Virtual Mentor
Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 191-291.
Ethical Questions Posed by Emerging Epidemics

From The Editor

NEW **Ethics in Action—**grants of up to $5,000 over two years to support ethics education and service projects. Apply now.

Essay Contest—*Virtual Mentor* is pleased to announce the twelfth essay competition for medical students, sponsored by the John Conley Foundation for Ethics and Philosophy in Medicine. This year's topic examines fairness in drug dispensing by physicians who practice in volunteer-based medical clinics. Read more

Educating for Professionalism

Clinical Cases

History of Medicine

Op-Ed

Medical Humanities

Resources

April Contributors

Upcoming Issues of *Virtual Mentor*

April: Ethical Questions Posed by Emerging Epidemics
May: Conflict of Values in the Clinical Setting
June: The Ethics of Sound Prescribing
August: Ethical Issues in Dermatology

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 194-196.

From the Editor

Of Men and Microbes: Physicians and the Ethics of Epidemics

On September 17, 1683, Dutch scientist Antony von Leeuwenhoek wrote a letter to the Royal Society of London describing microscopic observations made of dental plaque donated by a 17th-century gentleman with an aversion to personal hygiene. To his surprise and wonder, von Leeuwenhoek reported seeing, "...an unbelievably great company of living animalcules, a-swimming more nimbly than any I had ever seen up to this time...In such enormous numbers that all the water seemed to be alive" [1]. Von Leeuwenhoek and his contemporaries may have been delighted with their "animalcules," but in the centuries which followed it would become apparent that such organisms were also responsible for many of humankind's greatest woes, the dread specter of infectious diseases from typhus to plague that have ravaged humanity throughout recorded history.

Yet even without a full understanding of the microbial world he was among the first to describe, von Leeuwenhoek helped fuel paradigm shifts in not one but 2 distinct professions: science and medicine. It is easier, perhaps, to recognize the contribution of von Leeuwenhoek's discoveries to the later scientific achievements of such luminaries as Rudolf Virchow and Louis Pasteur, but we must not forget the parallel role of microbes in shaping the development of the modern medical profession. An understanding of the pathophysiology of infectious disease and the concomitant development of pharmaceutical agents with which to treat such infections ushered in a new breed of physician: one who could offer not only comfort, but also—sometimes—an actual cure. Alexander Fleming's penicillin gave way to Jonas Salk and the polio vaccine and then Donald A. Henderson and the WHO-led global eradication of smallpox. The future was bright; with a powerful armamentarium of antibiotic agents and vaccines, diseases that once devastated millions were no longer a threat, if they even existed at all.

And then came HIV/AIDS. And in the wake of a virus which has shattered our conceptions of illness, health, and infectious disease, society in general and physicians in particular have been forced to ask some difficult questions. When the individual autonomy so championed by biomedical ethics directly conflicts with the physician's obligation to protect the public health, which of these competing value systems takes precedence? How does the most universally recognized creed of the physician—*primum non nocere*—change in the face of an epidemic? Can some harm to a few be justified by the prevention of harm for the majority? And how does justice fit into the picture—do infectious diseases simply represent one more way in which the world can be divided into the haves and the have-nots?

At a time in which we find ourselves facing not only the global pandemic of HIV but also the threat of new emerging diseases—severe acute respiratory syndrome (SARS) or avian influenza—as well as re-emerging diseases we thought were gone—drug-resistant tuberculosis or methicillin-resistant *Staphylococcus aureus*—this April 2006 issue of *Virtual Mentor* asks us to consider the ethics of epidemics. In the first case commentary, Dr Parveen Parmar reminds us of physicians' responsibilities to monitor our own health as, like our patients, we too can be vectors of infectious disease. Dr Sarah Sutton, a clinician, and Dr Alison Thompson, a bioethicist, then tackle the thorny dilemma of quarantine and if—and how—the decision to impose it should be made. Next, Drs Feudtner and Wadleigh separately address the physician's dual obligations to patients and to family and self during an epidemic. Finally, Dr Mona Loutfy considers the use of randomized controlled trials in the clinical setting of an unknown infectious outbreak for which therapeutic options have not yet been evaluated.

In the journal discussion, Anya Likhacheva analyzes the lessons learned from SARS and how this emerging epidemic may guide our response to the next one. In a related clinical pearl, Dr Mark Dworkin walks us through the principles of disease surveillance and the steps individual physicians should take to contact local public health authorities with a case of an unknown or reportable infectious disease. And in her health law commentary, Sarah Fujiwara explains the legal basis for mandatory vaccination during a time of epidemic.

After considering some of the questions facing physicians involved with direct patient-physician encounters, we next turn our attention to questions on a social scale raised by infectious disease. In the medicine and society section, Alison Bickford compares the successes and failures of New York City and the states of the former Soviet Union in combating tuberculosis, a disease that was once eminently treatable but is now considered a re-emerging threat due to development of drug resistant strains. Using malaria as an example, Sean Murphy critiques the Western world's response to tropical infectious disease and reminds us of the devastating consequences for humanity when the diseases of the poor are marginalized.

The response to emerging infectious disease must also involve public policy, and so in the policy forum, Dr Maureen Kelley acknowledges that not all outbreaks are naturally occurring in her discussion of balancing bioterrorism preparedness with scientific and medical advancement. Dr Christine Grady contributes her policy analysis of the ethics of conducting clinical research trials in the developing world. Facing a key policy issue for physicians, Dr Martin Strosberg addresses the ethical dilemma of resource allocation in time of epidemic.

In addition, Michael Fumento reminds us that public perception is not always accurate in his op-ed piece arguing that the H5N1 avian influenza is not the looming threat it is often portrayed to be.

To acknowledge the important role infectious disease has played in the past, present, and undoubtedly future of medicine, this issue of *Virtual Mentor* concludes with a view of how far we have come and where we are headed. Jessica Mellinger puts modern

epidemics in perspective by evaluating the response to the much earlier 14th-century outbreak of the plague that decimated much of Europe. Dr Douglas Hamilton traces the development of a modern approach to managing infectious disease in the Center for Disease Control's Epidemiology Intelligence Service. And, continuing in a long tradition of using the visual arts to inform our reflections, Dr Kate Scannell concludes by presenting artist Timothy Grubbs Lowly's unforgettable drawing *Carry Me* as a reminder that as physicians we must choose, both individually and collectively, which patients and which burdens we will carry.

In considering the ethics of epidemics there are no easy answers. Treating infectious disease may have been one of medicine's first real triumphs, but antibiotics notwithstanding, neither the clinical nor the ethical challenges posed by such infections have diminished. Indeed, as the authors in this month's issue point out, the myriad difficulties presented by emerging disease will only continue. As individual physicians, as a profession, and as a society we must constantly evaluate the balance between safeguarding the public and protecting the rights of the patient. In short, physicians must recognize the inherent duality of our professional responsibilities. Furthermore, although the daily activities of most physicians center around patient care and not the legal or policy arena, we cannot afford to forget the broader implications of treating—or not treating—infectious disease. In our roles as individual patient or physician, we remain part of a global community: emerging infections challenge us to remember both.

Amanda J. Redig
MD-PhD student
Feinberg School of Medicine
Northwestern University

Reference Note

1. von Leeuwenhoek A. Excerpt from a letter dated September 17, 1683, to the Royal Society of London, and printed in the Philosophical Transactions of the Royal Society. Available at: http://www.ucmp.berkeley.edu/history/leeuwenhoek.html. Accessed March 20, 2006.

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 197-200.

Clinical Case

Autonomy and Public Health: When the Patient is a Physician

Commentary by Parveen Parmar, MD

Twenty-four hours after his visit to the internal medicine clinic, Luc Aston was not surprised to discover a raised swelling on the inside of his forearm where the PPD test for tuberculosis had been administered. During his childhood in France he had received the Bacillus Calmette-Guerin TB vaccine. Then midway through the first year of his emergency medicine residency he was diagnosed with a case of active pulmonary TB, most likely acquired from patient exposure. Following his diagnosis, Luc took a leave of absence until chest x-rays confirmed his response to drug therapy. Now returning to finish his intern year, he was still required by hospital policy to receive an annual tuberculin skin test despite his past medical history and the likelihood of a false positive result.

"I've had positive skin tests before so I'm not worried," Luc said later that day over lunch, after he and 2 friends, also residents, claimed a table in the back corner of the cafeteria. "I just wish I could shake this cold—I haven't been able to run much lately. But anyway," he continued, "my last x-ray 6 months ago was fine and I don't want to alarm anyone at the clinic by telling them the skin test was positive. I mean isn't that what you'd expect?"

"Wait a minute Luc," Sriranjani Patel, a third-year emergency resident, interrupted. "You really need to have another x-ray just to make sure. Are you saying you're not going to follow through with that?"

"Well, I don't really want to," Luc replied, pausing for a moment to cough. "Sorry about that," he continued. "I'm already behind because I took time off. Besides, I really don't want to start taking meds again. The side effects are not something I want to go through a second time, especially when I really think medication isn't needed. I mean come on," he said, pausing to cough again deeply. "I had TB but it's fine now—I don't want to be taking isoniazid at 6-month intervals for the next 4 years just because some doctor at the clinic gets nervous."

"Luc," Sriranjani started cautiously, "how long have you been coughing?"

"Sri, please!" Luc exclaimed. "Don't start with that. I just have a bit of a cold. I'm fine!"

"Any pleuritic chest pain? Night sweats?" asked Mark Theophilus, the third member of the group, and a second-year resident.

"Will you 2 stop trying to diagnose me?" Luc asked, tossing a wadded-up napkin onto his half-empty plate in exasperation. "So I'm coughing and it's a little tight when I breathe. I have a cold! You know, those things called viruses? If I go in and make a big deal about this," he said, gesturing to his arm, "they might start me on meds again and I don't want that. I'm fine, trust me, and I'd really appreciate it if you both just stay quiet about this. I had an x-ray 6 months ago and I don't have time to get another one right now so I'm just not going to mention the PPD [purified protein derivative skin test] results. Once this cold goes away," he paused, coughing again, "I'll be fine!"

Commentary

As this vignette unfolds, Luc the coughing intern may very well have a simple upper respiratory infection. On the other hand, having recently completed a course of multi-drug therapy for pulmonary tuberculosis he may have also relapsed into another case of active tuberculosis. As an emergency medicine intern with exposure to hundreds of children and elderly and immunocompromised patients, certainly Luc has a responsibility to report his symptoms and agree to a repeat chest x-ray. Yet, one can understand why he might be reluctant to do so, having just spent several months away from work taking unpleasant, often toxic, medications. This case presents an interesting dilemma that illustrates the challenges when 2 worlds collide. As both a patient and a physician, does Luc have the right to refuse health care in this situation?

Luc's colleagues are also in a unique position. They have a responsibility to respect the judgment and wishes of their friend, but at the same time they are also accountable to their patients, other colleagues, and themselves to fulfill the professional obligations of physicians. In facilitating Luc's return to work as a medical professional, possibly with a communicable disease, are they complicit in endangering the health and even the lives of their own patients? Beyond questions of professional ethics, if Luc does in fact have TB, this group of interns—and all exposed employees of the hospital—may themselves end up needing several months of multi-drug therapy. Can loyalty and respect for their friend's wishes justify inaction?

The Right to Refuse Treatment

Under the basic principle of autonomy, it is everyone's right to ignore his or her own health, for better or worse. The American Medical Association's *Code of Medical Ethics* reflects this position when it states that, "The patient has the right to make decisions regarding the health care that is recommended by his or her physician. Accordingly, patients may accept or refuse any recommended medical treatment" [1]. Patients regularly refuse proven therapies in favor of alternative or natural therapies, even after being fully informed of the risks of doing so [2]. As a practicing physician, I have even had patients die as a result of such decisions.

However, except in extraordinary circumstances such as quarantine, physicians must respect the patient's right to autonomy and self-determination in making decisions regarding health care, no matter how difficult, and even when it can affect public health.

For example, under some circumstances we respect the right of parents to decide not to vaccinate their children—we pray that herd immunity protects these children and ours [3]. Similarly, physicians often come to work when they have communicable diseases, from the flu to gastroenteritis. These highly contagious viral illnesses can be transmitted easily from person to person in the process of routine care, even with vigorous hand washing. With these precedents, doesn't Luc also have the right to refuse further care for his symptoms, even if, like a simple viral illness, his condition could endanger his patients?

Patient Safety, the Prevailing Concern

Despite such arguments, the fact remains that tuberculosis is far beyond a simple viral illness. It is a chronic, life-threatening, debilitating illness that is extremely difficult to treat and poses a tremendous threat to the public health. While most patients have no problem getting over a cold, recovering from tuberculosis is no small matter. Furthermore, developing TB can be an immediate death sentence for a patient with HIV or other immune deficiency. Immunodeficient patients, including those with AIDS, those on chronic steroids because of autoimmune disease, transplant patients, and the elderly and chronically ill make up a large percentage of the patient population of the average emergency room.

Consequently, given the threat that TB poses to the lives of his patients, Luc has a responsibility to report his symptoms, regardless of the personal difficulty this will cause. Luc the patient has a right to refuse care, but Luc the physician has the privilege of being a physician only so long as he protects the health of his patients above all else. His patients' rights trump his rights as long as he works in a hospital. The level of danger posed to patients' health by their physician's communicable illness is what determines when symptoms must be reported.

The Role of Colleagues

Luc's colleagues, as physicians, must focus on the health of their patients, even if this means disregarding the wishes of their friend. Active tuberculosis is far too serious a disease to allow an intern to become an unreported case. Certainly, his friends should start by offering Luc the chance to report his symptoms on his own. But if he does not, they should clearly state that they will inform their hospital's occupational health department of his symptoms. They should emphasize that they do not wish to betray him, but they would like to feel assured that patients presenting to the emergency room will not be exposed to a life-threatening disease. As physicians themselves, Luc's friends also have a responsibility to protect their own health—sharing lunch with a hacking TB case is hardly the way to do that.

Although this situation is undoubtedly a difficult one for Luc's colleagues—Who wants to face the possibility of having to confront a friend?—it is not without precedent. If Luc's colleagues noticed that his ability to provide patient care was impaired secondary to a drug or alcohol addiction, they would be ethically if not legally obligated to report their suspicions in the interest of patient safety [4]. It can easily be argued that a physician with an active case of TB poses as serious a threat to patient welfare as a physician under the influence of drugs. And even if Luc does not have TB and is

suffering from something more innocuous such as a respiratory virus, it is perhaps still the role of his friends to promote physician wellness by encouraging him to consider his own health needs. Regardless of whether Luc is suffering from TB or a respiratory virus, he illustrates the reality that physicians are as human as the patients they treat and, at times, may even become patients themselves.

Being a physician is an honor, not a right. With this honor come several clear responsibilities that must be upheld—even if our own rights, beliefs, and desires conflict directly with what is best for our patients. In accepting the responsibilities of this profession, we have agreed that our patients' needs must always come first. When we feel that we are unable to put our patients first, it is our responsibility to excuse ourselves from patient care in their interest.

References

1. American Medical Association. Opinion 10.01 Fundamental elements of the patient-physician relationship. *Code of Medical Ethics*. Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=browse&p_p=T&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-10.01.HTM&nxt_pol=policyfiles/HnE/E-10.017.HTM& Accessed March 7, 2006.
2. Astin JA. Why patients use alternative medicine. *JAMA*. 1998;279:1548-1553.
3. Calandrillo SP. Vanishing vaccinations: why are so many Americans opting out of vaccinating their children? *Univ Mich J Law Reform*. 2004;37:353-440.
4. American Medical Association. Opinion 9.031 Reporting impaired, incompetent, or unethical colleagues. *Code of Medical Ethics*. Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=browse&doc=policyfiles/HnE/E-9.031.HTM&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-8.21.HTM&nxt_pol=policyfiles/HnE/E-9.01.HTM& Accessed March 7, 2006.

Parveen Parmar, MD, a resident in emergency medicine at UCLA, is a graduate of Northwestern University's Feinberg School of Medicine where she helped found the school's chapter of Physicians for Human Rights.

Related Article

An Impaired Resident, March 2003

An Impaired Resident, September 2002

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 201-207.

Clinical Case

"I'm Sorry but You Can't Leave": Patients, Physicians, and Quarantine

Commentaries by Sarah Sutton, MD, and Alison Thompson, PhD

"I wonder if we'll get any more flu patients today?" thought Melissa Wagner, a fourth-year medical student in the middle of her emergency medicine clerkship. The large urban medical center affiliated with her medical school had already admitted 34 cases of a variant strain of influenza in the last 2 days. Across the city an estimated 250 people had become ill during the past 2 weeks, with the mortality rate hovering just below 20 percent. In an effort to control the spread of the deadly virus, both the state public health department and local medical centers were cooperating with strict quarantine procedures for individuals exposed to known carriers. Local news stations encouraged people to remain home, while medical personnel with known patient exposure were restricted from leaving their hospital or clinic until after a 24-hour observation period. Although Melissa had not yet come in contact with anyone later determined to have an active infection, she couldn't help but wonder about each new patient she examined.

Later that morning, Melissa's supervising resident directed her to a patient complaining of persistent abdominal pain. "His symptoms don't match with the flu," she told Melissa, "so I don't think you need the isolation mask and gown."

Five minutes into the exam and history, Melissa could feel her pulse start to quicken. Mr McIntyre may have come to the ER with abdominal pain, but now he was starting to complain of a headache and nausea accompanied by an elevated temperature of 100.2° that just 3 hours earlier had been 98.4°. Growing more and more nervous, Melissa immediately went to find Dr Martin, her supervising resident.

"He was in the waiting room for how long?" Dr Martin asked in despair, after the team promptly admitted Mr McIntyre with what was determined to be another case of influenza. "Three hours? We're going to have to quarantine everyone who was there!"

Accompanied by Dr Walker, the attending physician for the team, Melissa and Dr Martin made their way to the corner of the waiting room where the triage nurses had assembled the 12 people who had been exposed to Mr McIntyre. After calmly explaining the situation and the necessary 24-hour quarantine, Dr Walker asked if anyone had any questions.

"Yeah, I've got one," a large man with a swath of bloody gauze wrapped around his forearm snarled belligerently. "I've been bleeding all over the floor for an hour and now you're telling me I can't leave? I only saw that sick guy for 5 minutes!"

"I'm sorry sir—" Dr Walker began before he was cut off.

"I don't believe this," the man cut in. "This is such garbage. I'm supposed to be at my kid's soccer game tonight and then I work the night shift. What do you want me to do about that?" he asked before stalking away towards the bathrooms.

Six hours later, as Melissa walked towards the cafeteria, she realized that Nick—she learned his name after spending half an hour stitching shut the cut on his arm—was following her, occasionally looking over his shoulder towards the triage station. "Excuse me," he said quietly, glancing over his shoulder again. "I'm really sorry about before—I didn't mean to get so upset. It's just that I have so much to do today and I promised my son I'd make it to his game. I've…well, I've missed the last 3."

"Oh, that's okay," Melissa said. "I can understand why you'd be upset."

"But honestly, I don't have that flu," Nick replied. "I feel fine, I don't have a fever or any of those other things they keep talking about on TV, and that sick guy went into the back right after I sat down. Seriously. Five minutes later. You were so nice about doing my stitches—can't you help me out here? I really need to be at this game and I've been here for almost half the quarantine time. I could just walk out the side door and they'd never even notice I'm gone. Please don't say anything," he begged, glancing once more down the empty corridor and edging towards the door. "I'm fine, honest."

Commentary 1
by Sarah Sutton, MD

In this clinical scenario, both Nick and Melissa have suddenly been thrust into pivotal roles in a public health crisis. Nick is filled with anger, confusion, and frustration. He has been imprisoned and he does not understand why. Until this moment Melissa has been a patient advocate and a representative of the emergency room physicians; now she has been transformed into a deputy of the public health system. Her new role supersedes her previous roles—but it does not release her from her traditional obligations to her patients. State and federal public health officials have deemed the variant influenza an emergency warranting quarantine in her city. Melissa must obey the rules of quarantine, communicate the urgency of the situation, and engender the cooperation of the quarantined.

In addition, however, Melissa has had close contact with the ill patient and must be quarantined herself. She may be experiencing many of the same feelings as Nick, the man with the bleeding arm. Ultimately, sharing her understanding of the situation and her own feelings about it may be a key to enlisting the cooperation of the quarantined individuals.

Considering Isolation versus Quarantine

Melissa should first understand the difference between 2 distinct concepts, isolation and quarantine. In previous eras, these concepts were used interchangeably. The modern definition of isolation is the physical separation of persons with the active contagious disease. We use isolation on a day-to-day basis in the hospital—for example, in the case of patients with methicillin-resistant *Staphylococcus aureus*, with suspected bacterial meningitis, or with possible untreated pulmonary tuberculosis.

Quarantine, in contrast, is the physical separation of healthy individuals who appear to have been exposed to a person with active contagious disease [1, 2]. To minimize ongoing risk of infection, the quarantined are removed from those with active infection. For quarantine to be an effective tool, 2 factors should be involved in the underlying biological basis of the disease in question: (1) the disease process appears to be contagious and (2) there appears to be a reproducible incubation period. If individuals under quarantine remain healthy beyond the presumed incubation period, the quarantine should be lifted for those persons.

