**stat**: an abbreviation for the Latin *statim*, an adverb that signals a need—
for a surgical instrument, a medical supply or, as in this magazine, a short, compelling story—to be met without delay.

**FOCUS //**

**QUARANTINE** was one of many turn-of-the-century efforts to corral smallpox, as at this camp on St. John’s Island, off Singapore. The virus that once infected an estimated 50 million people a year with smallpox remains captive in two reserves, in Atlanta and central Russia. In May, World Health Organization delegates debated whether to set a deadline for destruction or to allow these caches of the virus to remain—but ultimately decided to postpone their decision for three years. Those in favor of destruction say that despite security at sites where the virus is kept, the world would be safer with the pathogen gone. Opponents argue that there may be hidden reserves that bioterrorists could exploit, and thus a small amount should be maintained to develop a more effective vaccine.

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A Healthy Investment
BY LINDA KESLAR

Of Medicare’s 43 million beneficiaries in 2006, the 10% who were the sickest and had the most complex health conditions accounted for 67% of annual Medicare spending. Over the past decade, the government has funded dozens of demonstration projects aiming to improve care and reduce the skyrocketing costs for such patients, yet there has been little evidence of improvement. One of the few exceptions is the Mass General Care Management Program, which began in 2006 and was funded by the Centers for Medicare & Medicaid Services. Eric Weil, a primary care physician and the medical director of the program, discusses how it became so successful that it’s being extended—and the major challenges to implementing it in other locations.

Q: Why does it cost so much to treat these patients?
A: Patients in the first three-year phase of the program were, on average, 76 years old, were being hospitalized more than three times a year and were taking more than a dozen medications. More than half had behavioral health problems, and the mortality rate was 16%. Quite simply, they are sick and getting sicker, so they’re likely to require a lot of care.

Q: Do they just need more care than typical 76-year-olds?
A: They need thoughtful attention to how their care is delivered. When I see one of these patients for the first time, I identify his or her key health issues and set up a care plan. I can prescribe all the right medications and make the necessary referrals, but it’s unclear after the patient has left my office that everything will go according to plan. That’s where the nurse care managers come in. I (and the other 200-plus participating physicians) work with them to coordinate patient care. I’m confident that when a patient leaves my office, there’s another person who knows the patient just as well as I do and that a potential gap in care is being addressed.

Q: The nurses make a lot of phone calls to be sure patients are taking their medications?
A: Yes, but they do much more. I depend on care managers to do whatever’s necessary to keep a patient out of the hospital. The care manager not only coordinates
a patient’s care with specialists but also works with a team that includes mental health professionals, pharmacists and social workers. For example, I have an elderly female patient who used to be admitted to the hospital every three to four months because of congestive heart failure. Now we have a nurse care manager calling her regularly and potentially even making home visits. She monitors a program we’ve put the patient on and works with a pharmacist to adjust her medications and make sure she’s taking them at the proper times. The patient hasn’t been back in the hospital for a year—amazing.

**Q:** With all that costly follow-up, resulting in improved patient outcomes, how did the program also achieve financial benefits?  
**A:** Better care results in less need for expensive hospital services. There was a 20% decline in hospital admissions and a 13% drop in emergency department admissions during the program’s first three years. CMS invested more than $8 million in the program; the savings from keeping patients out of the hospital have covered that amount and saved potentially an additional $7 million to $10 million. Essentially, for every dollar spent, the program saved at least $2.65.

**Q:** Were there disappointments?  
**A:** We were less successful in reducing the rate of readmissions. We make every effort to address gaps in care, improve quality and maximize coordination. But this is a very ill population of patients. Despite all of our good work, we can’t halt the progression of illness.

**Q:** Can this be a model for the entire country?  
**A:** The model is doable in most places; it would just need to be adjusted for every institution. However, if this program were in a remote location with small practices, which might require that nurse care managers work for (and drive to and from) several practices rather than be embedded in one, and with no electronic health record network, that would introduce a lot more challenges in coordinating care.

**Q:** How might such programs be funded eventually?  
**A:** The MGH demonstration project experimented with modifying the traditional fee-for-service model by adding a monthly management fee to support the additional care that we deliver to this population, paid by Medicare. Ideally, health reform will support the development of models to encourage care coordination.

