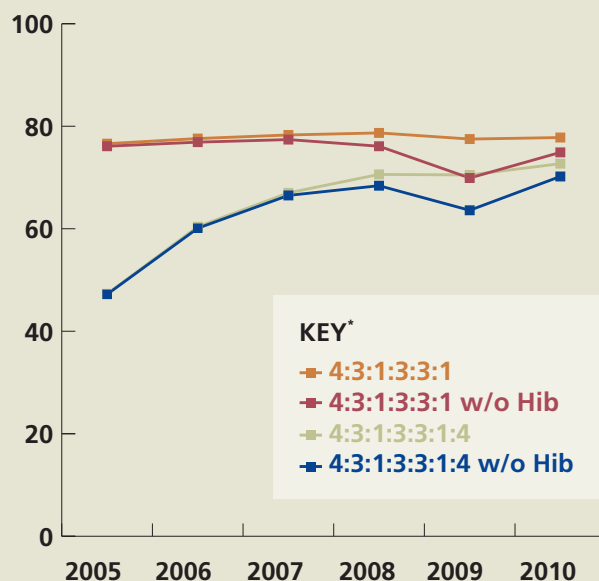
In addition to confusion about which vaccines are recommended, there also has been confusion about when vaccines should *not* be given. Many things that physicians and nurses once believed about vaccine contraindications are false. For example, it was widely believed that no one with an acute illness should receive a vaccine. In fact, a mild illness, with or without fever, is not a contraindication to vaccination. It was, and perhaps still is, believed that multiple vaccines might weaken the immune system. There is no evidence that supports this. Furthermore, despite the fact that more vaccines are given today than were 20 years ago, we actually are giving less antigen. The smallpox vaccine and the older form of DTP, which contained whole-cell pertussis, contained far more antigen (but still far less than if the patient developed the actual disease).

One way clinicians can try to keep children up to date is by using every clinic visit, rather than just well-child visits, to screen for and administer vaccinations that are due. Were we to rely on well-child visits alone, our current vaccination rates would drop dramatically. Systematic reviews of studies of vaccine delivery have identified a number of other strategies that have been shown to improve vaccination rates,⁶ including education and expanded access. Other interventions that work include reducing the out-of-pocket costs associated with vaccination, reminders/recalls, standing orders, and assessment and feedback of up-to-date rates for practices or individual practitioners. Day care, school and college requirements for vaccination, interventions in WIC settings and home visits also improve vaccination rates.

Vaccination registries also have helped clinicians with the delivery of vaccine.⁷ These computerized information systems are repositories of immunization records that permit clinicians and other vaccine providers to contribute and access information regarding a child's vaccine status. The Minnesota Immunization

FIGURE

Up-to-Date Vaccination Rates in U.S. Children 19 to 35 Months of Age



***EXPLANATION OF KEY**

4:3:1:3:3:1 refers to 4 doses DTP, 3 doses IPV, 1 dose MMR, 3 doses Hib, 3 doses HBV and 1 dose VZV

4:3:1:3:3:1 W/O HIB refers to 4 doses DTP, 3 doses IPV, 1 dose MMR, 3 doses Hib, and 1 dose VZV

4:3:1:3:3:1:4 refers to 4 doses DTP, 3 doses IPV, 1 dose MMR, 3 doses Hib, 3 doses HBV, 1 dose VZV, and 4 doses PCV

4:3:1:3:3:1:4 W/O HIB refers to 4 doses DTP, 3 doses IPV, 1 dose MMR, 0 doses Hib, 3 doses HBV, 1 dose VZV, and 4 doses PCV

The rates without Hib are shown to illustrate the effect of the national shortage of Hib from 2007 to 2009.

Information Connection (MIIC) is a network of seven regional registries covering the state. The Southeast Minnesota Immunization Connection, for example, serves the 11 counties including Olmsted in southeastern Minnesota. At Mayo Clinic, clinicians and nurses can access MIIC information about vaccines.

Attitudes and Misconceptions

The major obstacles to timely and complete vaccination delivery are not logistical. From the days of Edward Jenner and the development of the smallpox vaccine, negative attitudes and fear have led people to delay getting vaccinated or outright refuse to do so. A gauge of the problem is the rate of parents claiming non-medical exemptions for their children from school and day care requirements. Schools and day cares require parents to make sure their children are up to date on their immunizations, and when notified most parents arrange for their children to obtain the necessary vaccines. However, states allow exemptions. All states

Child, Adolescent and Catch-up Vaccination Schedules

To access the 2012 schedules published by the Advisory Committee on Immunization Practices, go to www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html.

permit medical exemptions; but some allow other exemptions as well. In a 2012 CDC survey with 47 states reporting, 43 allowed religious exemptions and 16 philosophical exemptions.⁸ In 2009-2010, the CDC found exemption rates ranging from less than 1% (Mississippi) to as high as 6.2% (Washington) for kindergarten children.⁸ Nonmedical exemptions ranged from 0.2% (Rhode Island) to 5.8% (Washington).⁸ Data were not available for Minnesota, and previous surveys conducted by the CDC did not examine state exemption rates.

A recent survey conducted by researchers in Wisconsin sheds some light on the reasons why parents in that state claim non-medical exemptions.⁹ Wisconsin had a 0.6% rate of medical exemptions and a 3.1% rate of nonmedical exemptions.⁸ Of the 779 parents sampled who claimed exemption, only 236 responded (30.3%) and of those, 70 were excluded as their children were indeed up to date on vaccines. The 166 remaining claimed exemptions for the following reasons:

- Vaccine might cause harm (57%)
- It would be better to get the natural disease (38%)
- My child is not at risk for the disease (37%)
- Autism (31%)
- Thimerosal (30%)
- Vaccine might overload the immune system (29%)
- Disease(s) not dangerous (20%)
- Vaccine might not work (16%)
- Ethical or moral reason (13%)
- Fetal tissue (10%)
- To get my child enrolled in school without hassle or delay (10%)
- Contrary to religious beliefs (1%)
- Encouraged by school officials (<1%)

More concerning, however, are the results of a survey of 1,490 parents whose children were up to date with the required vaccines in Wisconsin.⁹ Although only 48.4% responded,

- 23.4% agreed with the statement “Children get more vaccinations than that are good for them,”
- 33.7% endorsed the statement “I am concerned that children’s immune systems could be weakened by too many immunizations” and
- 14.5% agreed that “It is better for a child to develop immunity by getting sick than to get a vaccine.”

Where are these beliefs coming from? Many of these concerns arise from parents’ natural tendency to weigh the perceived benefits (difficult to do with a vanishing prevalence of and few reports about vaccine-preventable diseases) and perceived risks (difficult to keep straight with the frequent and outrageous claims of harm caused by vaccines) combined with the tendency in our culture to distrust “big government,” “big industry” and “big medicine.” We do not like being told what to do.

At the root of many parents’ reluctance to get the MMR vaccine is the fear of autism. This fear grew out of fraudulent

claims made by Andrew Wakefield and others in their 1989 *Lancet* article that raised safety concerns associating autism with measles and measles-containing vaccines.¹⁰ Other antivaccinationists claim that vaccines, when given to the very young or in combination, overwhelm the immune system. They claim that vaccines are unnecessary and that vaccine-preventable diseases began to disappear before the vaccines were routinely used. In addition, they claim that vaccine-preventable diseases no longer pose a threat and for that reason vaccines are no longer necessary. They also claim vaccines are not effective.