Quarantine has been a technique used to contain infections since before the existence of the germ theory of disease. The 2003 outbreaks of severe acute respiratory syndrome (SARS) in China, Hong Kong, Taiwan, Singapore, and Toronto revealed that quarantine can be an effective tool to halt infection in modern societies. Furthermore, quarantine is an integral part of public health plans for future outbreaks of potential emerging infectious diseases and some acts of bioterrorism such as release of smallpox virus.

The Challenge of Quarantine

After understanding the meaning of quarantine, Melissa should recognize how invoking it may pit 2 primary values against each other—personal autonomy and public welfare. In addition, Melissa should recognize the sudden (albeit temporary) supremacy of the public welfare needs. Normally our society upholds autonomy, the right of the individual to determine his or her actions, as a supreme value—unless there is a risk of harm to others. As a medical student, Melissa recognizes the right of a patient to refuse hospital admission despite severe pneumonia, to ignore her recommendations to stop smoking tobacco, or to choose not to fill a prescription for hypertension. It is her obligation to communicate the importance of her recommendations in a manner that the patient can understand; ultimately, however, the decision of whether or not to comply rests with the adult patient. Thus Melissa respects Nick's autonomy.

In most patient-physician relationships, the value of public welfare plays a minor or even nonexistent role. When federal and state public health authorities proclaim quarantine within a region, however, the public welfare is at grave risk. These officials have deemed the situation a public health emergency involving a contagious infection. In such a situation, the needs of the community temporarily supersede individual rights and freedoms. The unusually high mortality rate during this outbreak in Melissa's city clearly reaches the threshold of a public health emergency.

The Physician's Response

As she recognizes the sudden, unbalanced tension between the needs of public welfare

and those of personal autonomy, Melissa should act decisively and immediately. She should act as an extension of the public health system to prevent Nick from leaving the hospital. Because this patient has previously been belligerent, Melissa may need to ask security personnel to intervene. With assistance, she may be able to use her prior relationship with Nick to re-establish rapport and thereby prevent Nick's departure.

Once Nick returns, it is Melissa's obligation to address the needs of all her patients, the quarantined [3]. Research during the SARS outbreak in Toronto revealed that those who were quarantined commonly described feelings of isolation, uncertainty, desperation, powerlessness, and fear of illness and loss of income. What appeared to engender cooperation and coping were: clear, consistent information from health care workers, an understanding of the purpose of quarantine, clear expectations about behavior, and reassurance that immediate needs would be addressed [4]. It is important for members of the quarantined group to realize that being sequestered may keep their own families safe and that, by being removed from the clinically ill, they've lessened their own risk of acquiring influenza. As a medical student and a quarantined individual herself, Melissa is uniquely poised to communicate and reassure. Her ability to form a bond with the quarantined individuals will help them cooperate with this imposed separation.

In conclusion, during a public health crisis, the balance shifts from favoring individual rights to protecting the health of the community. In the situation of quarantine, each individual physician's role is to engender cooperation by communicating clearly and by acknowledging the natural fears and feelings of powerlessness that infectious disease outbreaks create.

References

1. Gostin LO, Gravely SD, Shakman S, Markel H. Quarantine: voluntary or not? *J Law Med Ethics*. 2004;32(4 Suppl):83-86.
2. Barbera J, Macintyre A, Gostin L, et al. Large-scale quarantine following biological terrorism in the United States: scientific examination, logistic and legal limits, and possible consequences. *JAMA*. 2001;286:2711-2717.
3. Lo B, Katz MH. Clinical decision making during public health emergencies: ethical considerations. *Ann Intern Med*. 2005;143:493-498.
4. Cava MA, Fay KE, Beanlands HJ, McCay EA, Wignall R. The experience of quarantine for individuals affected by SARS in Toronto. *Public Health Nurs*. 2005;22:398-406.

Sarah Sutton, MD, is a member of the Department of Infectious Disease at Northwestern University's Feinberg School of Medicine.

Commentary 2

by Alison Thompson, PhD

In this case scenario, Melissa confronts a fundamental ethical challenge facing clinicians in public health crises: being respectful of individual liberty while protecting the population from harm. The primary moral dilemma takes place when autonomous

individuals want to act in ways that threaten people's health. In this case, Nick wants to exercise his individual liberty to break quarantine, but, if he is allowed to leave the hospital, he may put the health of others at risk. The legal and moral duty to protect the public from harm trumps Nick's individual liberty because of the significant potential threat he poses to the community's health. However, it is important for Nick and others to understand why they are being asked to cooperate with public health measures such as quarantine and what the consequences may be if they are not compliant. Despite the ethical legitimacy of enforcing a quarantine, there are more nuanced aspects and moral dimensions to this case that are less clear-cut.

Proportions and Precautions

While it seems fairly certain in this case that the quarantine restrictions are not disproportionate to the threat being allayed, it may be that in other cases health measures are not proportionate responses to the risks. One criterion for assessing proportionate responses to health threats is the need for precaution in situations where there is a lack of good information with which to make decisions. It is important, therefore, that hospitals work closely with public health officials in times of crisis to ensure that everyone has accurate health information and that the least restrictive or coercive measures are employed when it comes to limiting individual liberty [1, 2].

The precautionary principle justifies taking a course of action that errs on the side of caution and that may require health measures that are more restrictive of individual liberty than they actually need to be. While Melissa would not be personally responsible for determining what public health measures ought to be enacted, she does have a responsibility to pass along to hospital decision makers (and perhaps even to governmental health officials) any new information about the influenza patients that may be relevant to how the outbreak is handled. By doing so, she can help ensure that public health measures to contain and manage the outbreak are both proportionate to the threat the disease poses to the public's health and that they reflect suitable precautions.

Considering Equity

Even if Melissa does have reason to believe that Nick's case is special and that he is not at significant risk of spreading contagion to the community, she should consider whether allowing him to leave would be fair to the others who are currently in quarantine. The principle of equity is important in such a situation, and Melissa's actions should preserve as many rights as possible for those in quarantine. While there may be unintended negative consequences for Nick if he has to remain in quarantine, it is arguably more important that citizens be treated equally in a public health crisis so that restrictions to individual liberty are not applied in a discriminatory manner. Equitable treatment is also vital because of the importance of solidarity—unequal treatment can undermine the sense of common purpose that is critical in managing a public health crisis.

In urgent situations, decisions have to be made that often result in collateral damage: imposition of a disproportionate burden on particular members of society, for example. In this case, those who are quarantined will bear some of that burden. As a result of

being quarantined, Nick will disappoint his son and will likely lose wages. The moral duty of reciprocity requires that society support those who suffer such consequences as a result of measures designed to protect the public from harm. While Melissa alone cannot ensure that Nick recoups his financial losses, she could arrange for him to contact his family in order to explain why he will not be attending his son's soccer game. Melissa could even volunteer to speak to his son to explain why his father is unable to attend. Though this is certainly beyond what is required of her, demonstrating compassion and understanding can help to ease the emotional burdens of those in quarantine. Nick's behaviour suggests that it may be necessary for Melissa to involve hospital security or police, who can help to ensure that he does not leave the quarantine area. While this may require more restrictive or coercive measures, Melissa should remind herself that Nick's compliance was originally requested on the same voluntary basis as everyone else's.

Melissa may realize as the night wears on that she, too, is facing significant risk while discharging her duty to care. Perhaps she has a family at home who she fears will be put at risk because of her occupational exposure. Melissa ought to seek reassurance from her supervisors and from the hospital's occupational health staff that everything is being done to make her working conditions and those of her fellow health care workers as safe as possible. This may mean providing access to masks, or perhaps the hospital ought to provide health care workers with antiviral medication for prophylaxis against the influenza. Hospitals and even governments have a responsibility to ensure that working conditions are safe for those who bear a disproportionate burden in discharging their professional obligations in a public health crisis [3].

Conclusions

This case appears straightforward at first, but there are many ethical issues embedded in a clinical scenario in which a significant threat to the public health emerges. While Melissa is not in a position to resolve every ethical problem raised by this case, she is in a position to advocate for Nick by seeing that the unintended negative consequences of his quarantine are mitigated. Furthermore, she can advocate for her own safety and for that of her colleagues. Finally, as a frontline health care worker, Melissa has a responsibility to keep hospital and public health decision makers apprised of any new and relevant information that can help promote a precautionary and proportionate response to the crisis.

References

1. Gostin LO. Influenza pandemic preparedness: legal and ethical dimensions. *Hastings Cent Rep*. 2004;34:10-11.
2. Upshur RE. Principles for the justification of public health intervention. *Can J Public Health*. 2002;93:101-103.
3. Singer PA, Benetar SR, Bernstein M, et al. Ethics and SARS: lessons from Toronto. *BMJ*. 2003;327:1342-1344.

Alison Thompson, PhD, is a postdoctoral fellow at the Centre for Research on Inner City Health at St Michael's Hospital in Toronto, Canada.

Related Articles
SARS Revisited, April 2006

Citizen Samaritans and Public Perils: Our Duties to Doctors, May 2004

Ethics of Quarantine, November 2003

The viewpoints expressed on this site are those of the authors and do not necessarily reflect the views and policies of the AMA.

The viewpoints expressed on this site are those of the authors and do not necessarily reflect the views and policies of the AMA.

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 208-213.

Clinical Case

Should I Stay or Should I Go? The Physician in Time of Crisis

Commentaries by Chris Feudtner, MD, PhD, MPH, and John Wadleigh, DO

"Hello, this is Bob," Dr Robert Yang said as he answered his cell phone after digging it out from underneath his couch cushions.

"Bob," the voice responded, "this is Jackson."

"Oh, Jackson—great, this reminds me," Bob replied while muting the volume on the football game. "Carol Wilson called this evening right after you left, and Bryan seems to have acquired another respiratory infection. I called in a refill on his antibiotics for the evening and scheduled him for you as an emergency appointment first thing tomorrow. I know with the avian flu going around the last thing you want is for one of your kids with cystic fibrosis to get pneumonia."

There was a pause on the other end. "Yeah, well, that's why I'm calling actually," Jackson said. "Look Bob, I know we've been in practice together for a long time and it's been great, truly it has. I mean you're Emily's godfather after all. The thing is, with this avian flu mess…" His voice trailed off.

"Jackson?" Bob asked, puzzled. "What are you trying to say?"

"What I'm trying to say, what I know I have to explain to you and Christine as my partners, is that I'm just not comfortable staying in the city if this is the beginning of an epidemic. Cathy and I are taking the kids to her parents tomorrow. We're driving, staying away from the airports and everything. I'm sorry Bob, but this is looking serious. And at some point I have to start putting my own kids first. Like I said, I've already talked to Christine—can you 2 cover for me?"

Commentary 1

by Chris Feudtner, MD, PhD, MPH

Catastrophe looms on the horizon as a spreading pandemic of virulent influenza threatens death and social pandemonium. Set against this dramatic backdrop, a physician has decided to flee with his family far from his home—and far from his medical practice and patients. In a late night telephone call, he informs his practice partner of his plans and seeks his cooperation. By vignette's end, key themes have been placed in stark opposition: the physician's obligations to his patients, his professional

colleagues, and society more generally versus his familial duties to his wife and children or to his own health and well-being.

Identifying a Framework

Is this framework of duties, which pits different obligations against each other, an effective way to think through this case? The existentialist philosopher and novelist Albert Camus, in his masterwork *The Plague*, initially frames the dilemma of the physician Bernard Rieux in terms of an "abstracted" sense of professional duty: after quietly reflecting on the history of the bubonic plague and its almost incalculable implications as his city is engulfed by the epidemic, Rieux rouses himself back to action, thinking that "the thing was to do your job as it should be done" [1]. More generally, ethicists have worked hard to define physicians' duties to patients as evidenced by the American Medical Association's *Code of Medical Ethics,* which specifically proscribes physicians from abandoning their patients. In the eyes both of the law and most ethicists, once a patient-physician relationship has been established, a physician is obligated to provide subsequent care until the relationship is terminated. Furthermore, termination of this relationship can occur properly only after the physician has notified the patient and ensured that medical care will be provided through some other arrangement [2]. The AMA has extended this line of thinking to prescribe appropriate physician behavior during epidemics, arguing that, "because of their commitment to care for the sick and injured, individual physicians have an obligation to provide urgent medical care during disasters. This ethical obligation holds even in the face of greater than usual risks to their own safety, health, or life" [3].

Viewed from this established perspective, censuring the fleeing physician is easy—perhaps too easy. This is not to say that I don't agree with the duties set forth by the AMA; I strongly believe in the obligation of physicians to remain responsibly committed to their patients and to help out when public health crises occur. Nor do I think that the vignette misrepresents the essential plot, motives, and conflict in a drama that has been replayed countless times over the centuries as innumerable physicians have fled from epidemics of plague, yellow fever, cholera, HIV, and most recently severe acute respiratory syndrome (SARS) [4-8]. No, the problem I see in analyzing this case chiefly in terms of duties is actually quite practical: such analysis is not effective in promoting better behavior because during times of crisis physicians (and many others) are likely to be more focused on understanding their personal risk rather than their professional duties. Furthermore, should an epidemic occur, the state is likely to use its authorized power to coerce needed medical personnel to perform emergency duties, and a dialogue on the nature of the duties of individual physicians misses a broader consideration of duties of the state to exercise its power fairly and effectively. These reasons for moving beyond a discussion of duties warrant elaboration.

Duties versus Risks

First, for individuals trying to decide what to do at a moment of moral crisis, the ethical definition of obligations too often provides little serious guidance for how one should behave in the face of conflicting duties. Speaking for myself, as a husband and father as well as a physician, I consider the key questions in this case to consist not of qualitative examinations of my obligations—I know these pretty well, and neither role, husband

and father or physician, always trumps the other. Rather, the 2 pivotal issues in my mind are: (1) a quantitative assessment of the degree of threat to which I would be exposing my family and myself by continuing to provide care to patients (ranging between 0 and 100 percent risk of morbidity or mortality), and (2) identifying across this range my threshold of moving from "acceptable risk" into the range of "too much risk," which is to say the point at which I would change my behavior. When would I decide to isolate myself from my family in order to protect them? When the risk of my transmitting the disease to them exceeded 1 percent, 5 percent, 10 percent? How long would I tolerate such a separation before balking? And when would the risk of my own death be sufficiently high (20 percent, 50 percent, 80 percent) that I would decide to abandon my post?

These questions are exceedingly difficult, evoking feelings of confusion, embarrassment, and almost pain in their contemplation. I know the answers would likely change under the influence of fear in the event of a real pandemic. Still, these quantitative judgments about how much I would put on the line to uphold one duty—not abandoning patients—while compromising another duty—protecting family from harm—are crucial for analyzing what physicians should and will do in such situations. Ethical analyses filled with duty-drenched language tend to stifle any forthright discussion of these judgments. To once again use myself as an example, am I displaying a disreputable disregard for a physician's duty by pondering where on the spectrum of family and personal risk I might abandon my post? Do concerns of being judged negatively by others promote better behavior or instead prevent more honest examinations of how I might act under almost unimaginable circumstances and thereby retard more realistic preparations to act ethically?

Considerations of Power

Second, at the level of a society attempting to formulate policy to handle a full-scale pandemic, a code of physician conduct that relies only on exhortations to honor one's duties will likely prove impotent. If the historical record teaches only one lesson, it is this: when confronted with a deadly epidemic, instead of moral persuasion, power will be what matters. Specifically, the power of the state or government operating through law and regulation is what will certainly be used to cajole or coerce unwilling physicians into compliance with official definitions of a doctor's duties during emergencies. For example, the Model State Emergency Health Powers Act (MSEHPA), crafted by The Center for Law and the Public's Health, and now introduced or enacted in total or in part by 44 states, proposes in section 608 that the public health authority would be empowered, "to require in-state health care providers to assist in the performance of vaccination, treatment, examination, or testing of any individual as a condition of licensure, authorization, or the ability to function as a health care provider in this State" [9-10].

Whether or not these powers would be enforced in the event of a pandemic and its aftermath remains to be seen. In previous epidemics, physicians who chose to abandon their posts or declined to care for certain patients did not appear, for the most part, to suffer punitive consequences. But, with the MSEHPA and other pieces of legislation in place, any debate about what physicians should do in the face of a public health crisis

should be supplanted by a debate about what powers the state should have to compel physicians to perform certain duties and how those state powers should be put into practice. Just like a military draft, the procedure of compelling physicians to serve should be administered justly, with the burdens and dangers of providing care distributed fairly among all physicians. And, just like a military operation, there would be a heightened reciprocal duty of the state and health care institutions to do everything in their power to safeguard the well-being of the physician conscripts. This would entail preparatory planning regarding not only adequate supplies of masks, gowns, vaccines, and antivirals but also housing (for physicians who elect to quarantine themselves from their families) and staffing plans (when physicians are in short supply, due either to the excessive numbers of patients or the absenteeism of other physicians) [11].

Conclusion

In the closing lines of *The Plague*, as the pestilence has abated and the city is liberated from quarantine, Camus (who beyond his initial exhortation of professional duty has offered innumerable insights regarding the individual and collective experience of confronting mortal danger) observes of his hero that, "as he listened to the cries of joy rising from the town, Rieux remembered that such joy is always imperiled" [12]. In many ways the same holds true today. Given that a pandemic is regrettably all too likely, we should fortify arguments about professional duties with more concrete discussion about levels of acceptable and unacceptable personal risk and with more focused dialogue about the appropriate use of power by the state or hospitals during times of crisis.

References

1. Camus A. *The Plague*. 1st international ed. New York, NY: Vintage Books; 1991: 41.
2. American Medical Association. Opinion 8.115 Termination of the patient-physician relationship. *Code of Medical Ethics*. Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=browse&doc=policyfiles/HnE/E-8.115.HTM&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-7.05.HTM&nxt_pol=policyfiles/HnE/E-8.01.HTM& Accessed March 15, 2006.
3. American Medical Association. Opinion 9.067 Physician obligation in disaster preparedness and response. *Code of Medical Ethics*. Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=browse&doc=policyfiles/HnE/E-9.067.HTM&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-8.21.HTM&nxt_pol=policyfiles/HnE/E-9.01.HTM& Accessed March 2, 2006. See also American Medical Association. Opinion 10.01 Fundamental elements of the patient-physician relationship. Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=browse&doc=policyfiles/HnE/E-10.01.HTM&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-9.132.HTM&nxt_pol=policyfiles/HnE/E-10.01.HTM& Accessed March 15, 2006.
4. Emanuel EJ. Do physicians have an obligation to treat patients with AIDS? *N Engl J Med*. 1988;318:1686-1690.
5. Freedman B. Health professions, codes, and the right to refuse HIV-infectious patients. *Hastings Cent Rep*.1988;18:S20-25.
6. Masur H, Emanuel E, Lane HC. Severe acute respiratory syndrome: providing care in the face of uncertainty. *JAMA*. 2003;289:2861-2863.

7. Powell JH. *Bring Out Your Dead: The Great Plague of Yellow Fever in Philadelphia in 1793*. Philadelphia: University of Pennsylvania Press; 1993.
8. Rosenberg CE. *The Cholera Years: the United States in 1832, 1849, and 1866*. Chicago, Ill: University of Chicago Press; 1987.
9. Gostin LO, Sapsin JW, Teret SP, et al. The Model State Emergency Health Powers Act: planning for and response to bioterrorism and naturally occurring infectious diseases. *JAMA*. 2002;288:622-628.
10. The Center for Law and the Public's Health at Georgetown and Johns Hopkins Universities. *Model State Public Health Laws*. Available at: http://www.publichealthlaw.net/Resources/Modellaws.htm#MSEHPA. Accessed February 27, 2006.
11. Kotalik J. Preparing for an influenza pandemic: ethical issues. *Bioethics*. 2005;19:422-431.
12. Camus, *The Plague,* 308.

Chris Feudtner, MD, PhD, MPH, is the director of research for the Pediatric Advanced Care Team and the Integrated Care Service at the Children's Hospital of Philadelphia. He is also a senior fellow of the University of Pennsylvania's Center for Bioethics.

Commentary 2
by John Wadleigh, DO

Physicians hold a special position in our society and, at a time of a potential medical crisis, we need to give society our best effort—not turn and run. In the case of a developing infectious epidemic for which evacuation is considered, physicians may want their families to leave in a reasonable and proper manner for a safer location. Furthermore, the evacuation of areas of potential crisis—a region with impending hurricane landfall, for example—is also an accepted means of balancing public health in a crisis situation. In either setting, however—epidemic or evacuation—medical professionals need to be available to provide appropriate care for our patients.

The physician in this case has chosen to leave the scene of an epidemic and is shifting the responsibility of caring for his patients to his partners. Something must be said here about "dumping" on one's associates. Deserting one's physician colleagues during a crisis and asking them to do what you do not wish to do places an unfair portion of the burden for fulfilling the profession's promise to society on select members.

Running foolishly into a situation that is known to be dangerous is not wise and is not suggested. On the one hand, the physicians facing a potential epidemic should not needlessly put themselves at risk by failing to observe appropriate precautions. On the other hand, physicians have a professional duty to stay to help in a coordinated and rational fashion during times of crisis. As members of a team functioning in a calm and intelligent fashion, we can work to balance these competing interests—protecting physicians as much as possible while helping our society in time of medical need.