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**By keeping patients out of the hospital, the program saved at least $2.65 for every dollar spent.**

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**BY THE NUMBERS // An Infernal Ringing**

12 Number, in millions, of Americans who in the 1990s were persistently plagued by tinnitus (from the Latin *tinnire*, “to ring”): a ringing in the ears or perception of sound where none is present.

16 Americans, in millions, for whom tinnitus is a chronic problem now; while there is no known cure, common treatments include hearing aids (which help cancel out the ringing by clarifying other sounds) and other devices that create ambient noise.

12 Common causes of tinnitus, some of which (hearing loss, consistent exposure to loud noise, and head or neck trauma) cause chronic tinnitus and others (certain medications, even wax buildup) just fleeting discomfort.

50 Americans, in millions, who are temporary or chronic sufferers.

260 Medications, most commonly aspirin and Alka-Seltzer, that include tinnitus as a potential side effect.

2 Main types of tinnitus: tonal (a continuous ringing) and pulsatile (a rhythmic pulsing, often in concert with one’s heartbeat).

744,000 American veterans in 2010 who received disability payments for tinnitus caused by head or neck trauma, or by such battlefield noises as grenades, helicopters and gunfire.

1.1 Number, in billions of dollars, paid to veterans for tinnitus disability in 2009.

10 Number, in millions of dollars, allocated to tinnitus research in 2009.
When almost 20,000 fake Viagra, Cialis and Levitra pills were seized from cargo at New York’s JFK Airport in February 2011, it was the latest high-profile incident of counterfeit drugs—medications bearing false information about what they contain or where they come from—infiltrating the United States. Though the problem is more acute in developing countries—bogus malaria and tuberculosis drugs alone may kill 700,000 per year—the United States is far from immune. Here are opportunities in the U.S. drug distribution system taken by scammers to slip in drugs with less-than-sterling pedigrees.

INFOGRAPHIC // Cheating the System
BY MEERA LEE SETHI // INFOGRAPHIC BY CARL DETORRES

It Fell Off a Truck
Stolen shipments can create a space for counterfeits to enter the supply chain. Genuine vials of Lemevir, a brand of insulin, were stolen shortly after leaving the manufacturer’s facility. The thieves compromised the drugs by failing to store and handle them properly; many patients reported adverse reactions.

Faking Ingredients
U.S. drug companies often outsource the manufacture of active and bulk ingredients. Doses of heparin, a blood thinner, were adulterated with a poison that mimics heparin’s reaction to lab tests. Eighty-one deaths were linked to the tainted drug, produced when a supplier of heparin bought the main ingredient from a Chinese company.

Diversion for Profit
Counterfeiters take advantage of discount programs to get hold of cheap drugs and resell them at much higher rates. One ring of criminals, for example, persuaded HIV/AIDS patients to fill cheap or free prescriptions for protease inhibitors; they also acquired drugs by posing as clinics and buying prescriptions at Medicaid prices.

A Shady Middleman
Counterfeiters sometimes pose as secondary wholesalers. In one instance, scammers diluted anemia drug Procrit with nonsterile tap water. Besides being too weak to work, the bacteria the drug contained was highly dangerous to the AIDS and cancer patients who took it. At least one patient’s medication was traced back to a secondary wholesaler.
ONLINE BUYER BEWARE
From holograms to RFID tags, authorities have made a number of attempts over the decades to thwart counterfeiters. To see a time line of their efforts, visit protomag.com/counterfeit.

REPACKAGING FAKES
Fake Lipitor, a cholesterol-lowering drug, was smuggled into the United States from Costa Rica and bought by a repackager. The fake pills contained at least some atorvastatin, the active ingredient in genuine Lipitor, but were not chemically identical. Patients complained they tasted strangely bitter.