Who are the antivaccinationists promoting these views? They are parents who are convinced their children have been harmed by vaccines, anti-medicine and anti-science coalitions, proponents of alternative medicine, religious groups and antigovernment groups. These groups often use names that suggest they are a source for balanced, if not official, information such as the National Vaccine Information Center. They attract those who are suspicious of modern medicine and the motives of public health officials. Because the antivaccinationists are vocal and because the Internet provides an affordable and convenient venue through which they can broadcast their messages, they are hard to ignore. As a result of their claims, an increasing number of parents are delaying vaccinating their children.

In their survey of the Portland metropolitan area, Robison and colleagues found a high number of parents limiting the number of vaccinations in the first nine months of life to one to two per visit.¹¹ At best, this means more clinic visits and longer delays before the child achieves immunity. However, fewer than 5% of parents who chose to limit the number of vaccinations were keeping up with the alternative immunization schedules proposed by Robert Sears, M.D., or Stephanie Cave, M.D.

..... Making the C.A.S.E.

The number of parents claiming exemptions or using delayed-vaccination schedules is troubling. Such hesitancy can and has led to outbreaks of vaccine-preventable diseases such as pertussis and measles. From 1989 to 1991, our country experienced epidemic rates of measles with 55,000 cases reported, 11,000 hospitalizations and 120 deaths. In the last two years, Europe has experienced similar rates. In 2011, Minnesota saw a number of measles outbreaks and more reported cases than any other state that year.

So what are we to do? Alison Singer, Ph.D., president of the Autism Science Foundation, says that physicians need to do more than educate or inform parents. Instead, we need to share our recommendations with the same conviction we have when recommending diagnostic investigations and treatment regimens. In addressing vaccine hesitancy, Singer advocates what she calls the C.A.S.E. method (see “Talking to Parents about Vaccinating their Child”). The C stands for corroboration. Physicians should corroborate or acknowledge parents’ concerns and find some point upon which they can agree, setting the tone for a respectful, successful conversation. The A stands for “about me.”

Talking to Parents about Vaccinating their Child

Alison Singer, Ph.D., president of the Autism Science Foundation, recommends using the C.A.S.E. (Corroborate, About me, Science, Explain) method when talking with parents about their concerns about vaccines. A conversation might go something like this:

First corroborate a parent's concerns: "There's certainly been a lot on TV and the Internet about vaccines and autism, so I can understand why you have questions."

Describe how you have studied the issue: "I always want to make sure I'm up to date on the latest information so that I can do what's best for my patients, so I've researched this thoroughly."

Bring science into the conversation: "The evidence does not support that the measles vaccine, the MMR or any vaccine causes autism. Dozens of studies have been done. None show a link. The Centers for Disease Control and Prevention, the American Academy of Pediatrics, the Institute of Medicine and others have all reviewed the data. All reached this same conclusion. Vaccines do not cause autism."

Explain why the child needs vaccines: "Vaccines are critical to preventing death, disease and disability. They prevent diseases that cause real harm. Choosing not to vaccinate does not protect your child against autism, but does leave her at risk for disease. Your child needs these vaccines."

Move from corroboration to describing what you have done to become knowledgeable and expert in vaccination. The S stands for science. Only then briefly relate the science. Finally, the E stands for explain. Explain that your advice is based on the science, making clear that this is indeed what is advised.

During a June 2012 workshop conducted by the Minnesota Chapter of the American Academy of Pediatrics, physicians and nurse-practitioners practiced using the C.A.S.E. method. They came to recognize the importance of the words and tone that they used, the ways they can connect with parents and the role they have in advising parents. They also discovered that this method is feasible in the office setting and provides structure and guidance that allows them to make their points without losing patience or focus. Most important, the method resonated with their idea of how they want to work to build and sustain relationships with parents and patients.

Conclusion

Routine vaccination does represent a public health triumph. Many vaccine-preventable diseases occur at rates that are less than 1% of the rate during the pre-vaccine era. Morbidity and mortality rates for many diseases have fallen dramatically as a result. But the number of vaccines that need to be given in a

timely manner to each year's new birth cohort is daunting. Combine this with complacency that develops in parents as a result of vaccination programs' success in making diseases disappear, and it is clear that we have a major public relations problem related to vaccines. Because the failure to vaccinate results in injury and death, it might be better considered a public relations tragedy. The hesitancy that parents feel about vaccinating their child—a hesitancy that appears to be growing—makes keeping children up to date on their immunizations even more of a challenge. But we have systems in place to protect the integrity of our vaccine programs and to address issues of affordability and availability. It is clear that physicians must rise to the challenge posed by vaccine hesitancy and eschew our tendency to focus on information transfer and technical requirements and instead embrace our role as clinicians and present parents with clear messages about the importance vaccinating their children. **MM**

Robert M. Jacobson is a consulting staff physician at Mayo Clinic and president of the Minnesota Chapter of the American Academy of Pediatrics.

Disclosure: Robert M. Jacobson has served in the last three years as a principal investigator for two multi-center vaccine studies funded by Pfizer as well as one funded by Novartis, all conducted at Mayo Clinic. He currently serves as a member of a safety review committee for one vaccine study as well as a member of a data and safety monitoring board for two other vaccine studies, all funded by Merck.

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Tick-Borne Diseases in Minnesota

An Update

By David F. Neitzel, M.S., and Melissa M. Kemperman, M.P.H.

■ Tick-borne diseases endemic to Minnesota include Lyme disease, babesiosis, anaplasmosis/ehrlichiosis, Powassan virus illness and Rocky Mountain spotted fever. Physicians need to be aware of these diseases and be vigilant about testing for them when patients present with acute febrile illness or rash within one month of potential tick exposure. In addition, they need to educate patients about these diseases and encourage prevention measures, especially use of tick repellents. This article reviews the epidemiology of these illnesses in Minnesota and the current recommendations for diagnosis and treatment.

Although Minnesota residents have long been aware of Lyme disease, physicians and other health care providers must continue to be vigilant about diagnosing and treating it, and educating patients about how to avoid it. Although Lyme disease remains the most commonly reported tick-borne disease in Minnesota and the United States, providers also need to be aware of—and teach their patients about—other tick-borne diseases that are now found in the state: babesiosis, anaplasmosis/ehrlichiosis, Powassan virus diseases and Rocky Mountain spotted fever. This article describes the clinical presentations, recommended laboratory assays, and treatment guidelines for Lyme and other tick-borne diseases (Table).

Epidemiology of Tick-Borne Diseases in Minnesota

Lyme disease (*Borrelia burgdorferi*), babesiosis (*Babesia spp.*), human anaplasmosis (*Anaplasma phagocytophilum*), one form of human ehrlichiosis (*Ehrlichia muris*-like agent) and Powassan virus illness are considered endemic to Minnesota and Wisconsin, where they are associated with bites from the blacklegged tick or deer tick (*Ixodes scapularis*). Rocky Mountain spotted fever (*Rickettsia rickettsii*), while most common in the South, also can occur in the Upper Midwest, where its primary tick vector is Minnesota's ubiquitous American dog tick or wood tick (*Dermacentor variabilis*). These and other tick-borne diseases also can be acquired when travelling to other states or countries where they are endemic.