Crisis Plans and the Local Physician
Crisis plans have a role to play in these situations. The plans are constructed to facilitate

the logistical management of a medical crisis such as an emerging infectious disease. We hope the "worst-case" scenario never occurs, but if necessary, a crisis plan prepared in advance can be implemented. Most crisis plans are designed by the Centers for Disease Control, Red Cross, and other large government and private agencies so that central controlling agencies can coordinate a widespread effort. As a result, private practice physicians are not commonly involved with crisis planning, but when a potential crisis is on the horizon, medical professionals should contact the local authorities and make themselves available. Local physicians who know the city, the clinics, the hospitals, and other local professionals are invaluable for the coordination of care in an area facing a crisis such as the one described in this clinical case. As a primary care physician I can be available for triage, education, immunization, initial diagnoses, and primary treatment. Depending on training, physicians in other specialties can be available for consultations or secondary and tertiary care. If local physicians don't address medical needs, the severity of the crisis is exacerbated.

John Wadleigh, DO, is in private practice in family medicine in Tucson, Arizona. He is a graduate of Western University of Health Sciences, Pomona, California.

Related Articles

Duty to Treat versus Personal Safety, May 2004

The Proposed Model State Emergency Health Powers Act, May 2004

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 214-218.

Clinical Case

Changing the Rules in Times of Crisis: Do Desperate Times Allow Desperate Measures?

Commentary by Mona Loutfy, MD, MPH

Dr Meredith Green hadn't slept in 38 hours. An as-yet-unidentified respiratory virus had overloaded the medicine service at the hospital where she was on staff, and, if the news reports were any indication, there was no end in sight. Preliminary reports suggested the infection could be related to severe acute respiratory syndrome, or SARS, but global medical communication had so far failed to establish anything beyond the fact that the virus was highly contagious, with devastating mortality and morbidity statistics. Roughly 10 percent of those who acquired it would die while another 10 percent would suffer brain damage as a consequence of the raging fevers the disease induced. Neither statistic seemed to be affected by supportive measures, but at the moment nothing else could be done.

Bleary-eyed, Meredith almost didn't see the man waiting for her outside the room of one of her patients. "Dr Green, Dr Green," he said, a note of panic in his voice as he moved away from the wall against which he had been leaning. "Dr Green, I know everyone is doing all they can, but my wife is getting worse. She's delirious now, with that fever you were telling us about."

"I'm so sorry, Mr Patterson," Meredith said as she moved to open the door. "I need to examine her again and work on getting that fever down. We're doing everything we can to stabilize her condition."

"That's just it," Mr Patterson replied as he followed Meredith into the room. "I know how hard you're working, but this is my wife! She's never been sick like this ever. And we have 3 children at home—she just has to get better. I've been doing some reading and something called interferon seemed to help with SARS. Everyone keeps telling me this is like SARS, and even if it's not, interferon is a powerful antiviral medication, isn't it? It could work, couldn't it?"

Meredith stopped and turned back toward the door as she pulled on the gown and gloves of respiratory isolation. "Mr Patterson, I know you want your wife to get better," she said, "but we can't just start treating her with every antiviral in the pharmacy. Interferon is a powerful drug with many potential side effects. No one knows what it might do in a case like this or how it might react with the other medications your wife needs to keep her fever down. We can't start experimenting on patients to find out."

"But why not?" Mr Patterson asked. "Right now she's dying—you warned us about what a fever that high could mean. She's a fighter, my wife, and I know if she could talk to you she would want to try anything, even if it might not work. I know I want you to. If it gives her even a chance it's worth the risk—it can't be worse than dying, can it?"

"But Mr Patterson," Meredith started to say.

"Please, won't you try?" he interrupted. "She's dying! Can't you make an exception when someone is dying?"

Commentary

The situation in which Dr Green finds herself is a difficult one and, surprisingly, not that infrequent. The case highlights the basic principles of biomedical ethics—nonmaleficence, informed consent, benevolence—in a setting faced by health care professionals during the course of an infectious disease outbreak or a life-threatening illness or both. In analyzing this case, I write as the physician who first used interferon in those infected with the severe acute respiratory syndrome virus (SARS) in Toronto. As a specialist and researcher in infectious diseases, I was positioned both ethically and clinically to use an old drug—interferon—in a new disease—SARS—and to investigate the results in the best way possible.

Analyzing the Principles of Medical Ethics

On graduation day, the guiding principle of medicine we swear to uphold is nonmaleficence. As proud new physicians, we take an oath to do no harm. Nonmaleficence applies to the case of Mrs Patterson: her husband is asking the treating physician to use a drug that is experimental, has not been tested for the treatment of Mrs Patterson's disease, has significant side effects, and could worsen her condition. Before any decision is made, each of these factors must be taken into consideration, discussed with Mr Patterson, and explained thoroughly so that he understands them. This case is further complicated by the fact that the patient cannot give her informed consent, thus her husband would be making the decision for her. Could his judgment be clouded by emotions and not reflect his wife's true wishes?

This question leads into a second important principle of medical ethics: informed consent. In its most basic definition, informed consent reflects the right and responsibility of every competent individual to advance his or her welfare. This responsibility is exercised by voluntarily consenting to or refusing recommended medical procedures based on a sufficient knowledge of the benefits, burdens, and risks involved. The ability to give informed consent depends on 4 components: (1) adequate disclosure of information; (2) patient freedom of choice; (3) patient comprehension of information; and (4) patient capacity for decision making. If these 4 requirements are met, then the patient can be said to have made an informed decision. In the current case, the patient cannot give consent or make an informed decision; this task is left to her husband. How can he understand the risks of using interferon when there is no relevant scientific data available for Dr Green to discuss or explain? Can genuinely informed consent truly be obtained in this situation?

The third crucial principle of medical ethics is benevolence. For physicians, this encompasses doing everything in our power to help our patients by preventing death or improving quality of life or both. Under certain circumstances, benevolence can temporarily supersede informed consent; in an emergency situation, for example, it is acceptable to implement procedures such as transfusing blood without consent if a patient's life is in immediate danger. In this case, Mrs Patterson has a life-threatening illness for which there is no accepted therapy. In such an instance, should we not at least try *something,* even if that something is investigational or of little benefit, because the outcome is inevitable and in trying an experimental therapy at least the physicians and family members know that everything possible was tried?

This is a complex question to answer and a difficult decision to make. If the inevitable outcome for the patient without experimental treatment is death, and the experimental drug is one with which we are familiar because of its use in other disease states, it is possible that an experimental application may not harm the patient and might even be of clinical benefit. Such an application is also likely to have psychological benefits for the family. In this situation, some physicians might decide to try using an experimental agent. In practice, it is not uncommon for physicians to use drugs "off-label," that is, to prescribe them for uses not listed on the FDA-approved package insert. As an example, antiretroviral drugs are not labeled for use in postexposure prophylaxis, but we prescribe them to prevent HIV transmission after sexual contact even without experimental data to support this decision. I am neither endorsing nor countering such a decision, but simply pointing out that such use is not unique to Mrs Patterson's case.

The final ethical point that must be considered when evaluating this scenario relates to the challenge of doing research in an outbreak setting or in fatal diseases with low incidence and prevalence. It is very difficult to conduct research in these settings, and many clinicians and researchers suggest that it might be impossible. Yet I believe it is critical to carry out research under these circumstances. We will never answer some of the most difficult and important questions in medicine without doing research on the treatment of rare and potentially fatal diseases. The situation with SARS taught us that we need to be universally prepared to carry out large randomized controlled trials (RCTs) in an outbreak setting to answer questions of how best to treat emerging infectious diseases that may recur or spiral into a pandemic.

The Toronto Experience

During the Toronto SARS outbreak, I utilized interferon treatment in 19 patients, after having reviewed *in vitro* data showing that interferon had the best activity against the SARS-associated virus among a panel of antiviral compounds tested. Together with other researchers in the laboratory and in radiology, I worked to develop an *a priori,* unbiased methodology for examining patient responses to this investigational agent. I would not have tried using interferon without the implementation of such a pilot study.

Furthermore, approval for the use of interferon had to be obtained from Health Canada; this involved speaking with 2 immunologists to get scientific data indicating that it was sound to give interferon in these cases and that doing so would not worsen the disease. In addition, it was necessary to gain approval from the hospital ethics

committee, the pharmacy and therapeutics committee, and the management advisory committee. All of these tasks were carried out in 48 hours, prior to using an experimental drug in patients with a new disease. It is also important to note that, in addition to the regulatory details, I also discussed the risks, benefits, and experimental nature of this treatment with each of my patients. Considerable work and time goes into the use of an experimental drug in a new disease; understandably, in the clinical case depicted here, Mr Patterson might not appreciate or be aware of all these crucial procedures. Even if Dr Green does decide to use an experimental agent to treat Mrs Patterson, she will not do so without considerably more action than a detailed conversation with her patient's husband.

A Case Close to Home

Recently, I have had first-hand experience of this issue from the other side. My mother was diagnosed with amyotrophic lateral sclerosis (ALS), a fatal disease that led to her death a mere 10 months after diagnosis. Earlier in the year she was diagnosed, there was a landmark breakthrough in ALS research, which found that the use of ceftriaxone was effective at reversing the nerve damage in ALS in a mouse model. However, the human clinical trials would not start until the following year and then only in the United States, thereby precluding my mother from a study for possibly the most effective treatment for this horrible progressive disease. Like Mr Patterson, I was faced with the option of asking my mother's specialist to use an experimental drug in a disease where we knew the patient was going to die, regardless of possible intervention on our parts. I asked myself, what is the harm in using an experimental drug in this situation? What if the patient herself were asking for the drug and understood the risks and benefits? Should we preclude such a patient from trying an experimental drug when all other treatment options have been exhausted? Interferon and ceftriaxone are drugs we use quite often in clinical practice, so we know their side effects extremely well. Can I transfer that knowledge to another disease state and use these drugs off-label when they have not been thoroughly investigated for this disease state?

Conclusions

Although Mrs Patterson's case presents many challenges, it is one that most physicians are likely to face at some point during their careers. Thorough consideration of the guiding principles of nonmaleficence, informed consent, benevolence, and the ethics of sound research can help guide the ultimate decision of whether or not to use an experimental therapy under dire circumstances. In my view, experimental treatment should always be used in a research setting, not as a haphazard clinical guess. An "n-of-1" for the use of an experimental drug is of no benefit to the patient, the family, others suffering from the disease, or the community at large. If, for example, a patient's condition improves after an experimental drug was given, do we attribute this improvement to the drug or to the natural history of the disease? Without a carefully designed research study—even a pilot study designed on very short notice—such a question can never be answered. The results of this "n-of-1" case can give false hope to other patients and their families who may then attempt a desperate search for an unproven treatment. If an experimental drug is not used in a research setting, any clinical results are of no benefit to other individuals with the same disease or to society as a whole.

In the case of Mr and Mrs Patterson, the most useful course of action for Dr Green is to investigate the effects of interferon for the treatment of the emerging respiratory virus, possibly in a pilot study or in a similar scientific matter. However, the gold standard of assessing the ultimate efficacy of a drug is through a RCT. Every effort should be made to carry out such a trial, even in diseases that occur either in outbreaks or that are life-threatening with a low incidence and prevalence rate. The benefits of such research are incalculable.

Mona Loutfy, MD, MPH, is an assistant professor at the University of Toronto. She holds a medical degree from the University of Toronto and an MPH from Harvard's School of Public Health.

Related Article
Clinical Trials and End-of-Life Decision Making, November 2004

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 219-222.

Journal Discussion

SARS Revisited

by Anya Likhacheva

Tambyah PA. SARS: responding to an unknown virus. *Eur J Clin Microbiol Infect Dis.* 2004;23:589-595.

For many people, the mention of SARS—the acronym for sudden acute respiratory syndrome—still evokes the widely broadcast images of a sea of cotton masks in international airports. Three years ago this upper respiratory illness caused a health scare around the globe. Paul A. Tambyah, an associate professor in the Department of Medicine at the National University of Singapore and a specialist in infectious diseases, rightly hails the virus as the first emerging infectious disease of the 21st century in his article "SARS: Responding to an Unknown Virus" [1]. In this publication, Tambyah discusses the measures taken to analyze and to prevent the global spread of this novel coronavirus.

By 2004, SARS cases had slowed just as mysteriously as they had started in Guandong province of southern China 2 years earlier, in December of 2002. Yet the legacy of unanswered questions the pathogen left behind should keep scientists, public health officials, epidemiologists, and ethicists occupied for a long time to come [2]. Why, exactly, should we revive discussion if it is no longer a pressing threat? After all, the SARS death toll is relatively low with 812 deaths worldwide [3]. What's more, the looming H5N1 avian flu virus is currently front page news. Even so, the SARS epidemic should not be filed away without appreciation of the lessons it taught. Although short-lived, SARS forced us to face the unpleasant reality of global pandemics and to address the ethico-legal dilemmas that result from hasty public health measures.

Looking at the Response to SARS

Tambyah's analysis of the response to SARS exposes the prevailing sense of loss and urgency this epidemic produced. At the time of the first case reports, so little was known about the virulence, transmission, and treatment of the disease that the situation harkened back to the 1918 influenza pandemic. In this context, Tambyah emphasizes the magnitude of the collaborative effort between scientists and physicians across the globe to characterize and contain the unknown infection. Without question, the best ammunition of the 21st century—science and technology—was mobilized to first sequence the genome of the SARS coronavirus and then share the findings quickly and efficiently. But even as that was being done, descriptions of new cases flooded the Internet, and public health officials were at a loss about which restrictive measures to

impose. There was no way to detect the virus early in the course of the disease [3]. To this day, the nature of the mutation that made human-to-human transmission possible and the precise mode of that transmission remain a puzzle. In the end, containment was handled by tried-and-true public health tools. The use of personal protective equipment, careful grouping of SARS patients within hospitals, travel restrictions, isolation, and quarantine all contributed to the eventual control of the outbreak [4].

Do public health officials deserve a pat on the back for stopping a worldwide pandemic? Preventive measures were taken quickly in part due to advances in information technology, but in the end the public health approach was not novel. The sudden disappearance of SARS is not fully understood, thus the threat of its eventual reappearance is still a possibility. Furthermore, SARS may pale in comparison to new emerging diseases. The conventional public health tools that proved so useful during the SARS outbreak may fail as we face viruses such as avian flu, a pathogen with an efficient means of international transportation by way of migrating birds. The SARS outbreak gave us a sense of vulnerability; our present scientific knowledge of the virus should not lull us into a false sense of security.

Learning from SARS

The urgency with which the SARS outbreak was handled highlights the central tension between efforts to protect both public health and the right of individuals to privacy [5]. In many countries the epidemic was treated as a threat to national security, with measures taken accordingly. In Dr Tambyah's home country of Singapore, the military was given the task of contact-tracing [5]. In this setting, he describes a "tendency to overprotect" against a disease with an unknown mode of transmission and without a definitive diagnostic test. The confidentiality of the patient-physician relationship was breached when the names of so-called "super-spreaders" were made public [5]. Such public health measures become injurious when they ostracize individuals and promote ethnic, social, or geographic discrimination. But when *does* protection justify transgressing privacy? The appropriate balance between a nation's obligation to safeguard its citizens' health and those same citizens' right to privacy is, indeed, hard to achieve. Unfortunately, this problem will resurface again and again as we face new infections. In his conclusion, Tambyah questions whether quarantine is truly necessary if another SARS outbreak takes place and whether super-spreading events are a reality. In light of the arguments he presents, we can hope that public health officials will make every effort to protect patients' privacy and make the decision to breach it only when reduction in morbidity and mortality for the members of the community can be guaranteed.

The SARS epidemic also highlights a lack of sophistication with regard to travel restrictions and their infringement on travelers' civil rights. As discussed above, health officials did not have many tools at their disposal to contain this invisible threat. The World Health Organization (WHO) issued unprecedented travel advisories, recommending SARS screenings for all travelers departing from outbreak areas [5]. As it later turned out, close contact was probably needed for efficient transmission, but at the time thousands of people who had not had close contact with infected patients were quarantined [1]. This meant that healthy individuals who may or may not have been

exposed to SARS were detained. Taiwan placed a 10-day quarantine on all individuals returning from countries on the WHO list. Of the 80 813 individuals who were quarantined, only 1 person was found to have laboratory-confirmed SARS [5].

In the US, the Department of Homeland Security authorized immigration and customs officials to detain any individuals who appeared to be ill with SARS [5]. Considering that no efficient diagnostic tests existed at the time, anyone could have been lawfully detained without due process. There is no doubt that quarantine of high-risk close contacts helped prevent further transmission of the virus, but the quarantine of low-risk travelers may not have had any impact. As Tambyah points out, since widespread dissemination of SARS via international air routes has not been proven, there is no good reason for strict travel restrictions if or when SARS resurfaces [1]. Unfortunately, in an age when one can board a plane in Tokyo and arrive in Los Angeles in a matter of hours, exotic killer diseases will continue to be fought at the expense of the basic right of freedom of movement.

Conclusions

Tambyah offers a comprehensive view of an unprecedented approach to a world pandemic in the 21st century. His detailed analysis also exposes the awkwardness of public health measures when the epidemiology of a new infection is not yet known. The SARS outbreak has demonstrated that health problems halfway across the world are no longer isolated. Globalization of commerce and culture also paves the way for globalization of infectious disease. And when nations perceive international epidemics as a direct threat to their security and prosperity at home, privacy and certain civil rights get set aside. In the context of new and emerging diseases, the SARS outbreak challenges us to consider whether our fear of deadly infectious diseases has surpassed our faith in the remarkable advances of modern medicine. We must also recognize that the decisions made during health emergencies can and will generate multifaceted and complicated ethical and legal dilemmas. Yet, as Tambyah's article demonstrates, in considering the challenges of a past outbreak, we can better prepare as a profession for the challenges of the future.

Questions for Discussion

- How has the advancement of individual rights changed the way societies handle infectious disease outbreaks?
- What are the long-term implications of the fear and terror that tend to infiltrate the realm of public health when it comes to emerging infectious disease?

References

1. Tambyah PA. SARS: responding to an unknown virus. *Eur J Clin Microbiol Infect Dis.* 2004;23:589-595.
2. Yardley J. After its epidemic arrival, SARS vanishes. *New York Times.* May 15, 2005. Available at: http://www.nytimes.com/2005/05/15/health/15sars.html?ex=1143349200&en=220b704e741d344c&ei=5070. Accessed March 24, 2006.
3. Tambyah PA, 593.

4. Pang X, Zhu Z, Xu F, et al. Evaluation of control measures implemented in the severe acute respiratory syndrome outbreak in Beijing, 2003. *JAMA.* 2003;290:3215-3221.
5. Gostin L, Bayer R, Fairchild AL. Ethical and legal challenges posed by severe acute respiratory syndrome. *JAMA.* 2003;290:3229-3227.

Anya Likhacheva is a third-year medical student at the University of Arizona and was the 2003 Outstanding Senior of the Department of Molecular and Cellular Biology.

Related Articles
"I'm Sorry, but You Can't Leave": Patients, Physicians, and Quarantine, April 2006

The Ethics of Quarantine, November 2003

Virtual Mentor
Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 223-226.

Clinical Pearl
Surveillance of Infectious Diseases Is Information for Action
by Mark S. Dworkin, MD, MPHTM

Surveillance is defined as the "ongoing, systematic collection, analysis, and interpretation of outcome-specific data for use in the planning, implementation, and evaluation of public health practice" [1]. Despite the density of this definition, physicians must understand what it means if they are to contribute to the maintenance of public health. Surveillance is the foundation upon which many of the public health successes we enjoy today are based. For example, polio has been eliminated from the United States and is on its way to being eliminated globally. Surveillance data have guided policies and programs, helped to marshal limited resources, and moved the world toward completely eradicating this disease that caused human suffering for generations. Such data guided and then confirmed global eradication of smallpox. Those unfamiliar with collection and analysis of infectious disease data may think it is merely "bean counting," but it is a field of study where new and important trends are identified with local, national, and global significance.

Surveillance Overview
In the United States, the responsibility for disease surveillance is typically shared by health care professionals, public and private laboratories, local and state health departments, and public health officials from several governmental agencies and departments. Various systems have been developed to track disease in humans, in animals such as birds or horses, and in insect vectors such as mosquitoes. All of these systems are currently being used to monitor West Nile virus activity, for example [2]. Effective surveillance of disease in humans begins with the health care provider. The term "health care provider" is defined broadly in some jurisdictions and may include physicians, nurses, physician assistants, nurse practitioners, infection control practitioners, chiropractors, dentists, and others. Thus it is important for all physicians to know the guidelines governing surveillance [3]. It is the responsibility of health care personnel, with the help of public and private laboratories, to diagnose and report cases of notifiable infectious diseases.

State legislation or regulations mandate that health care providers and laboratories report confirmed or probable cases of notifiable infectious diseases to their local or state health department, or both. Diseases that are reportable are typically chosen for that status because notification of the local or state health department triggers an important action that needs to be performed. Hence, surveillance is information for action. States have their own public health laboratory(ies) that assist in infectious disease

monitoring activities by providing infrequently performed or expensive tests that might otherwise be unavailable at the local hospital.