“Full of vagueness, groping, hedging, and ‘shot-gun’ prescriptions” is how Richard Cabot, a physician at Massachusetts General Hospital, characterized many diagnoses at the turn of the twentieth century. One hundred years ago, anxious to address this shortcoming, Cabot published Differential Diagnosis, an anthology of several hundred case studies that demonstrated how to discern the cause of an ailment. The book stemmed from Cabot’s founding, a decade earlier, of the “clinicopathological conference” (CPC), during which a physician would take to a stage and be presented with the case history of a deceased patient. The physician would then work out the diagnosis aloud, with audience members (mostly physicians and physicians-in-training) questioning him about his methods. In the end he would offer his diagnosis, which was then compared with the results of the patient’s autopsy. “It was a dramatic event,” says Christopher Crenner, chair of history and philosophy of medicine at the University of Kansas and a Cabot biographer, because participants risked being wrong in public view—and sometimes they were.

Cabot spread the case study approach to teaching by transcribing and publishing cases privately, then sending them to colleagues. When funding for the CPCs ran dry, The New England Journal of Medicine made them a staple—they have appeared in nearly every issue for the past 87 years as Case Records of the Massachusetts General Hospital. (Today an editorial team in the MGH pathology department vets cases for a doctor to present at his or her department’s grand rounds; a written copy of the CPC then appears in NEJM.)

As Cabot’s CPCs gained a wide audience, the method spread across the country and “became a powerful model for physicians to test their knowledge and skill as diagnosticians,” says Crenner. Moreover, says Nancy Lee Harris, editor of Case Records and a hematopathologist at MGH, “the CPCs are a chance for young physicians to read about how experienced clinicians get to a diagnosis.” Such a skill is essential because, as Cabot wrote, “cases do not often come to us systematically arranged like the account of typhoid in a text book of practice of medicine.” Doctors must learn to intuit a patient’s condition from a sometimes-limited set of clues. “Someone once told me that medical school teaches you to think like a scientist,” Harris says, “but the Case Records teach you to think like a doctor.”
POLICY WATCH //
Policing Physicians Online
BY LINDA KESLAR

A physician posting photos of himself drunk on Facebook. A YouTube video of medical students encased in body bags, drinking “blood” (actually chocolate) from plastic skulls. Those two incidents, cited by the American Medical Association as evidence that physicians aren’t immune to using social media unwisely, add to a growing body of evidence that proves the point. According to research published in The Journal of the American Medical Association, as many as 3% of tweets from 260 physicians with 500 or more followers during May 2010 included profanity, potential patient privacy violations, sexually explicit material, potential financial conflicts of interest or unsupported medical statements. And in a 2009 study published in the same journal, 60% of medical school deans surveyed dealt with students who had posted profanity, depictions of intoxication and sexually suggestive material online.

Though many physicians consider social media a tool for strengthening relationships with patients, interacting with peers and publicizing opinions on issues, such communications also pose questions of ethics, privacy and liability, according to the AMA. In November 2010, the organization issued the first national guidelines governing physicians’ use of social media. The AMA guidelines include general warnings against posting identifiable patient information. But because confidentiality issues may also arise when physicians allow patients to post on doctors’ blogs or Facebook pages, the rules include more technical advice, such as how to remove information patients post about their medical conditions. The AMA advice is meant not only to protect patients but also to help physicians avoid penalties that can be severe. Violations of the Health Insurance Portability and Accountability Act, which guards against unauthorized disclosure of individuals’ health information, may result in criminal fines of as much as $250,000 and imprisonment.

Yet the AMA will not be policing physicians’ social media activity; rather, it asks physicians to confront colleagues about bad behavior and to report problems to the AMA or state medical boards if trouble persists—actions most physicians are loath to take. “Watching doctors adopt Twitter, I’ve seen occasional violations of HIPAA and other disclosures that push the envelope,” says Bryan Vartabedian, a pediatrician at Texas Children’s Hospital in Houston who blogs and tweets. “But I feel uncomfortable messaging them to say they’re over the line.”

Still, many physicians welcome the guidelines. Katherine Chretien, a physician blogger, an associate medical professor at George Washington University School of Medicine and lead author of the two JAMA studies, calls the guidance “a good first step, because it’s been a little like the Wild West online.”