Lyme disease and human anaplasmosis are among the most common infectious diseases reported to the Minnesota Department of Health, and the number of cases has increased markedly since the 1990s. In 2011, nearly 1,200 confirmed

Lyme disease cases and nearly 800 human anaplasmosis cases were reported in Minnesota, a large increase from the approximately 300 and 25 cases, respectively, reported annually in the late 1990s. Most Minnesota patients were exposed to ticks in the eastern and northern parts of the state or in wooded areas in western Wisconsin. Increasing numbers of cases of babesiosis, human ehrlichiosis and Powassan virus infection have also been reported in recent years (72, 13 and 11 cases, respectively, in 2011). Seventeen cases of Rocky Mountain spotted fever, including one fatality, were identified in Minnesota between 2008 and 2011.

Ixodes scapularis ticks, which carry most of Minnesota's tick-borne diseases, are most abundant in hardwood, mixed hardwood or brushy areas and are active during most of the warm months of the year. Disease risk from *I. scapularis* is highest from mid-May through mid-July, coinciding with the primary feeding period of the tick in its nymph stage, when it is so small that bites usually go unnoticed. Spring and fall months also incur disease risk from adult *I. scapularis*. The ticks that transmit Rocky Mountain spotted fever, *D. variabilis*, inhabit wooded and grassy habitats and are active in spring and early summer.

Physicians and the public should be aware of the expanding geography of tick-borne disease risk in Minnesota. In recent years, *I. scapularis* and the diseases associated with it have emerged north and west of historically endemic areas of the state. The Minnesota Department of Health has recently confirmed *I. scapularis* as far north as the Canadian border and in many western Minnesota counties. If habitat and climate conditions are suitable, introduction of *I. scapularis* into new areas can result in tick establishment and local disease trans-

mission; therefore, it is appropriate to consider any hardwood or mixed-hardwood forests in Minnesota as a potential source of tick-borne disease acquisition.

Lyme disease and Rocky Mountain spotted fever occur in all age groups. However, children may be at greater risk because they may spend more time outdoors, be more likely to play in the woods and brush away from trails, or be less likely to check for ticks. In contrast, clinically apparent anaplasmosis/ehrlichiosis and babesiosis are most common in aging adults or people who are immunocompromised. Children and those with well-functioning immune systems are more likely to have mild or asymptomatic infections.

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Diagnosis and Management

All Minnesota medical providers should include tick-borne diseases in the differential diagnosis for patients with onset of febrile illnesses, expanding rashes or other indications of tick-borne disease within one month of spending time in wooded or brushy habitat. Many Minnesota residents, including those in nonendemic areas, are exposed to ticks when they are away from home, so health care providers should ask about possible tick exposure during travel. Because many tick bites go unnoticed, physicians should take into account the patient's exposure to tick habitats and the season of the year.

■ **Lyme Disease**

Lyme disease is caused by the spirochete *B. burgdorferi*. The incubation period for early Lyme disease is three to 30 days. The pathognomic erythema migrans rash is present in most but not all early cases. It is not always “bull's-eye” in appearance but does expand in size over time to 5 cm or more in diameter. If a patient has a single erythema migrans rash highly suggestive of Lyme and recent symptom onset (more than two to four weeks), *B. burgdorferi* antibody tests are not recommended because sensitivity is low at this stage of infection; such patients should be treated empirically. Disseminated Lyme disease may not be recognized or diagnosed for weeks or months.

Disseminated *B. burgdorferi* infections can involve dermatologic (multiple erythema migrans lesions), rheumatologic (arthritis with intermittent objective joint swelling), cardiac (second- or third-degree atrioventricular block), peripheral nervous system (cranial neuritis, radiculoneuropathy) and central nervous system (lymphocytic meningitis encephalomyelitis) manifestations.

Two-tiered serology of enzyme-linked immunosorbent assay (ELISA) or immunofluorescent assay (IFA) followed by a Western blot test (if ELISA or IFA is positive or equivocal) is recommended for diagnosing Lyme disease. Seroconversion to IgG antibodies on Western blot is expected for patients with symptoms lasting more than one month. For patients who have had signs and symptoms for more than a month or who do not have an erythema migrans rash, diagnosis should be based on evidence of IgG antibody on Western blot in addition to a clinically

compatible illness and not solely based on the presence of an IgM antibody.

Some members of the public and a small number of medical providers promote the existence of “chronic” Lyme disease as an active, post-treatment infection requiring antibiotics long-term. This premise is not supported by the medical literature. Persistent symptoms following proper treatment may be the result of lingering inflammatory processes, co-infection with another tick-borne disease or an unrelated process. Long-term or repeated treatment with antibiotics for “chronic” Lyme disease is not recommended, as evidence does not demonstrate the presence of viable *B. burgdorferi* after treatment with the correct antibiotic for the appropriate duration (two to four weeks).

In-depth diagnosis and treatment recommendations for Lyme disease are available through the Centers for Disease Control and Prevention (CDC) (www.cdc.gov/lyme/healthcare/clinicians.html) and the Infectious Diseases Society of America (IDSA) (www.idsociety.org/Lyme/). The American Lyme Disease Foundation (ALDF) also provides information, including images of erythema migrans lesions (www.aldf.com/lyme.shtml).

■ **Babesiosis**

Babesiosis is a potentially fatal malaria-like disease caused by intraerythrocytic parasites of the genus *Babesia* (*B. microti* in Minnesota). After an incubation period of up to eight weeks, clinical presentation can include but is not limited to fever, chills, sweating, myalgias, arthralgias, anemia and thrombocytopenia. Severe complications such as organ failure can occur.

The Minnesota Department of Health recommends polymerase chain reaction (PCR) testing for diagnosis of babesiosis or a combination of peripheral blood smears and serology. Blood smears do not identify all cases, especially if parasitemia is low. Similarly, serologic testing can be negative early in the course of infection. For patients in highly endemic areas, it can be difficult to determine whether positive serologic results indicate past exposure or current infection, although a four-fold change in titer between acute and convalescent specimens can suggest current infection. Because of these concerns, PCR is recommended over smears; but PCR sensitivity is not 100% either. Therefore, highly suspect cases should be treated and monitored with repeat testing.

Babesia parasites can be transmitted to patients through a blood transfusion. Currently, testing for *Babesia* is not a part of routine blood product testing and, therefore, transfusion-associated babesiosis should be considered in patients who develop fever and anemia after receiving cellular blood products. Suspect cases of transfusion-associated babesiosis should be reported promptly to the hospital blood bank, the associated blood donation agency and the Department of Health so that others who received the infected blood can be notified.

Severe babesiosis is treated with quinine plus clindamycin and may require red blood cell exchange. Continued monitoring for persistence of *Babesia* parasites with PCR or peripheral blood

TABLE

Tests and Treatments for Tick-Borne Diseases

TICK-BORNE DISEASE	TESTING	TREATMENT
LYME DISEASE	Serology not necessary for patients with a single erythema migrans lesion because antibodies might not be detectable for up to two to four weeks Serologic testing necessary for illness lasting more than one month; IgG antibody is expected	Complete treatment guidelines available from IDSA. Long-term or repeated treatment not appropriate
BABESIOSIS	PCR plus either serology or smear	Severe illness: quinine plus clindamycin; may also require red blood cell exchange and repeat monitoring for <i>Babesia</i> parasites Less severe illness: atovaquone plus azithromycin
ANAPLASMOSIS/EHRlichiosis	PCR plus either serology or smear	Empiric treatment with doxycycline
POWASSAN VIRUS ILLNESS	Serum and CSF from acutely ill patients can be submitted to the Minnesota Department of Health for serologic testing.	Supportive care and rehabilitation for patients with neurologic involvement
ROCKY MOUNTAIN SPOTTED FEVER	PCR or immunohistochemistry on skin biopsies from rashes. Antibodies usually not detectable until 1 week after onset, so serologic testing should consist of paired acute and convalescent sera.	Empiric treatment with doxycycline

smear may be necessary. Less severe cases are treated with atovaquone plus azithromycin.