Notification: the First Step

When a diagnosis of a reportable or "notifiable" infectious disease is made, physicians and other health care providers including infection control practitioners and hospital microbiology laboratories are required to notify their state health department by telephone, fax, mail, or by secure, Internet-based systems. A list of reportable conditions is usually readily available from local and state health departments. Reporting must occur within a determined time frame that varies for different diseases and is based on the immediacy of the need for the action. For example, when a diagnosis of invasive meningococcal disease occurs, the case typically must be reported within 24 hours so that prophylaxis can be promptly administered to close contacts and outbreaks can be quickly investigated to determine whether administration of meningococcal vaccine is needed. Alternatively, notification of a case of Hantavirus pulmonary syndrome does not require such an immediate response and, in the state of Illinois, may be reported within a 7-day time frame.

Those who investigate reports of notifiable diseases typically collect the minimum information needed to complete a basic investigation: patient name, patient demographics, and clinical history. Additional information is collected at the discretion of the state or local health department and varies with the disease in question. Reports of a vaccine-preventable illness might include details concerning the vaccination history of the patients involved. Reporting of a tick-borne disease might include a history of recent travel and participation in outdoor activities. Surveillance systems may be passive (provider initiated) or active (health department initiated). Active surveillance is typically superior to passive surveillance but involves additional cost and personnel time.

Data Evaluation

State health departments are responsible for assembling data collected from all local health jurisdictions. State agencies also do the following:

- Provide consultation or direct assistance to local jurisdictions when needed.
- Coordinate disease investigations when they involve more than one local health department's jurisdiction.
- Analyze disease-specific data.
- Disseminate the data to the stakeholders in the surveillance system.

Data summaries can be provided to a wide range of entities including health care institutions and nongovernmental agencies involved in health-related activities, legislators and other community leaders, federal agencies such as the Centers for Disease Control and Prevention (CDC), the United States Department of Agriculture (USDA), and the Food and Drug Administration (FDA). Compiled data can also be made available to the public.

Role of the Council of State and Territorial Epidemiologists

Standardized case definitions for each nationally notifiable disease are determined by the

Council of State and Territorial Epidemiologists, which meets annually. These definitions are periodically updated as new information becomes available [4]. States report their data on these conditions to the CDC where it is periodically analyzed and examined for trends, reported in the *Morbidity and Mortality Weekly Report*, and used for national prevention policy and planning. Other federal agencies also collect and review surveillance information. As an example, the USDA collects data on the presence of specific, confirmed clinical diseases in livestock, poultry, and aquaculture species from participating state veterinarians, while the FDA performs trace-back investigations to identify the source of contamination in reported food-borne disease outbreaks.

The Surveillance Ideal

Surveillance systems are intended to follow certain basic principles and are evaluated accordingly [5, 6]. Furthermore, surveillance should be reserved for conditions that have substantial public health consequences. Each system should have clearly defined objectives, and the actions taken in response to a reported case should be those considered useful for public health management. Surveillance systems should have simple case definitions, should not involve gathering difficult-to-access information, and should be flexible when new information is learned about a disease. Each system should also be sensitive enough to detect a high proportion of cases and to detect outbreaks (epidemics).

Surveillance systems must balance sensitivity (probability of a positive test among those with the disease) and specificity (probability of a negative test among those without the disease) in determining the parameters of disease reporting. An ideal system should have a high "predictive value positive," which means that the diagnostic criteria the system relies on would produce a majority of true-positive results rather than false positives; the person reported to have a given disease would actually have the disease, not a different condition with a similar pattern of clinical symptoms. For example, a botulism surveillance system that called for reporting of all patients with a hospital discharge diagnosis of paralysis would be very sensitive because nearly all hospitalized patients who truly had botulism would be reported. However, such a system would also lead to many reports of illnesses other than botulism and therefore have poor specificity and a low predictive value positive. Furthermore, each system should be representative so that it captures all cases, whether selection is based on demographics, clinical manifestation, or reporting sources. Finally, surveillance systems should have disease-specific reporting guidelines—immediate reporting for suspect bioterrorism outbreaks, for example—and realistic operating costs.

Legal Obligation to Report Notifiable Diseases

Typically, state laws mandate that physicians who are licensed to practice in a state learn which diseases are notifiable and the time frames within which they must be reported. The statutes and regulations that govern reporting often include language that imposes fines or imprisonment for failure to comply. Enforcement of such laws is rare, and underreporting is common. Understanding why surveillance is such a vital function of our public health system should help improve compliance. The implementation of electronic disease reporting systems throughout the United States will automate much

of the burden of infectious disease reporting, which should lead to more complete and timely reporting and improved recognition of outbreaks.

References

1. Thacker SB, Berkelman RL. Public health surveillance in the United States. *Epidemiol Rev.* 1988;10:164-190.
2. Huhn GD, Austin C, Langkop C, et al. The emergence of West Nile virus during a large outbreak— Illinois, 2002. *Am J Trop Med Hyg.* 2005;72:768-776.
3. Koo D, Caldwell B. The role of providers and health plans in infectious disease surveillance. *Eff Clin Pract.* 1999;2:247-252.
4. Council of State and Territorial Epidemiologists. *Position Statements for 2005*. Available at: http://www.cste.org/position%20statements/searchbyyear2005.asp. Accessed March 3, 2006.
5. Centers for Disease Control and Prevention. Updated guidelines for evaluating public health surveillance systems: recommendations from the guidelines working group. *MMWR.* 2001;50(No. RR-13):1-31.
6. Teutsch SM, Churchill RE, eds. *Principles and Practice of Public Health Surveillance.* New York, NY: Oxford University Press, Inc.; 2000.

Mark S. Dworkin, MD, MPHTM, is the state epidemiologist for infectious diseases and team leader for the Rapid Response Team at the Illinois Department of Public Health.

Virtual Mentor
Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 227-229.

Health Law
Is Mandatory Vaccination Legal in Time of Epidemic?
by Sarah Fujiwara

Imagine that Joseph Shoe, a 21-year-old student at a state university in Illinois, is spending 3 months in China for a summer study program abroad. While he is there, severe acute respiratory syndrome (SARS) breaks out in Canada and is traced back to China.

When SARS shows up in Canada, Illinois immediately creates a mandatory vaccine for all those who are currently in China or certain areas of Canada, or all those who plan to go there in the next few years. The new vaccination is commonly believed to be effective and is widely approved by the medical community. However, some in the medical community believe that the vaccination is worthless in preventing the spread of SARS and that it has injurious side effects.

Joseph feels confident that he will not contract SARS. He has been in China for a month, is perfectly healthy, and is not in the region of the outbreak. He is willing to submit to a physical but does not want the "experimental" vaccination and its side effects. He also feels that this mandatory vaccination affronts his bodily integrity and violates his 14th Amendment rights.

Discussion
The 14th Amendment asserts that no state shall make or enforce any law abridging the privileges or immunities of citizens of the United States or deprive any person of life, liberty, or property *without due process of the law* [1]. The Supreme Court recognizes a 14th-Amendment guaranty of substantive due process that protects US residents against arbitrary legislative actions; this constitutional guarantee requires that legislation not be unreasonable, arbitrary, or capricious and that it have a substantial relation to the legislative objective [2]. Essentially, though, this provision demands only minimal scrutiny or rational review of the enacted legislation; the law need only be rationally related to a legitimate government purpose to be declared constitutional. Further, the Supreme Court has recognized each state's "police power," which gives the state authority to enact health laws of every description, including quarantine and vaccination laws, to protect its citizens [2].

In 1905 the Supreme Court addressed mandatory vaccinations in regard to smallpox in *Jacobson v Massachusetts* [2]. There the Court ruled that the police power of a state absolutely included reasonable regulations established by legislature to protect public

health and safety [2]. Such regulations do not violate the 14th Amendment right to liberty because they fall within the many restraints to which every person is necessarily subjected for the common good [3]. Real liberty for all cannot exist if each individual is allowed to act without regard to the injury that his or her actions might cause others; liberty is constrained by law. The Court went on to determine in *Jacobson* that a state may require vaccination if the board of health deems it necessary for public health or safety [4].

When determining the legality of a statute enacted to protect public health and safety, the Court found it immaterial that a portion of the medical community thought the vaccination worthless or even injurious. The state has the right to choose between opposing medical theories and to refer the matter to a board composed of persons residing in the affected location who are qualified to make a determination. The courts do not become involved in legislation formed under the state's police power as long as it relates substantially to public health, morals, or safety and is not a plain, palpable invasion of rights secured by fundamental law [5]. Furthermore, it is immaterial whether or not the vaccine is actually effective, so long as it is the belief of state authorities that the mandatory vaccine will promote common welfare and is a reasonable and proper exercise of the police power [6]. It is of paramount necessity that a community have the right to protect itself from an epidemic of disease which threatens the safety of its members.

The Court decision in *Jacobson v Massachusetts* is just over 100 years old and has not been revisited in any meaningful way. The Court follows the doctrine of *stare decisis*, which directs it to follow existing judicial decisions when the same points arise in litigation unless there is sufficient justification for departing from precedent [7]. In this case the *Jacobson* Court's ruling has stood—not allowing a single individual to refuse vaccination while he or she remains within the general population on the grounds that to make such an exception would strip the legislative branch of its function to care for the public health and safety when threatened by epidemic disease [8]. This ruling prevails despite occasional injurious results from vaccinations and the impossibility of determining whether a particular person can be safely vaccinated. The only exception to a mandatory vaccination is an offer of apparent or reasonably certain proof to the state's board of health that the vaccination would seriously impair health or probably cause death [8].

Consequently, our student, Joseph, does not have a valid argument against the mandatory vaccination. It is established that vaccination to prevent an epidemic is well within the police powers of Illinois. Furthermore, he does not have a 14th Amendment liberty or due process argument because the vaccination is for the health and welfare of the state. Lastly, even if Joseph had a religious objection, it would most likely be dismissed because a compelling state interest may abridge religious freedom [9].

Questions for Discussion

1. In light of advances in preventing and treating infectious diseases, should there be more protection for individual liberty during disease outbreaks today than there was a century ago?

2. What sort of facts or background circumstances in a lawsuit might justify the Court's revisiting *Jacobson v Massachusetts*?
3. Who would be at fault if a vaccination administered to an individual in an epidemic causes that person's injury or death? What could this mean for the administering physician and the drug manufacturers?

Notes and References

1. US Const. Amend. XIV, §1.
2. *Jacobson v Massachusetts*, 197 US 11, 25 S Ct 358 (1905).
3. Ibid, 26.
4. Ibid, 27.
5. For instance, a state may abridge religious practices only when there is a compelling state interest and the law is substantially related to protecting this interest. Religious practices fall under strict scrutiny (as opposed to rational review), which is a higher standard of scrutiny because religious freedom is a fundamental right protected by the 1st Amendment. See for example, *McDaniel v Paty*, 435 US 618, 698 S Ct 1322 (1978).
6. *Jacobson*, 197 US, 35.
7. Black HC, Garner BA, eds. *Black's Law Dictionary*. 2nd pocket ed. St Paul, Minn: West Publishing Co.; 2001:661.
8. *Jacobson,* 197 US, 38.
9. See McDaniel, above. However, because the 1st Amendment receives strict scrutiny, the state would have to show that there is no other, less-intrusive method to accomplish their objective.

Sarah Fujiwara is a student at DePaul University College of Law and an intern at the American Medical Association during the spring 2006 semester.

Related Article

School Vaccination Laws, November 2003

Virtual Mentor
Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 230-234.

Policy Forum
Infectious Disease Research and Dual-Use Risk
by Maureen Kelley, PhD

The anthrax attacks in the United States in late 2001 served as a wake-up call for national security experts and reminded the scientific and medical communities that infectious disease outbreaks are not only caused by Mother Nature. One response to these attacks was to increase funding for research into infectious diseases, including select agents. Select agents are those biological agents and toxins that pose a potential threat to the public if deliberately or accidentally released [1]. Examples of select agents include the avian influenza virus, yellow fever virus, the pox viruses, the Marburg and Ebola viruses, the Japanese encephalitis virus, the anthrax bacillus, and the botulinum neurotoxins [2]. Yet conducting clinical and scientific research on select agents creates a serious ethical dilemma both for the researchers who use the agents and for the public; this situation is referred to as the dual-use risk.

The dual-use dilemma is this: in an effort to respond to existing and emerging infectious diseases, the same scientific information or products intended for good can also fall into the wrong hands and be used to threaten a population in an act of bioterrorism. All of the biological agents mentioned above exist in nature and either pose active infectious threats to large populations or could threaten wider populations in future natural outbreaks. Consequently, aggressive vaccine and treatment research is necessary to prevent and prepare for possible outbreaks. In the US, the Bioterrorism Preparedness and Response Act of 2002 was introduced to facilitate the development of new countermeasures to potential bioterrorist threats by accelerating development programs and stockpiling effective countermeasures [3]. By definition however, such research entails the use of live samples of an agent, inactive samples of an agent, or infected research animals. When reverse genetic engineering is used, genomic data for select organisms may be available and shared between investigators. Sometimes researchers will inadvertently create a more virulent strain of an organism while searching for mechanisms to disarm it or to create less virulent strains. Dual-use research may also make a nonpathogen virulent, create a strain that is resistant to antibiotics or antivirals, or develop a strain that is able to evade diagnosis [4]. Dual-use research thus presents several important problems in research ethics and public health policy.

Responsibility and Dual Use
At a fundamental level, dual use raises an old moral question in a new way. Should a person be held morally responsible for outcomes that are not intended and may be largely outside of her control? There are forward-looking and backward-looking

versions of this question. The backward-looking version arises when a negative outcome occurs and we wish to hold someone responsible, to lay blame, and to punish. The forward-looking version asks whether a person is morally bound to take preemptive precautions to avoid unwanted future outcomes. Recent public discussions about responsibility and dual-use research in the context of the bioterrorism threat resemble earlier moral debates in the history of science.

Both versions of the responsibility question were posed to Albert Einstein, Neils Bohr, and the other scientists of the Manhattan Project, first during the early work on atomic energy and then in the wake of the atomic bombing of Hiroshima and Nagasaki. Einstein and Bohr, in particular, struggled publicly and privately to sort out this question of personal responsibility. As Einstein said in an address at a Nobel Anniversary dinner, "Today, the physicists who participated in forging the most formidable and dangerous weapon of all time are harassed by an equal feeling of responsibility, not to say guilt" [5]. In the context of infectious disease treatment and vaccine development, if a researcher's intentions are good—to contribute to scientific progress or, in our case, to save lives in the event of an infectious disease outbreak—then how can we hold the researcher responsible for unintended and unforeseen malevolent use of the same scientific discovery?

We might ask whether the risk is truly unforeseen. We have some empirical evidence that the risk is probable, though the degree of probability is hard to estimate. We can look to the anthrax attacks in the US in 2001 and the sarin nerve gas attacks in Japan in 1995 as evidence of what is possible. And there are reports of terrorist groups' attempts to acquire the scientific expertise needed to carry out future attacks [6]. Research journal articles from the 1950s and 1960s that describe methods for isolating, culturing, identifying, and producing bacteria, including *Bacillus anthracis* were found in former terrorist camps in Afghanistan. Documents were also discovered there that outlined plans for recruiting individuals with PhD-level expertise and attending scientific symposia and conferences. The Japanese terrorist group Aum Shinrikyo, responsible for the 1995 attack on the Tokyo subway, has reportedly achieved a much more sophisticated level of weapons development and may be pursuing an independent bioweapons program in its own laboratories [6].

Although a large-scale biological attack has not yet occurred, reports like these raise valid concerns. If marginally skilled terrorists can accomplish bioweapons development with 50-year-old publications, what could expert terrorists accomplish using current findings and procedures? Given the possibility of the deliberate release of a select agent, one can reason from the public health perspective and argue that good intentions will not mitigate forward-looking responsibility for the consequences of malevolent applications of biodefense research. From the vantage point of ethical foresight, it would be irresponsible for the clinical and scientific communities not to anticipate this dual-use risk and seek preventive, protective measures that will minimize it.

Managing the Dual-Use Dilemma

The scientific community's response and that of US federal agencies to dual-use research are still evolving, but measures to date reveal a 2-pronged strategy: (1)

educating the scientific community, and (2) increasing security. To lay the groundwork for the first strategic arm, the US National Academy of Sciences published a detailed report that included recommendations for training molecular biologists and other researchers in the life sciences and educating laboratory staff about the risks of dual use [4]. A new advisory agency—the National Science Advisory Board for Biosecurity (NSABB)—has also been formed to oversee and guide the biosecurity response and the education effort. This advisory body is charged with developing a code of conduct that will help researchers in the life sciences to take preventive measures to minimize the risk that research organisms will be stolen or diverted for malevolent purposes [7].

Many universities and research centers are launching educational awareness initiatives aimed at clinical and scientific researchers in infectious diseases who work with select agents [8]. Better security measures will also be essential. This means more rigorous background checks for staff, graduate students, and faculty and tighter security for laboratories, stored samples, and research data. Most recently it has meant the expansion of the oversight role for Institutional Biosafety Committees, or IBCs. The details of IBC responsibilities in dual-use research are still being clarified, but IBCs will likely be asked to review research protocols on select agents, much in the way that institutional review boards oversee human subjects research. In the case of dual-use research, IBCs will be responsible for maintaining standards of biosafety and minimizing dual-use risk from within each research institution or university.

A Threat to Scientific Openness

The most controversial intervention in the name of biosecurity pertains to the publication of research data and methods. Until now, the editorial boards of medical and scientific journals have taken responsibility for judging, on a case-by-case basis, whether particular studies should be edited or withdrawn because the data or methods might aid terrorists. Within the last year, several controversial studies have caught the attention of the public, the scientific community, and NSABB.

In one case, the authors synthesized full-length poliovirus cDNA and then transcribed the artificial viral cDNA into viral RNA, thus making viral replication possible. The virus was then used to infect healthy cells to demonstrate that the artificial virus had the biochemical and pathogenic characteristics of the polio virus [9]. The publication of the study raised serious concerns that scientists were offering potential blueprints to terrorists for creating the same or similar viruses. Related concerns have been voiced about the online publication of genomic sequences. Genome analysis and nucleotide sequencing are important tools in the study of pathogenic microorganisms and in the development of diagnostic tools and vaccines [10].

Data sharing is central to the practice of science, but should the public have unrestricted access to information that might be used for malevolent purposes? What is the best way to monitor access without hampering free interchange and dialogue within the scientific community? Significantly restricting access to information in response to biosafety concerns could potentially have the dangerous effect of decreasing the transparency of scientific research to the wider public—an important feature of any citizen-supported institution in a liberal society.

Publication is the catalyst for many of the problems of security and responsibility discussed earlier. In cases where published data are available, or easier methods are already widely known, no benefit would come from censoring the scientific data. The tough case is novel information. Even in cases where novel methods are introduced, publication remains the primary means for scientists to share methods and results in the field of preventive measures and countermeasures.

Furthermore, excessive censorship and bureaucratic constraints on research and publication may have a chilling effect on select agent research. One way to balance intellectual freedom of publication and dual-use risk is to rely on existing institutional checks and balances. Editors can be trusted to exercise self-restraint in the publication of data and methods, with the aid of more detailed scientifically and ethically informed guidelines on dual-use risks. IBCs can serve as resources for scientists at the earlier stages of research, when they should be thinking ahead about potential dual-use concerns in publication. The paper might then be flagged when sent to editors, and consideration given to publishing partial data or methods, with complete methods available upon request for other investigators and research institutions.

These questions currently frame a heated debate within the scientific community, federal research oversight agencies, and, increasingly, the public media. As we work through the details of managing dual use, it is important to keep in mind the instrumental and symbolic value of transparency in research. Curtailing a terrorist's access to scientific research also curtails access by the general public and other scientists. Lack of transparency is, in that sense, a barrier to scientific progress. In light of the uneasy history of science, maintaining professionally significant transparency in politically charged areas of research such as biodefense is a prerequisite for building public trust. And public trust and awareness are central components in emergency preparedness.

The dual-use dilemma has yet to be resolved. The hope is that rigorous public dialogue and discussions within the scientific and medical communities will facilitate the development of educational guidelines, professional agreements, and institutional oversight that will provide reasonable safeguards against dual-use risk without unduly constraining the practice of infectious disease research aimed at the public good.

Notes and References

1. See the Centers for Disease Control and Prevention, Select Agent Program for the latest information on select agents. Available at: http://www.cdc.gov/od/sap/. Accessed March 16, 2006.
2. The official list of select agents is determined by Health and Human Services and USDA and can be found in US Federal Regulations: Agricultural Bioterrorism Act of 2002. *7 CFR Part 331* (2005); Possession use and transfer of select agents and toxins, *9 CFR Part 121* (2005); and HHS Final rule. Office of Inspector General. *42 CFR Part 73* (2005).
3. Bioterrorism Preparedness and Response Act, 42 USC 247d-6(h)(4) (2002).
4. National Academy of Sciences. Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology. *Biotechnology Research in an Age of*

Terrorism: Confronting the "Dual-use" Dilemma. Washington, DC: National Academies Press; 2004. Available at: http://fermat.nap.edu/books/0309089778/html. Accessed March 16, 2006.
5. Einstein A. *Ideas and Opinions*. New York, NY: Three Rivers Press; 1954:115.
6. Petro JB, Relman DA. Understanding threats to scientific openness. *Science.* 2003;302:1898.
7. For further information about NSABB, see: http://www.biosecurityboard.gov/.
8. For a publicly available training module on dual use, designed for graduate students and junior investigators, see: Southeast Regional Center of Excellence for Biodefense and Emerging Infections. The dual-use dilemma in biological research. In: *Core I. Policy, Ethics, and Law Core of the Southeast Regional Center of Excellence for Biodefense and Emerging Infections*. Available at: http://www.serceb.org/modules/serceb_cores/index.php?id=3. Accessed March 2, 2006.
9. Cello J, Paul AV, Wimmer E. Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template. *Science.* 2002;297:1016-1018.
10. Clayton RA, White O, Fraser CM. Findings emerging from complete microbial genome sequences. *Curr Opin Microbiol.* 1998;1:562-566.