Vartabedian says a good next step would be to provide case studies of real situations. For example, if a patient posts on a physician’s Facebook wall and the physician responds, that exchange could be viewed as establishing a physician-patient relationship. If that patient were to post a subsequent question and receive no reply, the physician might be held liable for not dispensing advice. Trouble could also arise if the patient lives in a state in which the physician isn’t licensed.

Despite such issues, Vartabedian felt compelled to respond when he received a Facebook message from a mother with a sick four-month-old. Rather than continue the discussion online, he called the mother and saw the baby the next day.

The legal ramifications will become clearer, says Rebekah A.Z. Monson, a health care attorney in Philadelphia. “There hasn’t yet been a landmark case about physicians and social media, but we’ll get there,” Monson says. Meanwhile, physicians—and patients—will need to tread carefully as they learn to make the most of these new media.

For physicians, the use of social media poses questions of ethics, privacy and liability.

What role should social media play in a physician’s practice? Tell us what you think at protoeditor@mgh.harvard.edu.
A superbug with a new drug-resistance gene: That’s how the popular press describes New Delhi metallo-beta-lactamase, NDM-1 for short. The more accurate description is even more troubling, because NDM-1 contains a slew of drug-resistance genes, including one that blocks carbapenems, a widely used class of antibiotics and currently one of the few last-ditch defenses against many drug-resistant pathogens. Even nonantibiotic approaches under study, as Proto described in the Fall 2008 issue (“The War on Superbugs”), are unlikely to defeat the bug anytime soon.

NDM-1’s arsenal of drug-resistance genes includes a group on a DNA segment called a transposon. Also called jumping genes, transposons tend to detach en masse from their chromosome and fuse with another one, sometimes after picking up pieces of free-floating DNA called plasmids.

Transposons and plasmids allow a bacterium to adapt rapidly, exchanging genes between individuals and species quickly. In the case of NDM-1, they allow any member of the Enterobacteriaceae family—a large group that includes Escherichia coli as well as bugs that can cause pneumonia and plague—to become a superbug.

“Because it has a whole string of resistance genes, there’s hardly any drug left to treat the disease,” says Robert Moellering, a Harvard Medical School specialist in the evolution of antibiotic resistance. “Some of these strains are resistant to everything.”

In addition to Klebsiella pneumoniae, NDM-1 has insinuated itself into E. coli, Enterobacter and Morganella, all common sources of human infection. In New Delhi—the densely populated center of the region from which NDM-1 has spread to North America, Europe, South America and Australia—a recent survey of community sewage and drinking water found NDM-1 to be widespread and present in no fewer than 11 bacterial species.

To fight back against the entire advancing army of drug-resistant bugs, researchers are experimenting with nonantibiotic approaches, such as defusing the proteins that make pathogens toxic. In theory, those approaches might work against NDM-1, but they’re still at very early experimental stages.

Among researchers and public health experts who study drug resistance, the sense of alarm is palpable. “The whole issue deserves massive urgency,” says University of British Columbia microbiologist Bob Hancock, whose work is focused on bolstering the body’s innate immunity against bacteria. “It takes 15 years to develop a drug. Just extrapolate the curves we’re seeing for any antibiotic resistance out to 15 years, and the situation looks extremely grim.”

**DEFINED //**

**hygiene hypothesis** [hi-jeen hye-pa-tha-sas] n: the notion that an almost obsessive emphasis on cleanliness in Western cultures has caused an increase in such autoimmune disorders as allergies and asthma.

In the past 50 years, asthma rates in the Western world have increased as much as threefold, and growing numbers of people have developed allergies. Since the late 1980s, studies have suggested a link to stricter hygiene standards, which have prevented children from frequently interacting with bacteria, fungi and other microbes. According to this hypothesis, exposure to a wide range of microbes early in life somehow conditions the immune system against asthma and allergies.

This symbiotic effect was documented most recently in a report published in The New England Journal of Medicine. German researchers examined the number and diversity of microorganisms to which 16,500 city and farm children were exposed, and discovered that a greater diversity of microbes correlated with lower asthma risk. James Gern, author of an accompanying editorial and former chair of the American Board of Allergy and Immunology, sees “promise that we’ll be able to identify treatments based on these observations.”