Diagnosis and treatment recommendations are available from the CDC (www.cdc.gov/parasites/babesiosis/health_professionals/index.html) and IDSA (www.idsociety.org/Lyme/).

■ Human Anaplasmosis/Ehrlichiosis

Although human anaplasmosis (formerly called human granulocytic ehrlichiosis) and several forms of human ehrlichiosis are clinically similar and are treated with doxycycline, the frequent interchangeable use of their names is incorrect. Human anaplasmosis is endemic to Minnesota and is caused by *Anaplasma phagocytophilum*, which infects neutrophils and is transmitted by *I. scapularis*. In contrast, human ehrlichiosis is caused by various *Ehrlichia* species. *E. chaffeensis*, which is endemic to southern states, infects monocytes and is transmitted by the Lone Star tick (*Amblyomma americanum*). The newly identified *Ehrlichia muris*-like agent, which appears to be endemic to Minnesota and Wisconsin, is likely transmitted by *I. scapularis*.

Reporting Tick-Borne Diseases

All tick-borne diseases must be reported to the Minnesota Department of Health. Reports need to include demographic, clinical and laboratory information. To report cases, please contact the tick-borne disease epidemiology staff at 651-201-5414 or download case report forms at www.health.state.mn.us/divs/idepc/dtopics/reportable/forms/tickborneform.html. Providers are encouraged to contact the Minnesota Department of Health for assistance with diagnosing suspect cases of Powassan virus illness or Rocky Mountain spotted fever.

The incubation period for human anaplasmosis and ehrlichiosis is three to 21 days. Signs and symptoms can include acute onset of high fever, chills, headache, myalgias, leukopenia, thrombocytopenia and elevated aminotransaminases.

Polymerase chain reaction tests provide the best sensitivity and specificity and can speciate *Anaplasma* and *Ehrlichia*. A peripheral blood smear for *Anaplasma* can also be performed, but smear sensitivity is often low. Serologic tests should include both *Anaplasma* and *Ehrlichia* or be paired with a PCR test, as *Anaplasma* and *Ehrlichia* can be cross-reactive on serologic assays. Any patient with illness suspicious for human anaplasmosis or ehrlichiosis should be treated empirically while test results are pending; doxycycline is the treatment of choice.

Anaplasma also has been transmitted through blood transfusion in Minnesota and should be considered in patients who develop a fever and thrombocytopenia post-transfusion. Contact the hospital blood bank, associated blood donation agency and Department of Health immediately about any suspect transfusion-related cases.

Diagnosis and treatment recommendations for human anaplasmosis and human ehrlichiosis are available through the CDC (www.cdc.gov/anaplasmosis/, www.cdc.gov/ehrlichiosis/ and www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm) and the IDSA (www.idsociety.org/Lyme/).

■ Powassan Virus Illness

Powassan virus, a tick-borne flavivirus related to West Nile virus, can cause severe neuroinvasive disease and death. Two Powassan virus lineages have been identified in North America, including one transmitted by *I. scapularis*. The incubation period for the disease is up to one month. Most patients diagnosed with Powassan virus infection have had encephalitis or meningitis. Less se-

vere illness from Powassan virus infection such as an acute febrile illness without neurologic involvement or even asymptomatic infection can occur. Serum or cerebral spinal fluid specimens from patients with central nervous system disease can be submitted directly to the Department of Health for testing. At this time, no commercial laboratories offer serologic testing for Powassan virus. There is no antiviral known to be active against Powassan virus. Clinical management involves supportive care and rehabilitation for patients with neurologic involvement.

■ **Rocky Mountain Spotted Fever**

Rocky Mountain spotted fever infects endothelial cells. Although it is endemic to much of the southern United States, it occurs in Minnesota only rarely. The incubation period is typically two to 14 days. Signs of illness can include fever, headache, maculopapular or petechial rash, myalgias, nausea and vomiting, and thrombocytopenia. Although the classic triad of symptoms for Rocky Mountain spotted fever is rash, fever and thrombocytopenia, the rash usually does not appear until two to five days after the onset of fever and might not be apparent when the patient first seeks medical care. The rash also may be atypical or absent in some cases. Therefore, the combination of fever, thrombocytopenia and exposure to tick vectors should prompt consideration of Rocky Mountain spotted fever.

Diagnostic tests for Rocky Mountain spotted fever include PCR or immunohistochemistry on skin biopsies from rashes. PCR testing on whole blood is not a sensitive testing modality because *R. rickettsii* does not widely circulate in the blood until the most severe stage of infection. Serologic testing by IFA can also be used but may be negative within the first seven to 10 days after onset. In some cases, the Department of Health can work with providers to arrange for additional testing including culture, PCR or IHC.

Up to 20% of untreated Rocky Mountain spotted fever cases and 5% of treated cases have fatal outcomes. Delayed treatment can dramatically increase the likelihood of severe infection involving hospitalization and death. To prevent severe disease, doxycycline should be initiated for any suspect cases while test results are pending, even in children; the risk for severe outcomes from Rocky Mountain spotted fever outweighs risk for dental staining as a result of treatment in this age group.

Diagnosis and treatment recommendations for Rocky Mountain spotted fever are available through the CDC (www.cdc.gov/rmsf/index.html and www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm) and the IDSA (www.idsociety.org/Lyme/).

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Prevention

Although these tick-borne diseases may present in multiple ways, the steps to prevent them are straightforward. During preventive and other health care visits, physicians and other providers should discuss the risk for tick-borne diseases and prevention measures with patients who live, work or recreate in tick-endemic areas. Personal protection measures such as using tick

Additional Information on Tick-Borne Diseases

- Minnesota Department of Health: Tick-borne disease epidemiology. 651-201-5414 and www.health.state.mn.us/divs/idepc/dtopics/tickborne/index.html
- Centers for Disease Control and Prevention: tick-borne diseases page. www.cdc.gov/ticks/diseases/index.html
- Infectious Diseases Society of America. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the IDSA. www.idsociety.org/Lyme/
- American Lyme Disease Foundation. www.aldf.com/

repellents, checking for ticks and wearing long pants are recommended for anyone who spends time in tick habitats. Although tick checks are important, even the most careful searcher might miss small nymphal ticks. Furthermore, although transmission of *B. burgdorferi*, the Lyme disease agent, involves at least 24 hours of tick attachment, transmission time for other tick-borne disease agents can be much shorter (eg, 15 minutes or less for Powassan virus; 12 hours for *Anaplasma/Ehrlichia* and *Babesia*), and transmission may occur before the tick is discovered. Therefore, use of effective tick repellents is strongly encouraged. These include repellents containing DEET (up to 30%), which is sprayed on clothing or skin, or those containing permethrin, which is pre-applied to clothing and lasts through multiple wearings and washings (permethrin-permeated clothing also can be purchased).