Maureen Kelley, PhD, is assistant professor in the Philosophy Department and Sparkman Scholar in Global Health in the School of Public Health at the University of Alabama at Birmingham.

Related Article
Physician-Scientists and Social Responsibility, September 2004

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 235-240.

Policy Forum

Ethics of International Research: What Does Responsiveness Mean?

by Christine Grady, RN, PhD

International research is essential to understanding and ultimately controlling emerging and long-standing infectious diseases. Yet, such research, when sponsored by developed-world entities (both public and private) and conducted in the developing world, is beset with inherent and complex ethical issues. An overarching ethical concern is the possible exploitation of vulnerable individuals or populations through research. Avoiding exploitation, usually understood as an unfair distribution of benefits, may be more of a challenge in international than in domestic research because of background disparities in health, health resources, and power between developed and developing countries [1-3].

Basic Research Protections

The fundamental ethical concerns in international research are similar to those that arise in clinical research done anywhere. In all clinical research, people are asked to assume risk and inconvenience in the interest of advancing health-related knowledge that may benefit individuals and society as a whole. As a result these individuals may be susceptible to exploitation and harm. Codes of research ethics, regulations, laws, and norms that guide clinical research have been promulgated to minimize the possibility of exploitation by carefully protecting participant rights and welfare. Thorough independent review to assure the rigor of the research question and design, assessment of potential risks in relation to benefits and attention to minimizing risk, fair subject selection, and informed consent are widely recognized provisions for protecting research subjects [4-6].

Reasons for Concern

So why the concern about the ethics of international research? After all, such research advances understanding of prevention, diagnoses, and treatment of prevalent and devastating diseases including HIV, tuberculosis, malaria, schistosomiasis, and others; this information is vital for the health of people in developing countries, as well as for global health. First, the growth of international clinical research in recent years has been staggering. Escalating resources have been devoted to studying important global diseases like HIV/AIDS, malaria, and tuberculosis [7]. At the same time, pharmaceutical, biotechnology, and device manufacturers have dramatically increased outsourcing of drug and product research to the developing world, especially to countries in Southeast Asia, Latin America, and Eastern Europe [8]. These developments arouse concern because research participants and populations in

developing countries may be particularly vulnerable to exploitation due to poverty; illiteracy; limited resources, education, and access to health care; and lack of familiarity or experience with research.

Second, some argue that research sponsors conduct studies in the developing world that would be declared unethical in industrialized nations, thus establishing double standards [9]. According to this view, sponsors choose to do research in the developing world because it is less expensive, subject to fewer regulatory constraints, and provides access to large numbers of treatment-naïve patients, thus allowing investigators to get away with meeting lower standards.

Several thoughtful groups have grappled with how to minimize exploitation and the likelihood of double standards in international research [10, 11]. Among their recommendations, each says that clinical research should be responsive to the needs of the host country community and that the host community should benefit from the research. The President's National Bioethics Advisory Commission, for example, recommended in 2001 that, "clinical trials conducted in developing countries should be limited to those studies that are responsive to the health needs of the host country" [3]. The World Medical Association's 2000 version of the Declaration of Helsinki states, "Medical research is only justified if there is a reasonable likelihood that the populations in which research is carried out stand to benefit from the results of the research" [12]. The UK's Nuffield Council on Bioethics advises national priority-setting for health care research so that it will be, "easier for host countries to ensure that research proposed by external sponsors is appropriate and relevant to its national health care needs" [11]. In their international guidelines, the Council of International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization advises, "before undertaking research in a population or community with limited resources, the sponsor and investigator must make every effort to ensure that the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community" [11].

Ruth Macklin pointed out in 2001 that behind this apparent agreement about responsiveness and benefit, there are serious controversies and many unanswered questions [13]. After 5 more years of considerable debate and enormous research growth, these questions remain largely unanswered. What does it mean to be responsive to the health care needs of a population? How should populations benefit from research? Clear answers to these questions are critical if research guidelines and requirements are to truly protect against exploitation.

The Question of Responsiveness

The requirement to be responsive suggests that research should address a question that is relevant and important to a host country and that the answer should be of potential benefit to that country. Must research then be limited to investigating a disease or condition highly prevalent in the country from which subjects are to be recruited and one that has been identified by that country as a high priority? Certainly in a country

where malaria is prevalent and a major cause of mortality in children, a study of a less toxic malaria treatment or a strategy for preventing malaria seems responsive to an important health need. By this criterion, a malaria study could be judged more "responsive" than a study of breast cancer or depression. But it doesn't necessarily follow that a study of breast cancer in a developing country would be wrong, unethical, or exploitative. Disease prevalence or burden cannot be the only criterion for defining responsive research.

CIOMS noted that "it is not sufficient simply to determine that a disease is prevalent in the population and that new or further research is needed: the ethical requirement of "responsiveness" can be fulfilled only if successful interventions or other kinds of health benefits are made available to the population" [11]. Others agree that responsiveness includes assuring that research results or products proven effective are made available to and viable in the host country [12, 14]. Research results certainly should be made widely available in a way that maximizes their value and usefulness. Collaboration with host country researchers, institutions, health policy makers, community groups, and others throughout all stages of research will assure dissemination of results and assimilation of important new knowledge. In the case of research trials that demonstrate the efficacy of a drug or biologic, plans for making those products available and promoting their licensure and affordability may also be important.

But here the devil is in the details, and there appears to be considerable disagreement in determining how this should work. Is the sponsor, the host country government, or some combination with or without assistance from others, responsible for making products available? Does making a proven product "reasonably available" entail offering it for free, at an affordable price, or just assuring that it can be purchased within the country? Is the reasonable availability requirement satisfied by submitting research data to the relevant regulatory agency for licensure, by subsidizing the manufacture or distribution of the product in the host country, by transferring the technology to the developing country, or by something else? Research ethics committees, sponsors, ministries of health, and others who make decisions about the acceptability of research need clarification in order to apply such requirements appropriately and consistently.

Linking Benefits with Responsiveness

Some have argued that the attention to making research products "reasonably available" is misguided. If the goal is to minimize potential exploitation of research participants, benefits are clearly important, but what matters is the level, not the type, of benefit that participants receive [15, 16]. There are many kinds of possible benefits associated with clinical research:

- Therapeutic benefits to study participants
- Useful and generalizable knowledge for the community
- Infrastructure and capacity building
- The addition of needed public health measures
- Training of research and clinical staff
- Ancillary medical benefits to participants or others

- The post-trial benefit of new drugs and other products
- Economic benefits
- Increased business, employment

In an effort to establish a fair level of benefit in every case, the particular type of benefits provided during and after the study for participants or for their community might appropriately depend on the type of research, the needs and background circumstances of the population, and their well-considered preferences.

In one survey, investigators conducting research in developing countries overwhelmingly agreed that the study population should benefit from research, and more than half of those doing intervention studies said that the interventions would be provided to the research population or others after the study for a year or longer [17]. However, more than half of the respondents were conducting observational or descriptive studies—not intervention studies; focusing "responsiveness" on making products available provides no guidance about appropriate benefits for these studies.

If a community of potential participants were to decide that in exchange for research participation what they most needed and wanted were unrelated health benefits such as mass vaccination or a new clinic building, should that be disallowed because it was not a product of the research*?* In one example, community representatives of an Indonesian island lobbied their ethics committee to allow a study of a malaria prevention drug because they wanted the general health care services and treatment for malaria offered by the study that were otherwise unavailable to them. The drug being studied was intended for use by Western tourists visiting regions where malaria is endemic and would not be useful to the island population, according to a presentation by Reidar Lie November 16, 2005 at National Institutes of Health. Is this study responsive to the community's needs? Would it be unethical for the ethics committee to allow this study to go forward?

Responsiveness, especially as a counterbalance to possible exploitation, is inextricable from considerations of the value of a particular research study and the benefits to participants and communities. Answering a question of social, clinical, or scientific value is an ethical requirement for all clinical research [18]. Responsiveness assumes value but then builds upon it. If the goal of responsiveness is to reduce the possibility of exploitation by making the particular research exchange fair in terms of benefits, then benefits should be decided on a study-by-study basis, dependent on the type of research, predicted risks, anticipated benefits to the sponsors and investigators, and needs and preferences of the host community. Checks and balances are needed for this process in the form of transparency and other mechanisms to avoid the possibility that those in a disadvantaged position agree to less than they should. If, on the other hand, responsiveness is meant to refer to broader obligations of global justice, so that sponsors and investigators are limited to conducting clinical research that rectifies background injustices or changes social structures to reduce vulnerability to exploitation, the requirements for researchers and sponsors are very different, and remain unspecified [19].

Conclusions

In the end, perhaps responsiveness in international research is best accomplished not through further specification of responsibilities laid out in international guidelines but through respectful and close partnerships with host country investigators, communities, ethics committees, and policy makers. True partners are aware of, committed to, and respectful of host community values, needs, norms, and social practices. Such partnerships would promote clinical research that is both valuable and designed to answer questions deemed important by those involved, and would engage in negotiation about benefits openly determined to be fair.

Notes and References

1. Wertheimer A. *Exploitation*. Princeton, NJ: Princeton University Press; 1996.
2. Macklin R. Avoiding exploitation. In: *Double Standards in Medical Research in Developing Countries*. Cambridge, UK: Cambridge University Press; 2004:99-129.
3. National Bioethics Advisory Commission. *Ethical and Policy Issues in International Research: Clinical trials in Developing Countries*. Vol. I. Bethesda, Md: National Bioethics Advisory Commission; 2001. Available at: http://www.bioethics.gov/reports/past_commissions/nbac_international.pdf Accessed March 2, 2006.
4. *US Code of Federal Regulations*. Public welfare. Protection of human subjects. 45 CFR 46 (1991).
5. Emanuel E, Wendler D, Grady C. What makes clinical research ethical? *JAMA*. 2000;283:2701-2711.
6. Emanuel E, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? The benchmarks of ethical research. *J Infect Dis*. 2004;189:930-937.
7. The budget for international research of the National Institute of Allergy and Infectious Diseases, the NIH institute with the largest international portfolio, increased fourfold from approximately $100 million in 2000 to $400 million in the 2006 President's Budget. Information courtesy of Office of Financial Management. NIAID/NIH. Bethesda, Md; 2006. The Bill and Melinda Gates Foundation has spent more than $9 billion on global health since its inception in 2000, and part of their portfolio is research. Available at: http://www.gatesfoundation.org/MediaCenter/FactSheet/. Accessed February 20, 2006.
8. Getz K. A swift predominance of ex-US sites. *Applied Clinical Trials*. Available at: http://www.actmagazine.com/appliedclinicaltrials/article/articleDetail.jsp?id=261633. Accessed March 7, 2006.
9. Macklin R. *Double Standards in Medical Research in Developing Countries*. Cambridge, UK: Cambridge University Press; 2004:1-31.
10. Nuffield Council on Bioethics. *The Ethics of Research Related to Healthcare in Developing Countries*. London, UK: Nuffield Council on Bioethics; 2002. Available at: http://www.nuffieldbioethics.org/go/print/ourwork/developingcountries/introduction. Accessed February 28, 2006.
11. Council for International Organizations of Medical Sciences. *CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects. Geneva 2002*. Available at: http://www.cioms.ch/frame_guidelines_nov_2002.htm. Accessed March 30, 2006.

12. World Medical Association. *Declaration of Helsinki, Ethical Principles for Medical Research involving Human Subjects.* Principle 19. Available at: http://www.wma.net/e/ethicsunit/helsinki.htm. Accessed February 20, 2006.
13. Macklin R. After Helsinki: unresolved issues in international research. *Kennedy Inst Ethics J.* 2001; 11:17-36.
14. Shapiro H, Meslin E. Ethical issues in the design and conduct of clinical trials in developing countries. *N Engl J Med.* 2001;345:139-142.
15. Participants in the 2001 Conference on Ethical Issues of Research in Developing Countries. Fair benefits for research in developing countries. *Science.* 2002;298:2133-2134.
16. Participants in the 2001 Conference on Ethical Issues of Research in Developing Countries. Moral standards for research in developing countries: from reasonable availability to fair benefits. *Hastings Cent Rep.* 2004;34:17-27.
17. Kass N, Hyder A. Attitudes and experiences of U.S. and developing country investigators regarding human subjects regulations. In: *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries.* Volume II. Washington, DC: National Bioethics Advisory Commission; 2001:B-38-B-39.
18. Emanuel E, Wendler D, Grady C, 2703.
19. London A. Justice and the human development approach to international research. *Hastings Cent Rep.* 2005;35:24-37.

Christine Grady RN, PhD, is head of the Section on Human Subjects Research in the Department of Clinical Bioethics at the National Institutes of Health. She is a senior fellow at the Kennedy Institute of Ethics, a fellow of the American Academy of Nursing, and a fellow of the Hastings Center. Her research interests include human subjects recruitment and international research ethics.

The views expressed are those of the author and do not represent those of the NIH, the US PHS, or the Department of Health and Human Services.

The viewpoints expressed on this site are those of the authors and do not necessarily reflect the views and policies of the AMA.

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 241-244.

Policy Forum

Allocating Scarce Resources in a Pandemic: Ethical and Public Policy Dimensions

by Martin A. Strosberg, PhD, MPH

With avian flu popping up around the globe, federal, state, and local governments along with hospitals are now fully engaged in pandemic preparedness planning. Undoubtedly, considerations of the history of the 1918 Spanish flu gives these efforts a sense of urgency. A 1918-like pandemic, under a worst-case scenario, would hit large regions of the country at the same time, thus forcing local communities to rely on their own resources; the duration of active infections would be weeks or even months. However, Hurricane Katrina, deeply embedded in the American consciousness, must also inform our preparedness planning. We remember the spectacular failure of federal, state, and local governments despite years of anticipating the disaster. And we remember the disturbing images of the poorest and most vulnerable populations being left behind.

Katrina raised fundamental issues of social justice. It is clear that no amount of planning and preparation can undo the cumulative political, economic, and social inequalities faced by a population as reflected in inequitable access to health care services and disparities in health status. In a pandemic, society would again be allocating scarce, life-saving resources. Quite simply, the health care systems would be overwhelmed.

Beyond social justice and allocation of scarce resources, other important ethical concerns raised by the specter of pandemic include the challenges of balancing individual rights against the community's public health needs and obligating health professionals to provide care in the setting of a communicable disease outbreak. Bioethicists have urged that the consideration of these points be incorporated into an ethical framework that structures the planning process. For example, based on experience with severe acute respiratory syndrome (SARS), the University of Toronto Joint Centre for Bioethics Pandemic Influenza Working Group has proposed a framework in *Stand Guard for Thee: Ethical Considerations in Preparedness* [1].

Some Operational Aspects of Social Justice

The 3 major operational components of pandemic response are:
1. Surveillance and detection;
2. Containment, including isolation, quarantine, and mass dispensing of vaccine;
3. Medical management in the home, hospital, and transitional facilities.

In a variety of ways, the means by which pandemic response is carried out has the potential to disproportionately impact the poor and vulnerable. For example, extensive quarantine could lead to loss of income and other deprivations.

Of these components, the challenges of medical management are particularly troublesome. It is quite clear that hospital capacity cannot be sufficiently expanded to meet the surge in demand that would occur in the face of an influenza pandemic. Hospital beds, equipment, and staff—themselves at high risk—would all be in short supply. Taking care of patients in their homes as long as possible might be the only alternative.

In 1918, 3 generations of family members typically lived close to and could provide support for one other. This is not the case today. Consequently, in the setting of an epidemic we must plan to deploy homecare services. Since there would likely be a shortage of workers to provide these services, volunteers would need to be recruited and trained. Furthermore, special efforts would have to be made to reach low-income areas and vulnerable populations living in crowded inner city neighborhoods or dispersed in rural areas. Those without sufficient support to stay at home would need to go to transitional facilities with staffed and equipped beds; such facilities could also help relieve pressure on hospitals.

Rationing

Above and beyond implementing systems to deliver services to traditionally vulnerable and underserved populations, a key challenge would be the rationing of resources in absolute shortage: vaccines, antiviral medications, and intensive care unit (ICU) beds and ventilators. We have already conducted a dry run of vaccine rationing; in the 2004 influenza season, the nation faced a temporary shortage of vaccine. The Centers for Disease Control and Prevention (CDC) developed a prioritization plan geared to the needs of high-risk populations, such as people over 65 with comorbid conditions, and the protection of essential workers, namely doctors and nurses. The CDC, however, did not provide guidance on how to ration vaccines within broad priority groups or how to make tradeoffs among subgroups. By default, the responsibility for these decisions passed to the local regions that expected a worsening shortage. Fortunately, the 2004 influenza season did not fully materialize as anticipated and the crisis passed. For 2005, the CDC published a new vaccine prioritization plan. Once again, however, in the event of severe vaccine shortage the really tough decisions were to be made at subordinate levels of government.

When prevention has failed and treatment is necessary, use of ICUs and antiviral medication such as Tamiflu come into play. While there has been relatively little policy development on vaccine and antiviral medication prioritization, several professional associations have thought long and hard over the years about ICU admission-discharge decision making, alternately called allocation, rationing, or triage [2, 3]. All hospitals have ICU admission and discharge policies, but most have been reluctant to follow them when required to make decisions that might appear to diminish the standard of care. Yet in a pandemic, where there would be little opportunity to transfer a patient to another hospital or to stretch resources to accommodate just one more patient,

hospitals would have to make tradeoffs. Put most starkly, the question is should an ICU patient who could potentially be saved but still requires the investment of time and resources—namely staff and ventilator—be discharged to make way for a patient who could be treated more efficiently, that is, with fewer human and other resources? Or are there other criteria that could be useful in setting priorities?

Setting Priorities

There are many reasonable approaches for allocating scarce resources. With regard to vaccine administration, priority could be given to those at highest risk of dying, to children and young people, or to health workers and others who are crucial in maintaining essential societal services. Such a definition could include individuals representing police, fire, sanitation, public utilities, and certain governmental departments. Other approaches to vaccine rationing include a lottery and first-come, first-served models. Different stakeholders will bring different values to the mix; there is no overarching moral principle that informs priority setting [4]. Accordingly, the Pandemic Influenza Working Group at the University of Toronto Joint Centre for Bioethics suggests that a priority-setting process should be reasonable, open and transparent, inclusive, accountable, and responsive. It argues that the more these procedural characteristics are incorporated into the decision-making process, the better the chance of engendering community trust and compliance [1]. The Public Engagement Pilot Project on Pandemic Influenza is an example of a vaccine priority-setting exercise that effectively elicited input from various stakeholders including public health experts and a cross section of citizens, including minority groups [5].

Implementation: The Planning Challenge

Unfortunately, other than in the case of organ transplants, governments at all levels have had little experience in engaging stakeholders in priority setting, let alone in explicitly rationing lifesaving resources. Furthermore, local government and local institutions must bear the burden of implementing policies. Even if achieved, community consensus on priorities is not enough. Can the policies be feasibly operationalized in a crisis situation where decisions must be made promptly and where there would be little time to make fine distinctions within and among priority groupings? If not, the policies must be modified. Absent a real crisis, their feasibility can only be estimated through the pandemic preparedness planning process.

We should not underestimate just how daunting the planning task is, given the complexity of joint action among public and private sector entities at federal, state, and local levels. Even if we spend another 50 years in the current World Health Organization (WHO) pandemic alert phase 3—human infection but no human-to-human spread—we do not have the resources, the political will, or even the collective sense of urgency to complete the *WHO Checklist For Influenza Pandemic Preparedness Planning* [6]. Inevitably, many decisions would have to be made in real time on an ad hoc basis drawing upon the emergency powers of state and local government. Nevertheless, despite these challenges, one fact remains clear: the time to act is now if we are to avoid Katrina-like catastrophes later.

References
1. University of Toronto Joint Centre for Bioethics, Pandemic Influenza Working Group. *Stand on Guard for Thee: Ethical Considerations in Preparedness*. November, 2005. Available at: http://www.utoronto.ca/jcb/home/documents/pandemic.pdf. Accessed on March 14, 2006.
2. American Medical Association Council on Ethical and Judicial Affairs. Ethical considerations in the allocation of organs and other scarce medical resources among patients. *Arch Intern Med*. 1995;155:29-40.
3. American Thoracic Society. Fair allocation of intensive care unit resources. *Am J Respir Crit Care Med*. 1997;156:1282-1301. Erratum in: *Am J Respir Crit Care Med*. 1998;157:671.
4. Veatch RM. Disaster preparedness and triage: justice and the common good. *Mt Sinai J Med*. 2005;72:236-241. Available at: http://www.mssm.edu/msjournal/72/72_4_pages_236_241.pdf. Accessed on February 26, 2006.
5. Public Engagement Pilot Project on Pandemic Influenza. *Citizen Voices on Pandemic Flu Choices*. Washington, DC: National Academy Press; 2005. Available at: http://ppc.unl.edu/publications/documents/PEPPPI_FINALREPORT_DEC_2005.pdf. Accessed February 26, 2006.
6. World Health Organization, *WHO checklist for influenza pandemic preparedness planning, 2005*. Available at: http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_4/en/index.html. Accessed on February 26, 2006.
7. Centers for Disease Control and Prevention. Tiered use of inactivated influenza vaccine in the event of a vaccine shortage. *MMWR Weekly*. 2005;54:749-750. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5430a4.htm. Accessed on February 26, 2006.

Martin A. Strosberg, PhD, MPH, is professor of health care management at the Graduate College of Union University, Schenectady, NY, and professor of bioethics at the Alden March Bioethics Institute at Albany Medical College, Albany, NY.

Related Article
Disaster Triage, May 2004

Virtual Mentor
Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 245-250.

Medicine and Society
Malaria and Global Infectious Diseases: Why Should We Care?
by Sean C. Murphy

The morning after Ronald Ross confirmed that mosquitoes formed a critical link in the lifecycle of the malaria parasite, he wrote in his notebook:

> …I have found thy secret deeds
> Oh million-murdering Death.
> I know that this little thing
> A million men will save [1].

In the US and Europe, Ross's prediction has come true. Although 1 million malaria cases occurred annually in the US throughout the 1930s, today the disease is virtually nonexistent. The story of malaria eradication in the US recounts the development of our health care infrastructure and the success of public health programs. However, in the developing world where such advances are absent, malaria rages as one of the worst infectious killers. And yet malaria is by no means the only one. Infectious diseases are the leading cause of global morbidity and mortality [2]. The "big 3" pathogens—HIV, tuberculosis, and malaria—cause hundreds of millions of infections annually and collectively kill more than 5 million people each year, mostly in sub-Saharan Africa and Asia. The great travesty of these statistics is that all 3 "perpetual" epidemics are preventable and largely treatable. Why do preventable, treatable diseases continue to weigh heavily on the poor? What are the ethical implications for the medical profession and society when drastic health disparities are perpetuated? What arguments can be made for changing the status quo? Since the history of malaria encapsulates our failure to combat global health threats, it is worth exploring the above issues as they relate to malaria in particular and all "forgotten epidemics" in general.

Poverty and Health
Bacterial, viral, and parasitic diseases cause approximately 163 000 deaths in the developed world annually (mostly among the elderly and those with compromised immune systems) compared to 9.2 million deaths (mostly among children) in the developing world [3]. Communicable diseases cause 56 percent of deaths in the poorest fifth of the world compared to only 8 percent in the richest fifth [4]. Infectious diseases are the world's leading killers of children and young adults [5]. By every measurable health statistic, the developing world is at an extreme disadvantage in matters of infectious disease.

In addition to morbidity and mortality, infectious diseases are bidirectionally linked to poverty. Malaria has micro- and macroeconomic consequences for affected regions: decreased income, tourism, and foreign investment and increased health expenditures [6]. In contrast, areas that control malaria realize higher life expectancies and economic gains. Malarious countries face far more than the parasite itself; they must also grapple with limited access to essential medicines or health care, poor hygiene and sanitation, low subsistence incomes, limited education, and scant health information.

Unfortunately, the developed world has not committed to addressing these problems. Ninety percent of health care dollars treat a mere 10 percent of the world's population. This skew is reflected in pharmaceutical portfolios; only 13 of 1233 drugs licensed from 1975 to 1997 were approved for tropical diseases, despite the overwhelming burden imposed by these diseases [7]. Current antimalarial drugs are being rendered ineffective by parasite resistance. Without colonial interests to mandate tropical disease research, and with these diseases virtually eliminated from developed countries, governments have refocused their attention on health problems at home. Meanwhile, as "acceptable losses," millions continue to die from malaria and other infections, leaving us with intensifying disease burdens among the poor, limited interest among the rich, and a dangerous and ever-widening gap between these spheres. According to public health expert Paul Farmer, the world's double standard for health is the leading bioethical problem of our time [8].

History of Infectious Diseases and Bioethics

As a discipline, bioethics is just beginning to address the health disparities that keep malaria and other infectious epidemics embedded in the developing world. While HIV/AIDS has garnered the recent attention of ethicists, malaria and tuberculosis have seen almost zero interest [5]. As discussed by Selgelid, there are several reasons behind the overlooked problem of global infectious diseases [5]. First, bioethics was founded to deal with increasingly complex issues of modern medicine, epitomized most recently by debates over euthanasia, organ transplants and stem cell research [5, 8, 9]. These interests directed the attention of medical ethicists to people who receive care, leaving those who don't—in particular, citizens of developing countries—to be addressed primarily as research subjects [8]. Secondly, bioethics emerged during a period of naïve belief that infectious diseases would ultimately be eradicated. Third, infectious diseases are often considered problems of the "other"—Africans, homosexuals, or drug users, for example [10]. Thus, Selgelid believes practical and psychological factors led ethicists to concentrate on problems facing mainstream, domestic patients rather than those overseas [5].

Four Arguments for Action

Despite a lack of bioethics commentary on tropical diseases, there are at least 4 major reasons why fighting malaria and other microbes worldwide is a "win-win" situation for donor and recipient countries [5, 11-14]. The arguments appeal to different constituencies, but collectively they provide a compelling case for aggressively combating global infectious diseases. As outlined below, such actions could (1) ensure human rights through justice, (2) secure domestic health, (3) create economic prosperity, and (4) bolster security and peace.

Ensuring human rights through social and global justice. Basic health care, equality, and justice are essential human rights. While enshrined in the declarations of the United Nations and other global organizations, in practice these principles are often ignored. Wars, poverty, political corruption, and moral indifference all contribute to injustice and poor health. As one of the worst evils plaguing humanity, disease is something that domestic and international organizations should work to abolish [5, 9, 15, 16]. In the words of J. Dwyer, "the health of an individual may depend on particular susceptibilities or exposures; the health of a population often depends on justice" [17]. Thus a fair and just society must form institutions and programs to combat preventable and treatable diseases while also supporting and stimulating research on all diseases. In doing so, society may eliminate inequitable conditions, including the poverty brought on by poor health.

Securing domestic health. Beyond appeals to public morality, it is a universal reality that governments worldwide must face the challenges of protecting the health and welfare of their citizens and safeguarding military and economic interests abroad. This fact has historically been a major force behind public health research in wealthy nations. For example, the federal government led the effort to eradicate malaria from the continental US during the mid-1900s. Even so, US climates remain suitable for malaria transmission; recent case reports of malaria in Americans without a travel history indicate that US-based transmission can occur [18]. However, malaria is generally absent from the country today because modern infrastructures, public health institutions, and prompt medical treatment keep the pool of infected individuals far below the critical threshold necessary for endemic or even epidemic transmission, both of which occur in the world's poorer countries. Today, the intense desire to protect domestic health funds aggressive research on threats from biological weapons (smallpox, Ebola), pandemics (influenza, HIV/AIDS), and emerging diseases such as severe acute respiratory syndrome (SARS) and West Nile virus. Although no less significant, study of established diseases of the developing world is lacking, specifically research into malaria, tuberculosis, and most tropical diseases.

Creating economic prosperity. Disease control has economic benefits for both developed and developing nations. The "big 3" diseases alone can collectively reduce the gross domestic product of some African countries by more than 20 percent [19]. Historically, donations to developing nations were perceived to have little material benefit to donors. Such "win-lose" thinking put economic and human rights proponents at odds. If, however, the economic argument is viewed with "non-zero sum" thinking (ie, "win-win"), as Folch and colleagues propose, then there are mutual economic benefits to disease control [19]. Health programs reduce disease, a cause of poverty, in turn stimulating economic growth. Healthy populations can develop stronger market economies, providing a basis for a free, democratic society. Long-term benefits to donor nations include the development, diversification, and maintenance of new markets [19]. Public-private partnerships and guaranteed delivery-contingent purchases are being offered to pharmaceutical companies to provide further incentive to study malaria, a disease they have avoided historically due to high research risks and low expected profits. This argument requires long-term resolve by governments and

corporations to balance the considerable initial investments with the delayed (but substantial) payoff of improved health.

Bolstering security and peace. Like the previous argument, the health-security nexus is being re-examined in the post-Cold War era as a major link to social disintegration and political destabilization [20]. Poor health measures including high mortality and low life expectancy reliably predict social unrest [5]. Healthy populations are more politically stable, more peaceful, and more likely to have productive relationships with allies. They are also better able to depose tyrannical or corrupt leaders and move toward a free and fair democratic society. This argument has been used to support global HIV/AIDS programs, perhaps the most socially destabilizing infection in the world today. Yet malaria and other microbes, causes of poverty themselves, also threaten security. Coupled with previously discussed economic rationale, these analyses are currently the most politically persuasive justifications for combating global infectious diseases [11].

Moving Forward

Despite the many reasons to improve the health of the poor, there remains no perfect antidote. Short- and long-term health and development projects will need to draw upon time-tested public health interventions and existing drugs while continuing to search for the drugs and vaccines of the future. Health and public infrastructures must be built anew. Even with drastically increased funding, there is no guarantee that our approach will eliminate health and social disparities.

Tropical diseases have recently generated new interest from public and private donors. A worldwide pledge to fight the "big 3" infections was initiated through the Global Fund to Fight AIDS, Tuberculosis and Malaria. Additional support has come from the Bill and Melinda Gates Foundation and others. The World Health Organization has an on-going Global Roll Back Malaria Campaign, which aims to halve malaria-related mortality by 2010 through improving national control programs, international cooperation, and local support. However, monetary commitment to the greater goal of eliminating poverty still falls far short of its annual funding goal [21].

Role for Medical Students and Physicians

Medical students and physicians play many roles that directly and indirectly impact patients, politics, and the poor. There is an urgent need for physicians to attend directly to the world's poor, and some even propose that medicine as a "vocation" demands this focus [8]. Medical schools can ensure that their graduates develop expertise and an appreciation of both foreign and domestic medical challenges. In addition to direct care, physicians need to be activists and advocates who teach and motivate, so that preventable, treatable diseases will no longer dominate the developing world. Physicians must lobby lawmakers and other institutions to ensure adequate funding for scientific research and public health programs. As medical students and physicians, we pledge to "do no harm." However, inaction toward the needs of the global poor, sick, and vulnerable is irresponsible and harmful. By addressing perpetual epidemics such as malaria, we begin to rectify health disparities that have become an unacceptable norm. There are plenty of reasons to act now, and all physicians can and should participate in this process of securing health and equality worldwide.

References

1. Ross R. *Memoirs, With a Full Account of The Great Malaria Problem and Its Solution.* London, UK: J. Murray; 1923:226.
2. Guerrant RL. Why America must care about tropical medicine: threats to global health and security from tropical infectious diseases. *Am J Trop Med Hyg.* 1998;59:3-16.
3. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet.* 1997;349:1269-1276.
4. Gwatkin DR. Global burden of disease [letter; comment]. *Lancet.* 1997;350:141-145.
5. Selgelid MJ. Ethics and infectious disease. *Bioethics.* 2005;19:272-289.
6. Gallup JL, Sachs JD. The economic burden of malaria. *Am J Trop Med Hyg.* 2001;64:85-96.
7. Trouiller P. Drug development outcomes for tropical diseases: 1975-1997. Paper presented at: Médecins sans Frontières/World Health Organization Workshop. Drugs for Communicable Diseases, Stimulating Development and Securing Availability; October 1999; Paris, France. Available at: http://www.accessmed-msf.org/prod/publications.asp?scntid=592001159122&contenttype=PARA&). Accessed February 28, 2006.
8. Farmer P. *Pathologies of Power: Health, Human Rights And The New War On the Poor.* Berkeley: University of California Press; 2004.
9. Dwyer J. Teaching global bioethics. *Bioethics.* 2003;17:432-446.
10. Joffe H. *Risk and "the Other."* Port Chester, NY: Cambridge University Press; 1999:37-55.
11. Fauci A. International health and tropical disease research: an NIAID perspective. Paper presented at: American Society of Tropical Medicine and Hygiene Washington Annual Meeting; Dec 11, 2005; Washington, DC.
12. Fauci AS. Emerging and reemerging infectious diseases: the perpetual challenge. *Acad Med.* 2005;80:1079-1085.
13. Lee J. Science and the health of the poor [editorial]. *Bull World Health Org.* 2003;81:473.
14. Mills A, Shillcutt S. Communicable diseases. In: Lomborg B, ed. *Global Crises, Global Solutions*. New York, NY: Cambridge University Press; 2004: 62-114.
15. Dwyer J, Global health and justice. *Bioethics.* 2005;19:460-475.
16. Rawls J, *The Law of Peoples*. Cambridge, Mass: Harvard University Press; 1999.
17. Dwyer J, *Global Health*, 463.
18. Iftikhar SA, Roistacher K. Indigenous Plasmodium falciparum malaria in Queens, NY. *Arch Intern Med.* 1995;155:1099-1101.
19. Folch E, Hernandez I, Barragan M, Franco-Paredes C. Infectious diseases, non-zero-sum thinking, and the developing world. *Am J Med Sci.* 2003;326:66-72.
20. United States Central Intelligence Agency. *The Global Infectious Disease Threat and its Implications for the United States. NIE-99-17D.* Available at: http://www.cia.gov/cia/reports/nie/report/nie99-17d.html. Accessed February 28, 2006.
21. Sachs J. *The End of Poverty: Economic Possibilities for Our Time.* New York, NY: Penguin Group; 2005.

Sean C. Murphy is an MD-PhD candidate at the Feinberg School of Medicine of Northwestern University in Chicago.

Related Article
Global Health Equity, April 2004

The viewpoints expressed on this site are those of the authors and do not necessarily reflect the views and policies of the AMA.

Virtual Mentor
Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 251-255.

Medicine and Society
Twin Epidemics of Multidrug-Resistant Tuberculosis: Russia and New York City
by Alison Bickford

Tuberculosis is currently one of the leading infectious causes of death in the world, with more than one third of the world's population infected and 8 million new cases each year, resulting in approximately 2 million deaths [1]. It is astonishing to think that only 20 years ago eradication of this disease seemed to be right around the corner. In 1953, shortly after the development of the powerful antibiotic isoniazid for treatment of tuberculosis, the number of cases in the United States began to drop. The United States Congress ceased direct government funding for the tuberculosis programs in 1972, and funding nationwide for prevention, screening, and treatment of the disease was greatly reduced. By 1985, the number of tuberculosis cases had reached an all-time low [2]. Tuberculosis was considered no longer a threat to public health.

Evolving Epidemics
In 1986 the number of new tuberculosis cases in the United States suddenly began to climb. At the same time, a similar phenomenon occurred in the Soviet Union: rates of tuberculosis, also at an all-time low, suddenly began increasing. By the early 1990s, both Russia and New York City had serious problems on their hands.

The factors contributing to these epidemics were remarkably similar in both locations. Russia and the United States had simultaneously decreased funding for programs designed to screen, diagnose, and treat tuberculosis. The transmission of TB is greatly influenced by social factors, and the collapse of the Soviet Union in 1990 with the resulting increase in homelessness, poverty, unemployment, and alcohol abuse facilitated the spread of tuberculosis in Russia. Russia's prisons began to fill with young men who had committed property crimes until the rate of incarceration stood second only to that of the United States [3]. Such overcrowded prisons filled with undernourished men became hot spots for tuberculosis transmission.

New York City, too, was experiencing all-time highs of homelessness, overcrowding, unemployment, and poverty. The newly declared "War on Drugs" filled New York City's prisons with homeless, unemployed, and TB-susceptible men. New York's large immigrant population and increasing rates of HIV infection also added to the quick rise in cases of tuberculosis: many immigrants brought latent tuberculosis with them and developed active disease in the harsh conditions of immigrant life in New York City. Furthermore, HIV infection predisposes an individual to contract tuberculosis and

allows for higher levels of active disease; HIV infection increases the efficiency of tuberculosis as well [4].

By 1993, the World Health Organization declared tuberculosis a global health emergency. It adopted a program developed 20 years earlier by the International Union Against Tuberculosis and Lung Disease (IUATLD) called DOTS, an acronym for Directly Observed Therapy Short Course. The DOTS program has 5 main principles, one of which involves ensuring—literally by direct observation—that each patient takes medication daily. The other principles include sputum smears to test for active pulmonary disease; administration of first-line tuberculosis drugs for 6 months; complete, standardized records of patients and outcomes; and political involvement in patient treatment [5]. Although the program has its flaws and limitations, DOTS should be enormously effective against normal strains of tuberculosis.

Neither Russia nor New York City was experiencing an epidemic of normal tuberculosis. Sporadic and inadequate treatment of patients during the 1970s and 1980s had led to strains of tuberculosis that were resistant to the standard first-line medications—the treatments used in the DOTS program. This distinguished these 2 tuberculosis epidemics from the more persistent and drug-sensitive tuberculosis in Eastern Asia and Africa. Tuberculosis resistant to 2 or more of these first-line drugs—usually isoniazid and rifampin—is classified as multidrug-resistant tuberculosis (MDR-TB). In both Russia and New York, single-drug-resistant tuberculosis and MDR-TB rapidly spread in overcrowded prisons and hospitals that were unprepared for highly infectious patients.

A Tale of 2 Responses

Here the similar stories began to diverge. In New York City, the biggest city in one of the wealthiest countries in the world, a tuberculosis task force was quickly mobilized. Screening, diagnosis, and treatment were provided free of charge. Infectious patients were isolated and nonadherent patients were detained to decrease the development and spread of MDR-TB. When an individual was found to have tuberculosis, the strain was identified and tested for drug resistance, so that the patient could be treated accordingly with second-line drugs [4]. Between 1996 and 2000, 80 percent of New York City's infected patients received the treatment they needed [6].

Not so in Russia and the other countries of the former Soviet Union. These impoverished countries with collapsed infrastructures did not have the resources to mobilize forces against this epidemic of drug-resistant disease. Although doctors in the Soviet Union had previously recognized and treated drug-resistant tuberculosis, medications and resources were in short supply in the 1990s. Russia became heavily dependent on international aid organizations for financial resources and tuberculosis medicines [7]. But international aid organizations were only interested in treating tuberculosis with DOTS. And DOTS was ineffective for MDR-TB.

In fact, DOTS was a spectacular failure in Russia, with cures reported in less than half of all treated patients [7]. This was due not only to high levels of MDR-TB but also to low rates of DOTS coverage because of opposition to the program from policy makers,

clinicians, and patients [8]. Tuberculosis became the leading cause of death in Russian prisons [7].

In 2002, the Green Light Committee (GLC) was established by the World Health Organization to increase access to treatment for MDR-TB. Reducing costs of second-line drugs has made treatment both feasible and cost-effective [9]. Finally, patients in Russia and all over the world are getting the treatment that was available to wealthier countries years before.

Global Implications

No one knows exactly how many cases of MDR-TB exist in the world, but it is estimated that right now 4 percent of tuberculosis cases are resistant to at least one drug. In 2001, approximately 17-25 percent of cases were classified as drug-resistant in Russia. In the penitentiary system, the percentages were much higher: 35-44 percent resistant, and 15-22 percent resistant to 2 or more drugs [3]. Incidence rates of tuberculosis are now falling in Russia and Eastern Europe, but it is difficult to know whether to attribute this downturn to effective treatment or to a general improvement in social factors leading to a decreased susceptibility in the population [5].

Debate continues about the value of testing for and treating patients with MDR-TB in developing countries. Testing for drug resistance requires time and equipment; second-line drugs are considerably more expensive than the first-line drugs, and the treatment course is prolonged from 6 months to 2 years. Some opponents argue that the extra cost of these treatments could be better spent increasing access to first-line treatments [9].

But MDR-TB, by definition, does not respond to the first-line treatments used in the DOTS program. Although cases of tuberculosis can conceivably resolve on their own, a decision not to treat MDR-TB because of the cost of testing or of the drug regimen often amounts to a death sentence for the person suffering from the infection. Furthermore, patients with untreated, active MDR-TB continue to spread their disease within their own families and communities. If they receive ineffective treatment with the cheaper first-line drugs, increased drug resistance may develop thus worsening the cycle.

The control of tuberculosis raises many ethical questions, including the allocation of resources; the dispute between a patient's right to refuse treatment and the protection of the community; and the care of those on the fringes of society, including the homeless, drug and alcohol abusers, and prisoners. One obvious question posed by the twin tuberculosis epidemics in New York City and Russia was whether or not we should use finite financial resources to provide costly treatments to a minority of patients. Is it worthwhile or cost-effective to treat MDR-TB? From both ethical and public health perspectives it is clear that MDR-TB must be detected and treated in poorer countries as it is in wealthier countries, a conclusion that has implications for the treatment of HIV in poor and developing countries [10]. It is also apparent that tuberculosis (like other infectious diseases) will not be eradicated until predisposing social factors like poverty, homelessness, malnutrition, and unemployment are mitigated.

Another lesson learned from these twin epidemics is that we cannot let our guard down when an infectious disease appears to be easily treated or virtually eradicated. Decreased vigilance and lack of funding for tuberculosis prevention and treatment were clear precursors to the epidemics in Russia and New York City. The rate of new cases of tuberculosis in Russia may be on the decline, but efforts cannot be reduced. As more patients receive treatment with second-line drugs, resistance to these drugs will increase, and new antibiotics will have to be developed and distributed to prevent a new, untreatable epidemic. Vigilance must be maintained in the United States as well: although New York is no longer a hot spot for tuberculosis, many citizens exposed to the disease in the 1990s still harbor latent infections that could be activated at any time. As long as tuberculosis exists in the world, immigrants and travelers will bring disease across international borders. It cost approximately $1 billion to quash the burgeoning epidemic in New York City—a financial burden that could have been avoided with continued screening and careful monitoring of patients taking tuberculosis medications [11].