Patients should be counseled that *I. scapularis* carries most of Minnesota’s tick-borne diseases and that these ticks are most abundant in wooded or brushy areas; in addition, even a slight risk for Rocky Mountain spotted fever warrants protection against bites from *D. variabilis* in grassy areas. Although preventive measures are important during warmer months of the year (March through November), they are most important between May and mid-July. Patients should also be made aware that tick-borne diseases besides Lyme disease can explain an acute febrile illness occurring within one month of exposure to tick habitat (with or without known tick bites).

Some aspects of tick-borne disease diagnosis and treatment such as postinfectious illness or persistence of antibodies can be confusing for patients. In addition, they may be concerned about “chronic” Lyme disease after hearing non-evidence-based information. When treating patients for a tick-borne disease, physicians should discuss the meaning of antibody tests, the certainty of the diagnosis and whether treatment is empiric or supported by laboratory evidence, and the need to balance the risks and benefits of antibiotic therapy. **MM**

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Streptococcus pneumoniae Serotypes

Nine-Year Experience at a Level-One Trauma Center

By Ramy H. Elshaboury, Pharm.D., Robert L. Bergsbaken, B.S., M.T., and John C. Rotschafer, Pharm.D., FCCP

■ *Streptococcus pneumoniae* isolates from adults hospitalized with invasive pneumococcal disease (IPD) were collected at Regions Hospital in St. Paul from 2002 through 2010. Of 200 sequential, nonduplicative isolates collected and serotyped, serotypes 3, 7F and 19A were found to be the most common. Since 2008, all IPD cases have been caused by non-PCV7 serotypes. This article describes the study and its findings. It also provides an overview of the three vaccines used to protect against IPD.

S*treptococcus pneumoniae* is a leading cause of bacterial pneumonia, meningitis, bacteremia and otitis media. According to the World Health Organization, it is responsible for up to 1 million childhood deaths annually, mostly in Africa and Asia. The Centers for Disease Control and Prevention (CDC) estimates the death rate from invasive pneumococcal disease (IPD), which is caused by *S. pneumoniae*, in hospitalized patients in the United States to be as high as 14%. Several factors contribute to mortality, including host, microorganism (pneumococcal serotype) and therapy.¹ Studies have established inverse relationships between the carriage prevalence of a serotype and invasiveness, and between disease severity and invasiveness.^{2,3}

There are more than 90 known pneumococcal serotypes based on antigenic differences in capsular polysaccharides.^{4,5} A recent meta-analysis concluded that among patients with bacteremic pneumonia, the risk of death varies by serotype.⁶ The serotypes most associated with an increased risk of death were 3, 6A, 6B, 9N, 19F, 19A and 23F.⁶ A similar correlation between serotype and risk of death for patients with meningitis was not apparent. Seven serotypes are included in the 7-valent pneumococcal conjugate vaccine (PCV7), which became available in 2000 for vaccination of children (Table 1). At the time of its development, these seven serotypes

accounted for 80% of IPD in children younger than 6 years of age in the United States.⁷

Before PCV7 became available, the incidence rate for IPD in the United States was 23.2 cases per 100,000 population and 59.7 cases per 100,000 population in people 65 years of age and older.⁸ By 2002, the overall rate of invasive disease dropped to 13 cases per 100,000.⁹ However, an increase in the prevalence of non-PCV7 serotypes in the past decade, especially serotype 19A, prompted the development of a newer vaccine with expanded coverage.^{10,11}

Subsequently, a vaccine that included an additional six serotypes was introduced in 2010. PCV13 was first indicated for children 6 weeks to 5 years of age; but since, it has been approved for use in adults 50 years of age and older. Finally, the 23-valent pneumococcal polysaccharide vaccine (PPV23) was first approved in 1983 for pneumococcal vaccination in adults and children 2 years of age and older.¹²

Hospitals are now required to collect and report their rate of pneumococcal vaccination for all patients age 65 years and older, regardless of admission diagnosis, as well as for those 5 to 64 years of age with a high-risk condition. These data will be available to the public starting in October 2013.¹³

In this article, we present our experience with *S. pneumoniae* serotypes sequentially isolated from sterile sites in adult patients at Regions Hospital, a

Level 1 trauma center in St. Paul, which had an average of more than 100,000 patient days per year between 2002 and 2010.

Methods

Sequential, nonduplicative *S. pneumoniae* isolates from sterile sites in adult patients hospitalized at Regions Hospital between 2002 and 2010 were

TABLE 1
Serotypes Included in
Pneumococcal Vaccines

SEROTYPE	7-VALENT	13-VALENT	23-VALENT
1		X	X
2			X
3		X	X
4	X	X	X
5		X	X
6A		X	
6B	X	X	X
7F		X	X
8			X
9N			X
9V	X	X	X
10A			X
11A			X
12F			X
14	X	X	X
15B			X
17F			X
18C	X	X	X
19A		X	X
19F	X	X	X
20			X
22F			X
23F	X	X	X
33F			X

sent to the Minnesota Department of Health for serotyping. Information about the culture source of each *S. pneumoniae* isolate was not made available to the investigators. Pneumococcal antisera was used for identifying and typing *S. pneumoniae* by means of the capsular reaction test (Quellung reaction).¹⁴ Institutional Review Board approval was not sought because the retrospective data collection was anonymous and did not affect patient care.

Results

Altogether, 200 isolates were collected and serotyped between 2002 and 2010. The number of isolates collected per year ranged from 14 to 29 (median = 22). Thirty-four distinct serotypes were identified (Table 2). Of the 200 isolates, 26 (13%) were serotypes that are included in the PCV7 vaccine, 113 (56.5%) were serotypes included in the PCV13 vaccine, and 152 (76%) were serotypes included in PPV23. It should be noted that all isolates collected since 2008 were non-PCV7 serotypes.

The most common serotypes were 3, 7F and 19A, accounting for 11%, 11.5% and 13%, respectively, of all 200 isolates. The incidence of IPD cases involving these serotypes has been increasing since 2005 and peaked in 2009, when they represented 67% of isolates. Serotypes 6A, 12F and 22F were the next most common. They accounted for 5.5%, 6% and 4.5%, respectively, of all 200 isolates.

The number of isolates with non-PCV13 serotypes ranged from five to 16 per year (median = 10). The incidence of IPD cases involving these serotypes peaked in 2004, when they represented 64% of isolates; but it has generally remained stable since 2002. The number of isolates with non-PPV23 serotypes ranged from one to nine per year (median = five). Non-PPV23 serotypes represented 45% of isolates in 2005.