References

1. Small PM, Fujiwara PI. Management of tuberculosis in the United States. *N Engl J Med.* 2001;345:189-200.
2. Tiruviluamala P, Reichman LB. Tuberculosis. *Annu Rev Public Health.* 2002;23:403-426.
3. Yerokhin VV, Punga VV, Rybka LN. Tuberculosis in Russia and the problem of multiple drug resistance. *Ann NY Acad Sci.* 2001;953:133-137.
4. Paolo WF Jr, Nosanchuk JD. Tuberculosis in New York City: recent lessons and a look ahead. *Lancet Infect Dis.* 2004;4:287-293.
5. Dye C, Watt CJ, Bleed DM, Hosseini SM, Raviglione MC. Evolution of tuberculosis control and prospects for reducing tuberculosis incidence, prevalence, and deaths globally. *JAMA.* 2005;293:2767-2775.
6. Murray JF. A century of tuberculosis. *Am J Respir Crit Care Med.* 2004;169:1181-1187.
7. Farmer P, Campos NG. Rethinking medical ethics: a view from below. *Developing World Bioeth.* 2004;4:17-41.
8. Atun RA, Samyshkin YA, Drobniewski F, et al. Barriers to sustainable tuberculosis control in the Russian Federation health system. *Bull World Health Organ.* 2005;83:217-223.
9. Mukherjee JS, Rich ML, Socci AR, et al. Programmes and principles in treatment of multidrug resistant tuberculosis. *Lancet.* 2004;363:474-481.
10. Kim JY, Shakow A, Mate K, Vanderwarker C, Gupta R, Farmer P. Limited good and limited vision: multidrug-resistant tuberculosis and global health policy. *Soc Sci Med.* 2005;61:847-859.
11. Gupta R, Irwin A, Raviglione MC, Kim JY. Scaling-up treatment for HIV/AIDS: lessons learned from multidrug-resistant tuberculosis. *Lancet.* 2004;363:320-324.

Alison Bickford is a third-year student in the Medical Scientist Training Program (MD-PhD) at Northwestern University's Feinberg School of Medicine.

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 256-260.

History of Medicine

Fourteenth-Century England, Medical Ethics, and the Plague

by Jessica Mellinger, MPhil

In the 20th and 21st centuries, human immunodeficiency virus (HIV), severe acute respiratory syndrome (SARS), and the threat of bioterror attacks have raised questions about the role of the physician in response to epidemics. Modern medical ethics, with its precepts of beneficence, nonmaleficence, and respect for patient autonomy, focuses almost exclusively on the relationship between the doctor and patient. As a result, this ethical framework is less well-equipped to deal with the relationship of the physician to society as a whole. Personal autonomy is often at odds with public health ethics, which stress the needs of the population over the needs of the individual.

The emphasis on the personal over the public applies to physicians as well as to their patients. Indeed, in the face of modern epidemics, the concept of a "duty-to-treat"—although explicitly and forcefully stated in the professional codes of the 19th and early 20th centuries—has been in conflict with a physician's autonomy in determining whom he or she will treat [1].

While the ethical challenges of today may be new, the threat of epidemic is not. It was present when, in 1354, Henry, first Duke of Lancaster and grandfather of Henry IV, began writing a devotional treatise. Composed of daily entries, *Le Livre de Seyntz Medicines* (*The Book of Holy Medicine*) is unique among medieval devotional literature in that it contains the most extensive known use of medical metaphors and imagery to describe religious experience. The book is a catalogue of Henry's sins, expressed as various wounds and diseases, followed by a similar account of spiritual remedies in the form of common medieval medical treatments [2]. What ultimately moved Henry to write this work remains a mystery, but coming so soon after the first arrival of the Black Death in England in 1347, it is not hard to imagine that the swift and devastating mortality of the disease made an impact.

Life in a Time of Sudden Death

The first wave of the Black Death occurred between 1347 and 1351, arriving most likely from China, and killing approximately one quarter to one third of the European population within 2 years [3]. In some locations, historians estimate that as much as 60 percent of the population died. After this first onslaught, the plague remained endemic for the next 300 years, returning every so often to cull the population. While epidemics such as the Black Death were dramatic in their devastation, medieval life was accompanied by the constant fear of death. Even without the plague, the average life

expectancy for women was about 29 years and for men, only 28. In such harsh times, the greatest fear of all was *mors improvisa*, an unexpected death coming before confession and forgiveness of sin [4]. This fear only increased during the plague when hundreds of thousands of people sickened and died, often within just a few days. It was also this fear which "gave rise to a genre of devotional literature designed to inspire good works and foster an appropriate sense of contrition in the reader" [5].

Henry's text is one example of confessional works designed to invoke contrition. The first half of the *Book of Holy Medicine* is devoted to descriptions of his sins as wounds that afflict various parts of his body—the head, eyes, ears, nose, mouth, hands, and heart. Henry portrays himself as the patient and Christ as the physician. In one passage, he describes his sin as an open wound that needs treatment, saying,

"I could have helped myself and cut off the [festering] limb by true confession and repentance of the heart…I should have chastened my flesh and cut away, not only the fire of sin, but the heat of the flesh by abstinence and other hardships, so that the fire's passage would have been cut off, so that it could have gone no further" [6].

In addition to spiritual healing, as a nobleman Henry of Lancaster would have had access to the best medical care, even though it would have been of little help in the face of the plague. In addition, the accidents, injuries, and diseases responsible for the short life spans of the time were largely beyond the scope of the medieval medical practitioner to cure. As a result, medieval physicians focused largely on prevention.

Medicine during the Middle Ages was conducted by a wide variety of practitioners, ranging from herbalists and conjurers to surgeons and university-trained physicians. Though there were some differences between medical training in Oxford and in Europe, they were largely similar with emphasis placed on theology and liberal arts for the first 7 years, followed by 3 additional years of study to obtain an "MD degree" [7]. Liberal arts training included the *trivium*(grammar, logic, and rhetoric) and the *quadrivium* (mathematics, music, geometry, and astronomy). As reflected in the *trivium*, reasoning, discussion, and debate were the skills most important to be learned. Further medical training was largely provided by set texts, mainly classic medical authors including Avicenna and Galen [7]. Some universities required clinical training with a physician (to be arranged by the student) and still others, particularly in Bologna and Montpelier in the early to mid-1300s, required attendance at an anatomical dissection. But the basis of becoming a physician rested on one's ability to know the reasons for sickness and to know how illness fit into an intellectual theory about health. It was this intellectualism that was critical to distinguishing "the learned physician who knew the reasons for things [from] the hireling with a knack for healing" [7]. Many physicians had taken holy orders of some kind [8].

Surgery was a distinctly separate and, for the most part, lesser craft and was not widely practiced by physicians, owing in part to the manual labor necessary to perform it as well as to the blood loss inherent to the process. In fact, papal bull forbade clergymen from shedding blood for any reason, including surgical procedures. Following ancient Greek medical theories, university-educated physicians subscribed to the humoral

theory of illness and strove to treat disease first by placing it within the appropriate intellectual framework and then by balancing the humors—phlegm (phlegmatic), black bile (melancholic), yellow bile (choleric), and blood (sanguine)—often through purgatives and enemas [4, 5].

When Henry of Lancaster began writing his treatise, little was known about how the plague was spread. Multiple theories of its cause were held, from God's vengeance to contagion to the established medical view that an individual's susceptibility to plague stemmed from personal imbalance of humors [9]. Physicians stepped into the breach to provide support, medical advice and even spiritual counsel for those wealthy patients who could afford a full-time physician [4]. But, were physicians obligated by any overarching principles of professional ethics to treat the sick during this time of epidemic? Do today's discussions of personal autonomy or public health ethics have any precedent in the deadly epidemics of the past?

The Medieval Profession of Medicine

In an attempt to discover ethical codes throughout history, some ethicists have proposed at least 3 conditions necessary for the development of a duty-to-treat ethic [1]. First, physicians would have had to recognize that they were at risk of becoming infected. Theories of contagion and polluted air as causative of disease were present in medieval times and gave rise to the prescription of strong smelling herbs and fumigation with pungent woods as ways to ward off plague [3]. However, the theory of infection and the identification of microorganisms would come many years later. Lacking effective treatments, physicians recommended personal hygiene (such as it was) and well-being as the cornerstones of prevention, with an emphasis on dietary prescriptions to balance the humors.

Second, establishment of a professional ethical code for epidemics requires an organized profession of medicine. With its multiple unlicensed practitioners, the practice of medicine during the mid-14th century was far from organized. The cohesive medical profession we know today simply did not exist in the Middle Ages—"Brewers who practiced surgery, abbots who delivered babies, friars who wrote medical books, a chancellor of the exchequer who doctored the king, a Cisterician surgeon—all were involved in healing, and all were involved in other pursuits" [10].

While the Hippocratic Oath was certainly known to medieval physicians, there is little evidence that it substantially influenced their practice [11]. The ethical principles of beneficence and nonmaleficence have been found in Hippocratic writings, although the actual precept of *primum non nocere* cannot be directly attributed to Hippocrates despite many attempts to do so [12]. Furthermore, the Hippocratic Oath did not set forth ethical principles for the event of an epidemic but focused instead on the patient-physician relationship. And even these principles were not universally acknowledged; during the medieval plague years, the prevailing wisdom was simple: "flee early, flee far, and return late" [13]. It has been noted that something of a duty-to-treat ethic did exist during this time, but it stemmed from the powerful Christian virtues of charity and service to the poor rather than from a sense of professional obligation [1]. These sentiments are certainly echoed in Henry's *Book of Holy Medicine* as he consistently

appeals to Christ the physician to heal him. "To you, [most sweet Lord] Jesus Christ, I come as to a doctor" [14].

Finally, a public expectation of the duty to treat is necessary for the ideal to take hold; there must be a "social contract" between physician and patient (or even physician and society) that such a duty to treat exists [1]. There is little evidence that such a social contract existed during the Middle Ages. What little expectation there may have been would have likely centered around the notion of the Christian duty to treat the sick.

The history of the medieval plague years throws into stark relief the ethical vacuum that doctors of the time had to fill on their own, falling back on religious convictions, personal compassion, or pragmatic concerns for self-preservation as the basis for their actions. Public expectations of physicians during epidemics are, even today, a point of some contention, with few explicit guidelines on a physician's duties during an epidemic. Indeed, much of our current discussion of the ethics of epidemics arises from the uncertainty surrounding the responsibilities of either a single physician or physicians as a group during the time of an outbreak. Still, much in the history of medicine and in the social development of the physician remains unknown. In the face of limited evidence, we must remember,

Perhaps the most celebrated physician ever is Hippocrates yet we know literally nothing about him. Neither do we know anything concrete about most of the medical encounters there have ever been. The historical record is like the night sky; we see a few stars and group them into mythic constellations. But what is chiefly visible is the darkness [4].

Notes and References

1. Huber SJ, Wynia MK. When pestilence prevails: physician responsibilities in epidemics. *Am J Bioeth.* 2004;4:W5-W11.
2. Henry's text is written in Anglo-Norman. For this paper, quotations are taken from EJ Arnould's edition of the manuscript published by the Anglo-Norman Text Society. Henry of Lancaster. *Le Livre de Seyntz Medicines (The Book of Holy Medicine).* Arnould, EJ, ed. Oxford, UK: Anglo-Norman Text Society; 1940. No complete modern English translation of Henry's work exists, but an excerpt has been translated into modern English in Bartlett AC, Bestul TH. *Cultures of Piety: Medieval English Devotional Literature in Translation.* Ithaca, NY: Cornell University Press; 1999:19-40.
3. Porter R. *The Greatest Benefit to Mankind: A Medical History of Humanity from Antiquity to the Present.* London, UK: Fontana Press; 1997:122
4. Rawcliffe C. *Medicine and Society in Later Medieval England.* London, UK: Sandpiper Books Ltd; 1995. 1-28, 105-125.
5. Rawcliffe C, 5. See also Hanley M. *Medieval Themes and Topics.* Available at: http://www.wsu.edu/~hanly/chaucer/coursematerials/humours.html. Accessed March 27, 2006.
6. Henry of Lancaster, 165, lines 16-18, 21-27. Author's translation.
7. Porter R, 114.
8. Porter R, 110.
9. Porter R, 124-125.

10. Getz F. *Medicine in the English Middle Ages*. Princeton, NJ: Princeton University Press; 1998:19.
11. Davey LM. The oath of Hippocrates: an historical review. *Neurosurgery*. 2001;49:554-566.
12. Smith CM. Origin and uses of *primum non nocere*—above all, do no harm! *J Clin Pharmacol*. 2005;45:371-377.
13. Porter R, 123.
14. Henry of Lancaster, 159, lines 1-5. Author's translation.

Jessica Mellinger, MPhil, is a third-year medical student at Northwestern University's Feinberg School of Medicine. Prior to starting medical school, she studied the history of medicine as a Rhodes Scholar at Oxford University.

Related Article
Professionalism and Medicine's Social Contract with Society, April 2004

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 261-264.

History of Medicine

The Epidemic Intelligence Service—The Centers for Disease Control and Prevention's Disease Detectives

by Douglas H. Hamilton, MD, PhD

Introduction

The Epidemic Intelligence Service (EIS) of the Centers for Disease Control and Prevention (CDC) is a unique 2-year postgraduate program of service and on-the-job training for health professionals interested in epidemiology. Since 1951, approximately 2600 EIS officers—CDC's "disease detectives"—have graduated from the program. In addition to the training gained through investigating disease outbreaks, natural and man-made disasters, and other public health emergencies, the program provides formal instruction to its trainees through courses in epidemiology, biostatistics, public health ethics and law, evaluation of surveillance systems, scientific writing, and prevention effectiveness. The 2-fold mission of EIS is training and service. One of the many ways that EIS delivers on its service mission is by forming the backbone of CDC's ready-response capability. When CDC is called upon to furnish epidemiologic assistance to our public health partners both domestically and internationally, an EIS officer is often the first one dispatched to the site.

Historic Overview

The EIS was the brainchild of Dr Alexander D. Langmuir, chief epidemiologist at the Communicable Disease Center (later renamed the Centers for Disease Control and Prevention) following his recruitment from a faculty position at Johns Hopkins University in 1949. One of Langmuir's first priorities upon assuming his new post was to recruit epidemiologically qualified personnel for the young agency. His initial efforts identified only 2 physicians who were interested in the position, and neither candidate was trained as an epidemiologist [1]. Dr Langmuir subsequently proposed that CDC establish a program to train epidemiologists for public health service. After initial attempts to fund this training program failed, Dr Langmuir changed his tack and argued that the United States needed a trained cadre of epidemiologists who could be available to detect and respond to a clandestine biologic attack, presumably by the Soviet bloc [2]. Congress responded with funding for the new program, and the first class of 22 trainees was enrolled in July of 1951. Although the stated rationale for the program was biodefense, Dr Langmuir later wrote, "The ultimate objective of this program is to promote a wider understanding and appreciation of epidemiologic approaches to the problem of disease control in war and peace" [1].

The early activities of the EIS focused on responding to limited public health emergencies and supplying technical consultation to state and local health departments. A watershed event was the development of the first formalin-inactivated vaccine for polio—the Salk vaccine. The vaccine was released amid great fanfare on April 12, 1955, the 10th anniversary of the death of President Franklin D. Roosevelt, perhaps polio's most famous victim. Dr Langmuir had established a plan of surveillance for polio, largely in anticipation of vaccine failures. At the time, the future of the polio vaccination campaign was in jeopardy due to pleas that vaccinations be stopped in the face of vaccine-induced cases of the disease. In response, Dr Langmuir traveled to Washington, DC, where he lobbied for and received permission to institute an emergency national surveillance program for polio. This effort required the commitment of the entire cohort of EIS officers at that time, 11 second-year and 32 first-year officers.

On April 25, a report of a baby in Chicago with polio, inoculated 9 days earlier, was reported to CDC. An EIS epidemiologist arrived to investigate the next morning. The following day, an EIS officer in Napa, California, called to report a second case. By the end of that day, a total of 6 cases had been identified. By May 6, vaccine produced by the Cutter Company was implicated as the likely source of infection. Vaccine distribution was temporarily suspended until the factory could be checked and appropriate safety measures instituted [3]. During this incident, CDC, through EIS, demonstrated its ability to respond rapidly to a public health emergency.

In the 50 years of the EIS program's existence, training has expanded beyond the original emphasis on infectious diseases to include all aspects of public health. In many ways, these changes reflect the evolution of the mission of the agency as a whole—CDC has grown from the Communicable Disease Center to become the Centers for Disease Control and Prevention. This evolution is clearly demonstrated by an examination of the types of epidemiologic assistance (EPI-AID) investigations conducted during the first 5 years of the program, 1952-1956, compared with those conducted during the most recent 5-year period, 2001-2005. During the first 5 years, 100 percent of the EPI-AID investigations were for infectious disease problems. During the last 5 years, infectious disease has continued to be a prominent focus (80 percent), but environmental (9 percent), chronic (3 percent), injury (4 percent), and other (5 percent) health-related problems have also been investigated. The international component of the program is also more apparent, with 17 percent of the investigations responding to international challenges. Of particular note is that during both periods, 4–5 percent of the investigations involved Category 1 biologic terrorism agents [4].

EIS Response to September 11, 2001

On Tuesday, September 11, 2001, CDC moved quickly to respond to the terrorist attacks in New York City (NYC) and at the Pentagon by activating its Director's Emergency Operations Center (DEOC). EIS personnel were among the first to help staff DEOC. Later that day, 2 EIS officers were deployed to NYC to assist the Department of Health and Mental Hygiene with hospital needs and surveillance of injuries to citizens and rescue workers. Health authorities were also concerned that a clandestine biologic weapon release might coincide with the attacks on the World Trade Center. Three days later, on September 14, 34 more EIS investigators were deployed to

establish the syndromic surveillance system among 15 hospitals in Manhattan and the surrounding boroughs. Still others were assigned to Washington, DC, to help establish syndromic surveillance around the Pentagon.

On October 4, 2001, the Florida Department of Health received a report of a possible case of inhalation anthrax in a Palm Beach resident. The Florida EIS officer immediately investigated the case report. That same day a team of 6 EIS and other CDC staff were flown in to assist with the investigation, and 4 EIS officers were sent to North Carolina to investigate the activities of the case-patient who had recently visited that state. Following the identification of a patient associated with the NBC studios in New York with cutaneous anthrax, 10 of the EIS investigators assigned to NYC syndromic surveillance spent the next 4 days helping collect epidemiological data, clinical samples, and counseling NBC employees. Over the next 4 weeks, an additional 27 EIS officers participated in the anthrax investigation in NYC.

Fifty EIS staff went to Washington between October 17 and January 14 to assist with the investigation of anthrax exposure in a letter sent to Senator Tom Daschle. As the investigation was expanded and postal system dissemination of the agent was discovered, EIS officers were also deployed to New Jersey and Connecticut. A total of 113 EIS officers were in the field during the anthrax investigations, and most of the rest of them assisted with staffing of the DEOC or state response centers.

In its initial response to the anthrax event, EIS established surveillance, tracked exposed individuals, and collected epidemiologic data to identify risk factors for exposure and disease. As the investigation shifted from the initial phase of "crisis response" to "consequence management," EIS officers became increasingly involved in the efforts to provide antibiotic prophylaxis to potentially exposed workers; their duties here included data collection, logistical management, and risk communication.

Other Large-Scale Deployments

Since the events of September 11 and the subsequent anthrax outbreaks, EIS has been asked to assist with CDC's response to other large-scale public health emergencies. Although these have not been biologic terrorism events, certain characteristics of all large-scale deployments are comparable. During the fall of 2002 West Nile virus spread across the southern and midwestern United States. EIS conducted investigations in Arkansas, Georgia, Illinois, Louisiana, and Mississippi, assisted with the director's emergency operations in Atlanta, and led nationwide studies of West Nile virus transmission associated with human tissue transplantation and blood transfusion.

A much larger and more intense public health response occurred after identification of severe acute respiratory syndrome (SARS) during the spring of 2003. Again, EIS played an early and important role in the CDC response. EIS officers were the first personnel detailed to Director's Emergency Operations Center when it was activated. As with any biologic terrorism event, the EIS served as CDC's primary surge-capacity resource. During the course of the SARS outbreak, 102 of 161 EIS officers participated in CDC's response efforts, while field-based staff assisted with activities in their individual states. Seventeen of the 102 were deployed internationally.

Following in the wake of Hurricanes Katrina and Rita, EIS officers at the disaster sites helped establish surveillance for injuries and illness in the affected areas, conducted needs assessments among displaced persons, investigated disease outbreaks, and temporarily replaced local public health workers forced to evacuate by the storms. During the 6 weeks after Katrina's landfall, EIS participated in 105 field deployments and another 18 assignments to DEOC.