The serotypes identified by Weinberger et al. as being associated with an increased risk of death in adult bacteremic patients with pneumonia included serotypes 3,

TABLE 2
Streptococcus pneumoniae Serotypes Isolated between 2002 and 2010

SEROTYPE	2002	2003	2004	2005	2006	2007	2008	2009	2010	TOTAL
1	-	-	-	-	1	1	3	-	-	5
3	2	5	1	3	2	2	-	5	2	22
4	1	2	1	-	1	-	-	-	-	5
6A	3	-	-	2	1	1	2	1	1	11
6B	-	2	1	-	1	-	-	-	-	4
7C	-	-	-	1	-	-	-	-	1	2
7F	2	-	1	2	2	2	3	4	7	23
8	-	3	2	1	-	-	1	-	-	7
9A	2	-	-	1	-	-	-	-	-	3
9N	-	-	-	-	1	1	-	1	1	4
9V	-	4	-	1	1	-	-	-	-	6
10A	-	-	1	-	-	-	-	2	-	3
11A	1	-	-	-	-	-	-	-	-	1
12F	1	3	4	-	-	-	1	1	2	12
13	-	-	1	-	-	-	2	-	-	3
15A	-	-	-	3	-	1	-	-	-	4
15B	-	2	-	-	-	-	-	-	-	2
15C	-	1	-	-	-	-	1	1	2	5
16F	-	1	-	-	-	-	-	-	1	2
17F	-	-	-	-	2	-	-	-	-	2
18C	2	-	-	-	-	-	-	-	-	2
19A	2	-	2	1	2	2	5	5	7	26
19F	1	2	2	-	-	-	-	-	-	5
20	1	-	1	-	1	-	2	-	-	5
22F	-	-	1	3	4	1	-	-	-	9
23A	-	-	1	-	-	1	-	-	-	2
23B	-	-	-	-	-	-	-	1	-	1
23F	1	1	1	-	-	1	-	-	-	4
31	-	-	-	-	-	1	-	-	-	1
33F	1	1	2	-	-	-	-	-	1	5
34	-	-	-	1	-	-	-	-	-	1
35B	1	1	2	-	-	-	-	-	-	4
35F	-	-	1	-	-	-	1	-	2	4
38	1	1	-	1	-	-	2	-	-	5
TOTAL	22	29	25	20	19	14	23	21	27	200

6A, 6B, 9N, 19A, 19F and 23F.⁶ These serotypes accounted for 76 of all 200 isolates (38%). The incidence of IPD cases involving these serotypes increased after 2005, peaking in 2009, when they represented 57% of isolates. Finally, the serotypes most frequently associated with drug-resistant pneumococcal infections, 6A, 6B, 9V, 14, 19A, 19F and 23F,^{4,5} were found in 56 isolates, representing 28% of

all 200 isolates. These serotypes have represented 20% to 32% of isolates each year over the past nine years.

Discussion

Based on our nine-year review of *S. pneumoniae* serotype distribution, serotypes 3, 7F and 19A were most common year after year. Results showed an increase in the incidence of cases of IPD involving

the three serotypes since 2004. No PCV7 serotypes have been isolated since 2008. However, an increase in the incidence of cases involving serotypes associated with an increased risk of death in adult bacteremic patients with pneumonia, as identified by Weinberger et al. was observed.

Recent data from the U.S. National Immunization Survey and the Minnesota Department of Health showed the statewide vaccination rate among children 19 to 35 months of age was 95.3% \pm 2.8 between 2009 and 2010 (children receiving at least three doses of the PCV series). This was an increase from a rate of 77.3% \pm 6.5 in 2004. In 2006, the Minnesota Behavioral Risk Factor Surveillance System, which conducts an annual telephone survey of state residents about health-related behaviors, estimated the vaccination rate in adults 65 years of age and older to be 71.1%, compared with 51.9% in 1999. Despite the increasing immunization rates, data showed the overall number of isolates collected per year in this institution has remained fairly stable. They also showed only 13% of serotypes identified are included in PCV7 compared with 56.5% in PCV13 and 76% in PPV23. Furthermore, four of the six most common serotypes identified (3, 6A, 7F and 19A) are not included in PCV7 but were added to the newly formulated PCV13.

A recent analysis by the CDC's Active Bacterial Core Surveillance Program, which monitors the incidence and epidemiologic characteristics of certain infectious diseases, showed a 45% relative reduction in IPD incidence since the introduction of the PCV7 vaccine in 2000. Although a reduction in PCV7-type IPD incidence was noted between 2002 and 2007, an increase in the number of non-PCV7 serotypes was also noted during that period.¹¹ Our results were in agreement with these findings. Our study showed a stable number of IPD cases per year at our institution, and since 2008, all were caused by non-PCV7 serotypes. This serotype replacement phenomenon has been noted since the introduction of PCV7.^{10,15}

Our study and others validate the current CDC recommendations for the administration of a supplemental dose of PCV13 for children who have received an appropriate series of PCV7 vaccines as indicated. The Food and Drug Administration's recent approval of PCV13 for adults 50 years of age and older presents a new challenge and opportunity for clinicians. Because of differences in coverage and immune response between the PPV23 and PCV13 formulations, clinicians should be aware of local serotype distribution to determine which product to use in adult patients. Clinicians should bear in mind, however, that the CDC Advisory Committee on Immunization Practices (ACIP) recently voted to recommend the PCV13 vaccine for adults 19 years of age and older with immunocompromising conditions. Final ACIP recommendations regarding the routine use of PCV13 in adults are forthcoming.¹⁶

Our study had strengths and limitations. The fact that it was a retrospective observational single-center study limits our ability to generalize the findings. Also, information about the site of infection, clinical diagnoses and patient demographics were lacking because of the anonymous and retrospective nature of the data collection. It is unlikely that these limitations affected the results, although information about site of infection and age could have improved the comparison with available national data. A major strength of the study is that the data represent nine consecutive years of experience in this institution. To our knowledge, this is the first local report on *S. pneumoniae* serotype distribution in this community. Continued surveillance is needed to further monitor the distribution of *S. pneumoniae* serotypes and the burden of IPD in the community following the introduction of the new PCV13 vaccine. **MM**

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Antiretroviral Medications as Prevention

Will the New Paradigm Reverse the HIV Epidemic?

By Keith Henry, M.D.

■ Fifteen years after recognition of the AIDS epidemic, the development of potent antiretroviral therapy (ART) resulted in a significant reduction in HIV-related morbidity and mortality for persons in resource-rich regions of the world. Now 30 years after the HIV/AIDS epidemic began, we have learned that potent ART also decreases transmission of HIV and that judicious use of antiretroviral medications in people who do not have the virus but are at high risk for contracting it (Pre-Exposure Prophylaxis or PREP) can protect against HIV infection. We now have the necessary tools to significantly decrease the scope of the epidemic in the decades ahead. Whether we use them—that is, provide antiretrovirals prophylactically or conduct widespread testing for HIV and treat all people who are found to have the virus—will depend on the concerted actions of societies, governments, public health authorities, clinicians and individuals.

When the AIDS epidemic was first recognized in 1981, few people would have predicted that 30 years later an estimated 30 million people would have died from the disease and that 34 million would be living with the virus. The seemingly endless series of bad reports about climbing death rates, severe suffering, and many failed treatment efforts during the first 15 years of the epidemic obscured a large scientific effort to identify the cause (the human immunodeficiency virus or HIV) and subsequently dissect the lifecycle of HIV. The initial pay-off materialized in 1995-96 with three key breakthroughs: 1) development of a clinically available test to measure HIV levels in the blood (HIV plasma levels or viral load), 2) discovery of new drugs targeting different aspects of the HIV lifecycle (reverse transcription and protease activity), and 3) recognition that the use of three drugs at the same time can essentially shut down HIV replication and lead to major clinical benefit. Use of three active antiretroviral drugs at once was termed highly active antiretroviral therapy (HAART or potent ART).

In the United States and other western countries, use of potent ART led to dramatic declines in AIDS-related morbidity and mortality, confirming the clinical benefit observed in pioneering clinical trials. This development led to *Science* maga-

zine recognizing potent ART as the scientific breakthrough of the year for 1996.¹ But potent ART regimens are expensive. In the United States, a typical regimen costs more than \$18,000 a year. However, the availability of generic forms of the medicine (which can cost less than \$1 per day) as well as funding for use of those generics through the President's Emergency Plan for AIDS Relief have resulted in access to treatment for millions of individuals in Africa and other parts of the world.² These dramatic advances in treatment of HIV were not accompanied by similarly dramatic advances in HIV prevention (efforts to develop a vaccine, for example, have been disappointing). Recent events have changed the situation so that we now consider ART itself as the key factor for HIV prevention. This article highlights the evolution of AIDS/HIV prevention and the progression of ART from a purely clinical intervention to the centerpiece for present and future prevention efforts.

Floundering Prevention Efforts

HIV prevention traditionally focused on educating persons at high risk as well as the general population about the virus and how it is transmitted, encouraging condom use (which was not widely accepted and involved a modest cost), providing needle exchange programs (which were neither broadly ac-

cepted nor utilized), and testing high-risk persons—as knowing one’s HIV status increases safe behavior (an estimated 22% of HIV-infected persons in the United States are currently unaware of their status). The steady rate of new HIV infection in this country (estimated to be 40,000 to 50,000 cases per year over the last decade) or in the world (down slightly but still estimated to be 2.6 million cases in 2009) underscores the failure of standard HIV prevention efforts.

..... The Potential of Potent ART

One area where prevention efforts have been immensely successful is in reducing mother-to-child transmission (vertical transmission) of HIV. In the United States, broad adoption of HIV testing for pregnant women and use of potent ART to prevent vertical transmission has resulted in a reduction in the transmission rate from approximately 30% to less than 2%. The first report of this model of testing for HIV and using ART, published in 1994,³ was an early indicator that ART might be the key to more effective HIV prevention. But it would take almost two decades to confirm that finding in the broader population.

In 2000, researchers working in Uganda published a sentinel paper clearly linking the risk of heterosexual transmission in discordant couples (one HIV-positive and one HIV-negative) to the plasma HIV level.⁴ Since potent ART regimens generally result in plasma levels below the detection limit (in recent studies 75% to 80% of patients started on potent ART typically have HIV levels less than 50 copies/mL after a year of therapy), it was expected and later observed in natural history studies that potent ART significantly reduced sexual transmission of HIV (92% reduction in one meta-analysis⁵).

..... Preventing Sexual Transmission of HIV

Considerable circumstantial evidence suggested that potent ART could effectively prevent HIV transmission; but conclusive evidence from a randomized clinical trial was lacking until 2011, when the results of the HTPN 052 study were presented.⁶ In that study, 1,763 discordant couples (one member had HIV with CD4 counts between 350 and 550 cells/mm³, which is above the WHO threshold for starting ART) from nine countries were randomized 1:1 to immediately receive ART (early group) or start ART after the CD4 count of the member with HIV declined or they developed HIV-related symptoms (late group). The primary endpoint was prevention of HIV transmission to the uninfected partner. Of the 28 linked transmissions, only one occurred in the early therapy group, yielding a 96% decrease in transmission compared with the late group (all participants received regular safe-sex counseling, condoms, and regular screening for and treatment of other sexually transmitted diseases). The importance of this study was underscored when *Science* magazine awarded ART for prevention as the most important scientific breakthrough for 2011.⁷

Because of the increasing potency and safety of new antiretroviral medications, there has been interest in evaluating the effec-

tiveness of ART for prevention of HIV infection in people who are at high risk for acquiring it (men who have sex with men and people who engage in high-risk behaviors with people who are HIV-positive or who do not know their HIV status). After initial animal studies hinted that pre-exposure prophylaxis (PREP) might be effective if administered at least one day prior to viral exposure, human studies began. The IPrEx Study, published in late 2010, was the sentinel PREP study.⁸ In the study, 2,499 HIV-seronegative men or transgender women who have sex with men were randomized to receive emtricitabine/tenofovir (FTC/TDF), a combination of two antiretroviral drugs, as a single pill or a matching placebo. After a median of 1.2 years, the FTC/TDF arm saw a 44% reduction in the rate of HIV infection compared with the placebo arm. In a subsequent analysis based on measurement of drug levels,⁹ taking the daily tablet four or seven times a week resulted in estimated HIV protection rates of 96% and 99%, respectively.

Results from this and other studies highlight how critical good adherence is to the efficacy of PREP. Given the available data

Milestones on the Pathway to ART as Prevention

- 1981** First AIDS cases described
- 1983/84** Discovery of HIV as the cause of AIDS
- 1994** Administering Zidovudine during pregnancy reported to decrease risk of vertical transmission
- 1995** Increased use of plasma HIV RNA monitoring for ART effectiveness
- 1996** Development of highly active antiretroviral therapy (HAART)
- 2000** Study in Uganda finds risk for heterosexual transmission of HIV correlates with plasma HIV levels
- 2010** iPrEx Study reports PREP decreased risk for HIV infection for high-risk men who have sex with men
- 2011** HTPN 052 study reports use of potent ART decreased risk for transmission of HIV by 96%
- 2012** U.S. panel recommends all HIV-positive persons be treated for both clinical and public health benefits

and the urgent need to decrease the HIV infection rate among men who have sex with men, the CDC issued interim guidelines for the use of PREP for people in that risk group.¹⁰ The Food and Drug Administration has now approved FTC/TDF for use as PREP. Outside of the research setting, a number of questions remain about the optimal use of PREP: Who should pay for it? How should we monitor adherence? How should we promote safe behavior? And who will provide the required supervision?

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Test and Treat

The concept that a lower HIV viral load decreases the risk of transmitting HIV has been adopted for use at the community level. Studies done in San Francisco and Vancouver have found a correlation between the calculated community viral load¹¹ and decreasing rates of new HIV infection despite greater survival among people who are HIV-positive (an increasing percentage are on ART and have low or undetectable viral loads). That success resulted in the San Francisco and New York City health departments recommending that all at-risk persons be tested for HIV and that all people who test positive be started on ART (for both clinical and public health benefits). This strategy for HIV control has been termed “test and treat” and is currently being evaluated in numerous settings throughout the United States. Recently, the Department of Health and Human Services Panel for ART in Adults recommended that all HIV-positive persons be treated for both clinical and public health benefits.¹²

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Obstacles to Success

Despite advances in our knowledge about how to decrease HIV infection, a number of obstacles stand in the way of reducing HIV transmission. There is legitimate concern that awareness of the effectiveness of ART will result in sexual disinhibition that could result in increased risk for HIV as well as other sexually transmitted diseases. In addition, only an estimated 28% of all HIV-positive persons in the United States are currently receiving treatment and have suppressed viral loads, highlighting major deficiencies in our health care system and in people’s awareness about HIV and the need to take responsibility for their health.¹³ The National AIDS Strategy¹⁴ includes plans to incorporate many of the advances in prevention outlined in this article; but federal funding is currently billions of dollars short of what is needed to do so.¹⁵ The severe recession has curtailed a wide range of U.S. and international health initiatives.¹⁶ At a time when added funds are needed for testing and treating HIV-infected persons, it may be difficult to find resources for expanding use of PREP (the cost of the FTC/TDF pill is \$500 to \$800/month). On a positive note, it is anticipated that in the next 12 to 18 months the Minnesota Department of Health will be able to provide data on the community viral load and the extent to which people are receiving treatment for HIV. This will allow resources to be targeted to where they can be most effective.

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Conclusion

After more than 30 years, we have acquired the knowledge and tools to curtail the HIV/AIDS epidemic, with judicious use of antiretroviral medications as the cornerstone of prevention strategies. Although future advances (ie, better generic drug options, microbicides and vaccines) will improve HIV-control efforts, the question that remains is one of resolve. Do we as a society have the will to do what it takes to broadly implement the strategies that are available in order to prevent countless future HIV infections (and save billions of dollars as a result)? Success will require the concerted actions of societies, governments, public health authorities, clinicians and patients. **MM**

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Eat Your Broccoli—or Else!

By John Egan, M.D.

Reflections on the Supreme Court's decision to uphold "ObamaCare."

On June 28, the Supreme Court announced its 5-4 decision in support of the Patient Protection and Affordable Care Act, a signature piece of legislation for the Obama administration. It came as a surprise to most that Chief Justice John Roberts, a George W. Bush appointee, sided with the liberal members of the Court and wrote the majority opinion upholding the law that has come to be known as "ObamaCare." In the weeks leading up to the decision, few if any of the prognosticators predicted that Roberts would be the swing vote to uphold the law.

Roberts wrote dozens of pages arguing with reasoned sophistication about one of the most interesting and divisive issues involved in the decision: the individual mandate. "The Federal Government does not have the power to order people to buy health insurance," he wrote in his opinion (available online at www.supremecourt.gov/opinions/11pdf/11-393c3a2.pdf). Yet in the end, he allowed the individual mandate to survive—in much the same way my mother convinced me to eat my vegetables as a child. Do it, or face the consequences.

The law states that all Americans "shall carry health insurance" by 2014 and individuals who can afford health insurance but choose not to purchase it will be assessed a "shared responsibility penalty." Both pundits and appeals courts have been (and continue to be) divided on whether this component of the law is constitutional.

In making its case, the federal government argued that the Commerce Clause grants Congress the authority for the mandate. In case you didn't pass the bar just for fun after medical school, the Commerce Clause is the part of the Constitution that grants Congress the power to make laws that affect interstate commerce. If not supported by the Commerce Clause, the government contended that the "penalty" was still permis-

sible as a tax on those who choose not to purchase insurance.

As many remember, Justice Scalia famously asked during oral arguments whether the Commerce Clause gave Congress the power to force people to buy broccoli. After all, broccoli could limit health problems and potentially help to bring down health care costs, he reasoned.

This broccoli argument has its roots in a Supreme Court decision from 1942. In that case, Congress attempted to prevent a farmer from growing more wheat than allowed by law to feed his livestock. By growing more wheat, he wouldn't have to buy wheat on the market, an action that contributed to reduced demand and thus lower prices for wheat. The Supreme Court supported the law because it regulated action—growing excess wheat—that affected interstate trade. The question is whether the Commerce Clause also applies to inaction that can affect the price of goods.

Justice Ruth Bader Ginsberg, a liberal member of the Court, argued that because all will need health insurance at some point, Congress had the right to mandate that all purchase it under the Commerce Clause. If the young and healthy did not buy health coverage, insurance would cost more for those who did purchase it. The cost of insurance would also increase when uninsured individuals found themselves unable to pay unexpected medical bills, as the cost of unpaid care would eventually fall to those who have insurance in the form of higher premiums to make up for the loss.

Roberts rejected Ginsberg's argument. He deemed that Congress did not have the power to make young and healthy Americans pay for insurance they did not want and might not need for years into the future. Roberts agreed with a more narrow interpretation of the Constitution that permits Congress to regulate existing commerce but not create new commerce, which it would then regulate. Roberts also said the individual

mandate may be “necessary” for the law to work but was not “proper”—leaving it up to the states to decide whether to force people to buy insurance (for example, “RomneyCare” in Massachusetts).

I tend to agree with Ginsberg more than Roberts with respect to health insurance being a unique commodity and subject to regulation via the Commerce Clause. Ginsberg argued that by not buying health insurance, individuals were essentially purchasing “self-insurance”—meaning they would pay for unexpected health care costs out of pocket before the government and insurers are called on to foot the bill. It follows that the uninsured have an effect on commerce just like the farmer did on the market for wheat in 1942. By not purchasing insurance, the uninsured cause a nominally decreased demand for health insurance, which raises prices. Yet, they still need a measurable amount of health care, and if they cannot pay for it, this too influences costs.

Ultimately, Roberts agreed with the conservative wing of the Court in rejecting the individual mandate as unsustainable under the Commerce Clause. “The Commerce Clause is not a general license to regulate an individual from cradle to grave, simply because he will predictably engage in particular transactions,” he wrote. The mandate was summarily dismissed because there is “temporal limitation in the Commerce Clause,” according to Roberts’ ruling. This decision sets significant precedent, limiting Congress’ powers profoundly in the future, and is a boon for conservatives in the long run.

Nevertheless, the real surprise came when Roberts agreed that the penalty for choosing not to buy health insurance effectively amounted to a federal tax. Congress’ authority to tax is broad, and it can tax practically anything it wants—as we know all too well. Even though Congress does not have the power to force individuals to purchase insurance, it can tax those who choose not to carry it. “The shared responsibility payment merely imposes a tax citizens may lawfully choose to pay in lieu of buying health insurance,” Roberts wrote. Those with sufficient income will now be subject to a 2015 penalty to the IRS, and will have to pay an addition percentage of their income if they fail to obtain health insurance by 2014.

A reading of the majority opinion should give us an appreciation for the intellect and judiciousness of the Court, expressed at a time when it has been viewed as divided by political ideologies. The decision is not likely to be a true game changer—Roberts remains a conservative justice with the track record to prove it. But this instance of diminished partisanship on the bench is a breath of fresh air.

Indeed, Roberts limited Congress’ power with respect to the Commerce Clause; but he also demonstrated his ability to overcome ideological leanings with the kind of balanced reasoning not expressed by the Supreme Court in recent memory. To begin the case, Roberts had to deftly fudge semantics to sidestep the Anti-Injunction Act, enabling the Court to hear the case in the first place. Then he prudently limited the Commerce Clause.

Finally, he had the court consider the penalty as a tax “only because we have a duty to construe a statute to save it, if fairly possible.” In doing so, he skillfully elevated his standing in the Court above colleagues on both sides and saved legislation that seeks to improve the nation’s health.

What have we learned from the Supreme Court’s momentous decision? Congress cannot make you buy broccoli. However, Congress can tax you if you don’t buy broccoli (if ever such law were passed). Thus, the Supreme Court’s decision on the individual mandate for health insurance might be summed up this way: “Americans, eat your broccoli—or else!” **MM**

John Egan is a third-year internal medicine resident at Abbott Northwestern Hospital in Minneapolis and serves on the Abbott Northwestern Ethics Committee and the MEDPAC Board of Directors. For the record, he doesn’t like cooked broccoli and does not have a law degree. He notes that sound reasoning is sometimes limited in both politics and in government.



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Dancing to Death

By Greg Poland, M.D.

Too small to see,
Too many to defeat.
We circle, probing one another.
You to invade and exploit,
Me to defend.
Who will win this dance of death?

You bring sickness, tears and death.
Invader, exploiter, hijacker of dreams.
Your single focus indifferent to me.
Selfish.

I sense you without knowing,
Until it's too late.
Mobilizing silent knights of defense.
We, a death dance,
Terminal, unforgiving, predetermined.
Who will win this ancient of wars?

Greg Poland is the Mary Lowell Leary Professor of Medicine at the Mayo Clinic. He describes himself as a physician-scientist, author, speaker, poet and provocateur.