Conclusion

Although the EIS program was created in response to the potential threat of a biologic attack, the driving philosophy of the program from its inception has been to train epidemiologists to respond to the whole spectrum of public health emergencies. We believe that the skills acquired by these epidemiologists equip them to respond to a biologic terrorism event. EIS officers continue to offer daily, ongoing support to CDC and to our state, local, American Indian/Alaska Native, and international partners. In recent years, EIS has repeatedly risen to the challenges posed by large-scale public health emergencies and has successfully supported CDC's public health mission as well as that of other federal government agencies.

References

1. Langmuir AD. The Epidemic Intelligence Service of the Center for Disease Control. *Public Health Rep.* 1980;95:470–477.
2. Langmuir AD, Andrews JM. Biological warfare defense: 2. The Epidemic Intelligence Service of the Communicable Disease Center. *Am J Public Health.* 1952;42:235-238.
3. Etheridge EW. *Sentinel for Health: a History of the Centers for Disease Control.* Berkeley: University of California Press; 1992.
4. Thacker SB, Dannenberg AL, Hamilton DH. Epidemic Intelligence Service of the Centers for Disease Control and Prevention: 50 years of training and service in applied epidemiology. *Am J Epidemiol.* 2001;154:985–992.

Douglas H. Hamilton, MD, PhD, is a captain in the US Public Health Service and the director of the Epidemic Intelligence Service Program at the Centers for Disease Control and Prevention in Atlanta, Georgia. He received both his medical degree and doctoral degree in microbiology from Vanderbilt University.

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 265-270.

Op-Ed

The Threat of an Avian Flu Pandemic is Over-Hyped

by Michael Fumento, JD

"It is only a matter of time before an avian flu virus—most likely H5N1—acquires the ability to be transmitted from human to human, sparking the outbreak of human pandemic influenza." So declared Dr Lee Jong-wook, director-general of the World Health Organization last November [1].

Fortunately, the assertion is as mistaken as it is terrifying.

Looking to the Data

The best-kept secret of the current fuss and, sadly enough, hysteria over H5N1 is that the virus has been in existence well beyond its highly publicized Hong Kong appearance in 1997; the virus was initially discovered in Scottish chickens in 1959 [2]. The virus has therefore been mutating and making contact with humans for 47 years. If it hasn't become pandemic in that half a century, it's hardly inevitable that it will.

Indeed, blood samples collected from rural Chinese in 1992 show 2-7 percent of those sampled were infected with some variant of H5; by extrapolation to the larger population, this equates to many millions of people [3]. Experts such as microbiologist Peter Palese of the Mount Sinai School of Medicine in New York believe that more than a million of these infections could have been H5N1 infections, although samples were not tested for variants of neuraminidase, a surface antigen, the "N" in H5N1 [4].

The Chinese data demonstrate that if H5N1 were going to become pandemic in humans, " it should have happened already," Palese wrote in an e-mail on February 3, 2006. "Probably an H5 can't make it in humans," he suggests, referring to the virus's ability to go beyond the original host. This cross-species infection can occur via either mutation or "reassortment." Reassortment means a host is infected by RNA segments from 2 different flu strains, giving rise to a third strain combining various traits—including theoretically one with the virulence and pathogenicity of H5N1 and the human-to-human transmissibility of an A or B strain of seasonal flu.

The Chinese serological data also help supply evidence that discredits the notion that H5N1 kills half its victims [5]. The 50 percent figure reflects bias selection in that it is based only on those who become sick enough to come to the attention of authorities [6].

Furthermore, if H5N1 isn't the particular strain likely to start a pandemic, there's no reason to expect that any virus will cause a pandemic in the near future. Yet a near-future pandemic seems to be our only serious public health concern.

More Prepared than We Think

In reality, our ability to handle a potential pandemic is more than trivial. Everyday, stockpiles of the neuraminidase-inhibiting antivirals, Tamiflu and Relenza, continue to grow, while manufacturing plants are converted to produce even more. New antivirals such as peramivir are being tested on the grounds that they may be as effective, or more so, than current antiviral standbys. These new drugs are also touted as superior in their ability to stave off resistant influenza strains because they are administered by injection, rather than by means of the readily abused Tamiflu pills and oral solutions [7, 8].

Vaccines are currently in development using reverse genetics to replicate only the antibody-provoking part of the virus. This speeds up the process of "seeding" chicken eggs to grow vaccine and prevents an avian virus from killing the avian egg [9]. Furthermore, eggs are being replaced by cell culture growth conditions in vaccine production. Several types of vaccines are already produced in this medium and H5N1 vaccine soon will be. This technology could triple the speed of vaccine production [10].

The potential to develop the capacity to stockpile vaccines instead of producing annual batches is promising. Two different research teams have used a crippled adenovirus as a carrier for a hemagglutinin surface protein (the "H" in H5N1) to provide complete protection from H5N1 in rodents. Regardless of whether the vaccine was made from a 1997 H5N1 strain or a 2005 strain, it offered cross-protection against the other [11, 12]. Scientists at Chiron Corporation tested blood from people who had received an experimental vaccine against a 1997 strain of H5N1 bird flu and found that it provoked a powerful cross-reaction from a strain that killed several Vietnamese in 2004 [13]. These data counter the oft-heard claim that we can't develop a vaccine until H5N1 becomes pandemic, since the pandemic strain will necessarily differ slightly from the current strain found in birds [14].

Considering Historical Precedent

With each new human case of avian flu, we're warned yet again that pandemic H5N1 could be upon us any time, long before we're prepared. These pronouncements reflect media ignorance of how viruses change and a failure on the part of those who know better to correct them. Despite what we commonly hear, H5N1 is not mutating, even slowly, toward becoming a pathogen capable of causing a pandemic.

There are no evolutionary pressures upon H5N1 to become more efficiently transmitted either from bird to human or from human to human; the virus mutates randomly. No thief listening with a stethoscope is picking a lock on Pandora's pandemic box one tumbler at a time. Rather, as one mutation brings the virus closer to human transmissibility, another is just as likely to draw it farther away.

We're also routinely told that we're "overdue" for a pandemic, with H5N1 the likeliest cause. Insert the search terms "avian flu," "pandemic," and "overdue" into Google and

you'll get about 35 000 hits. The director of the National Institute of Allergy and Infectious Disease, Anthony Fauci, insists we're "overdue," explaining that there were 3 pandemics in the 20th century and the last was in 1968. It's been 38 years since the last pandemic [15]. Yet the time between the second and third pandemics was only 11 years. There's no cycle. As risk communication experts Peter Sandman and Jody Lanard say, the "overdue pandemic" is mere superstition [16].

The Role of Modern Medicine

More harm comes from working assumptions that the next pandemic could be on par with the worst in history, the 1918-1919 Spanish flu. The main champion of this worst-case scenario is University of Minnesota School of Public Health professor Michael Osterholm. He extrapolates the estimated death toll from the Spanish flu to today's population and generates an oft-quoted estimate of 180 to 360 million deaths worldwide were such a pandemic to occur today [17].

The comparison certainly gets headlines, but regardless of either the virulence or pathogenicity of any human-to-human transmissible flu, it's folly to ignore almost 8 decades of medical advances. In 1918 there were no antiviral medications. You couldn't map out a viral genome, much less do so in about a week's time as was done with severe acute respiratory syndrom (SARS) 3 years ago [18, 19]. In 1918, there was absolutely no hope of developing a wide-scale vaccine before the pandemic burned out on its own. Most importantly, perhaps, there were no antibiotics and no pneumococcal polysaccharide vaccine (PSV). One PSV injection protects against 23 of the deadliest types of pneumococcal bacteria, has proven effective in reducing deaths secondary to influenza infection, and can be delivered well in advance of any pandemic [20]. Developments in communication and transportation have greatly advanced in the last century, ie, the ability of people to get to places where a vaccine is being delivered.

Indeed, the value of antibiotics is perhaps the most overlooked distinguishing factor between the historic influenza pandemic and any pandemic that would occur today. Another champion of the Spanish flu paradigm is Laurie Garrett, author of the alarmist 1994 book *The Coming Plague* [21]. Garrett wrote an influential *Foreign Affairs* article in 2005 declaring that while, "most strains of the flu do not kill people directly," the Spanish flu "was a direct killer." She adds, "Had antibiotics existed, they may not have been much help" [22]. She couldn't be more wrong.

There are real indications that the Spanish flu was more likely to kill directly than subsequent pandemics. But even here, anecdotal evidence of people suddenly dropping dead on trolley cars can be deceiving. "Often influenza victims seemed to recover, even returned to work, then suddenly collapsed again with bacterial pneumonia," explains John Barry, in his 2004 Spanish flu book, *The Great Influenza* [23]. In 1918, most people died in the fashion of subsequent flu epidemics and pandemics. "Autopsy records from New York City found that most of the deaths [from Spanish flu] occurred at the end of the first week and beginning of the second," according to a phone interview with University of Virginia virologist Frederick Hayden on October 15, 2005.

Researchers at Stanford University have assembled a Web site that quotes from the medical journals of the time, such as this from the *British Medical Journal* of 1918: "The principal danger of an influenza infection was its tendency to progress into the often fatal bacterial infection of pneumonia." Commenting generally on these journals' observations, the Stanford site says, "It was this tendency for secondary complications that made this influenza infection so deadly" [24].

Barry writes that even *without* modern drugs, "doctors could help. They could save lives. If they were good enough, if they had the right resources, if they had the right help, if they had time" [25]. This illustrates another tremendous difference between 1918 and now. *Now* we have *their* experience.

Conclusions

There is no gain in spreading an epidemic of hysteria. One price we're already paying is that people take antivirals like Tamiflu before they have any symptoms of disease. This contributes to viral resistance to medications, as it has in southern Vietnam [26]. Another problem with public hysteria is that while we stockpile Tamiflu and utilize other expensive, second-line measures that should be reserved for those situations in which a pandemic has taken hold, we ignore first-line measures that can prevent the development of a pandemic in the first place. These options include vaccinating poultry, eliminating infected flocks, and showing Asian farmers how to have as little contact with their birds and bird droppings as possible.

To some extent these actions are already under way, but many of the regions most directly affected include impoverished nations that cannot afford vaccinations for all poultry and may not have funds to reimburse farmers for killing all suspect birds. The result is endangered fowl left unvaccinated and alive. Developed nations need to become as involved as possible in containment efforts of developing nations, providing both expertise and financial support. To the extent that there is any risk of pandemic avian flu, it can be reduced to zero by eliminating bird-to-human transmission [27].

In conclusion, the panic we induce today will come back to haunt us. Americans still remember the swine flu fiasco in which a single death led to hysteria followed by a national vaccination program that itself appeared to cause an outbreak of disease [28]. SARS led to 750 stories in the *New York Times* and *Washington Post*—about 1 per death worldwide [29]. Indeed, SARS fell rather short of the *New Scientist* claim that, "it now seems clear that in the absence of a cure or a vaccine, SARS could eventually kill millions" [30]. The false fears we sow today we shall reap in the future as public complacency if a monster truly appears at the door.

Notes and References

1. Knox N. WHO: "Matter of time" before pandemic strikes. *USA Today*. November 7, 2005. Available at: http://www.usatoday.com/news/world/2005-11-07-who-flu_x.htm. Accessed February 3, 2006.
2. World Health Organization. *Avian Influenza A(H5N1)—Update 31: Situation (poultry) in Asia: Need for a Long-term Response, Comparison with Previous Outbreaks*. March 2, 2004. Available at: http://www.who.int/csr/don/2004_03_02/en. Accessed February 3,

2006.
3. Shortridge KF. Pandemic influenza: a zoonosis? *Semin Respir Infect.* 1992;7:11-25.
4. Palese P. Influenza: old and new threats. *Nat Med.* 2004;10:S82-87.
5. For example, see ABC News Primetime. *Are We Ready for the Bird Flu?* Laurie Garrett segment. Available at: http://www.abcnews.go.com/Primetime/Flu/story?id=1170177&page=1. Accessed February 3, 2006.
6. Thorson A, Petzold M, Nguyen TK, Ekdahl K. Is exposure to sick or dead poultry associated with flu-like illness?: Population-based study from a rural area in Vietnam with outbreaks of highly pathogenic avian influenza. *Arch Intern Med.* 2006;166:119-123.
7. Barroso L, Treanor J, Gubareva L, Hayden FG. Efficacy and tolerability of the oral neuraminidase inhibitor peramivir in experimental human influenza: randomized, controlled trials for prophylaxis and treatment. *Antivir Ther.* 2005;10:901-910.
8. Hubbard R. Flu drug put on fast track. *Birmingham News.* January 18, 2006. Available at: http://www.al.com/business/birminghamnews/index.ssf?/base/business/113757973711140.xml&coll=2. Accessed February 3, 2006.
9. Nicolson C, Major D, Wood JM, Robertson JS. Generation of influenza vaccine viruses on Vero cells by reverse genetics: an H5N1 candidate vaccine strain produced under a quality system. *Vaccine.* 2005;23:2943-2952.
10. Becker A. Momentum builds for cell-culture flu vaccines. *CIDRAP News.* June 27, 2005. Available at: http://www.cidrap.umn.edu/cidrap/content/influenza/ general/news/june2705cell.html. Accessed February 4, 2006.
11. Hoelscher M, Garg S, Bangari DS, et al. Development of adenoviral-vector-based pandemic influenza vaccine against antigenically distinct human H5N1 strains in mice. *Lancet.* 2006;367:475-481.
12. Gao W, Soloff AC, Lu X, et al. Protection of mice from lethal H5N1 avian influenza virus through adenovirus-based immunization. *J Virol.* 2006;80:1959-1964.
13. Mackenzie D, Choo K. Bird flu: kick-start vaccination or face the consequences. *New Sci.* Available at: http://www.newscientist.com/channel/health/mg18825215.900 Accessed February 4, 2006.
14. Schultz J. Bird flu vaccine won't precede pandemic. Quoting Daniel Lucey, co-director of the Biohazardous Threats and Emerging Diseases graduate program at Georgetown University: "There is no H5N1 pandemic so there can be no pandemic vaccine." *United Press International* Web site. Available at: www.upi.com/ConsumerHealthDaily/view.php?StoryID=20051128-054641-9412r. Accessed February 4, 2006.
15. Grady D. Odds of bird flu pandemic proving difficult to calculate. *Deseret News.* Available at: http://deseretnews.com/dn/view/0,1249,615156470,00.html. Accessed February 3, 2006.
16. Sandman P, Lanard J. Pandemic influenza risk communication: the teachable moment. December 4, 2004. Available at: http://www.psandman.com/col/pandemic.htm. Accessed February 3, 2006.
17. Osterholm M. Preparing for the next pandemic. *N Engl J Med.* 2005;352:1839-1842.
18. Marra MA, Jones SJ, Astell CR, et al. The genome sequence of the SARS-associated coronavirus. *Science.* 2003;300:1399-1404.
19. Canada's high-tech cancer fight. *Toronto Star.* March 20, 2004:F04.
20. Vila-Corcoles A, Ochoa-Gondar O, Llor C, Hospital I, Rodriguez T, Gomez A.

Protective effect of pneumococcal vaccine against death by pneumonia in elderly subjects. *Eur Respir J*. 2005;26:1086-1091.
21. Garrett L. *The Coming Plague*. New York, NY: Penguin Books; 1995.
22. Garrett L. The next pandemic? *Foreign Affairs*. Available at: http://www.foreignaffairs.org/20050701faessay84401-p10/laurie-garrett/the-next-pandemic.html. Accessed February 12, 2006.
23. Barry J. *The Great Influenza: The Epic Story of the Deadliest Plague in History*. New York, NY: Penguin Books; 2004:251.
24. Stanford Program in Human Biology Web site. *The Medical and Scientific Conceptions of Influenza*. Available at: http://www.stanford.edu/group/virus/uda/fluscimed.html. Accessed February 4, 2006.
25. Barry J, *The Great Influenza*, 316.
26. de Jong MD, Tran TT, Truong HK, et al. Oseltamivir resistance during treatment of influenza A (H5N1) infection. *N Engl J Med*. 2005;353:2667-2672.
27. Perez D, Sorrell E, Donis R. Avian influenza: An omnipresent pandemic threat. *Pediatr Infect Dis J*. 2005;24:S208-S216.
28. Sencer DJ, Millar JD. Reflections on the 1976 Swine Flu Vaccination Program. *Emerg Infect Dis*. 2006;12:29-33.
29. World Health Organization. *Summary of Probable SARS Cases with Onset of Illness from 1 November 2002 to 31 July 2003*. Available at: http://www.who.int/csr/sars/country/table2004_04_21/en/index.html. Accessed on February 4, 2006.
30. MacKenzie D. SARS much more deadly than first estimated. *New Sci*. Available at: http://www.newscientist.com/article.ns?id=dn3662. Accessed February 4, 2006.

Michael Fumento, JD, a senior fellow with the Hudson Institute in Washington, DC, is an author, journalist, and attorney specializing in health and science issues.

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 271-276.

Medical Humanities

Art, AIDS, and Ethics

by Kate Scannell, MD

On New Year's Eve, my friends and I donned our thermal raincoats and set out from our motel rooms in search of the Laguna Art Museum. For years we have gathered in this tourist town to greet the new year at the ocean's uncertain edge. Often, the southern California weather provides a dramatic backdrop to our experience, and 2006 was no exception—flooding city streets, umbrella-flipping winds, horizontal rains, ocean waves lurching towards shore.

Carry Me, 2002; by Timothy Grubbs Lowly. Drawing on toned panel 108 x 48 inches. Collection of Andreas Waldburg-Wolfegg. Reproduced by permission of the artist and Laguna Art Museum.

This year, the museum was hosting A Broken Beauty: Figuration, Narrative and the Transcendent in North American Art, an exhibition of postmodern works exploring the meaning of human embodiment. As the program brochure explained, the exhibition's title originated with the French philosopher Simone Weil, "who saw a symbiotic relationship between beauty and brokenness that she felt was essential to our understanding of the complexities of the human condition in the modern world" [1]. The featured artists aspired to represent the relationships between physical, mental, or spiritual brokenness and the quest for personal or collective redemption and hope.

While instantly drawn to the exhibition, I also feared that I would be made to view artwork that romanticized suffering or merited display on sentiment alone. I entered the museum as a physician mindful of real patients who suffered ingloriously and without hope, as a troubled witness to the early AIDS epidemic, and as a New Year's celebrant cautiously marking her tenth-year anniversary of cancer survivorship.

But an hour later and ready to leave the museum, my friends found me staring meditatively at a 9-by-4 foot monochromatic drawing by Chicago artist Timothy Grubbs Lowly. Entitled Carry Me, the haunting work depicts his severely disfigured and incapacitated

daughter, Temma, who is held up to our bird's-eye view by 6 women. (See figure) The accompanying text explains that the artist conceived the drawing in witness of his daughter, wondering what it might mean to be a human being physically and psychically "ultramarginalized." In the end, he envisages Temma as the self-sufficing answer, one that precedes and dismisses the question, and he imagines her voice: "Carry me, this is who I am, broken in mind, broken in body" [2]. And as observers of the drawing, we are asked to examine our own view and experience of Temma, while the women who carry her await our response.

AIDS in the Picture

This drawing now solidly inhabits my mind, and it routinely surfaces to consciousness when I think about my professional coming of age in the 1980s during the outbreak of the AIDS epidemic. The drawing has come to render, both graphically and in a wholly affecting way, a question of epidemic proportion that stretches from the present back to my tenure on the AIDS ward: How do we view and locate ourselves in relationship to each other during a terrifying and desperate human predicament?

To explain this, it is necessary to picture the AIDS epidemic as it appeared nearly a quarter century ago when it first spilled onto the human canvas. From my point of view as a newly minted doctor beginning medical practice in San Francisco, the epidemic looked like this: young gay men swiftly disabled, swiftly disfigured, swiftly dying; doctors and nurses looking helpless, perplexed, or afraid; public figures proclaiming from pulpits and soapboxes their harsh judgments about the strange new disease and its primary carriers.

Fear of contagion was itself epidemic. Men afflicted with AIDS often saw their families suddenly drop out of sight. They received termination papers from employers, eviction notices from landlords. William Buckley, Jr suggested that they be branded with tattoos; Lyndon LaRouche proposed that they be quarantined.

During the 1970s and 1980s, we were celebrating astronomical successes in life-prolonging medical technologies that regularly conferred incremental legitimacy and clout to our profession. But when AIDS arrived, with its swift and certain death sentence, defying the robust trajectory of our professional narrative and its burgeoning paradigm of cure, many of us were thrown into a tailspin.

During this chaotic time in the early epidemic—when the cause of AIDS was unknown, when no diagnostic test or treatment was available, when we realized we were all standing at the dark dawn of a fatal new epidemic—insistent questions demanded personal answers from everyone: Where do I stand—in or out—of this big picture? How do I relate to the brokenness of these young men's lives? What, if any, obligation do I have to carry them?

The Social Construction of Doctors and Patients

People answered these questions differently, demonstrating on a grand scale our culture's disparate views and valuations of the ultramarginalized lives of gay men with AIDS and the obligations of society and medicine to carry them. And within the

medical profession, remarkable disagreements erupted over whether doctors were even obligated to provide care for people with AIDS.

At the epidemic's raw beginning, many physicians refused to treat people with AIDS—that is, to even consider them as "patients" to whom medical care was owed. A study conducted in 1987 reported that 54 percent of 4100 medical internists surveyed nationally believed they had the right to refuse treatment to AIDS patients [3]. Another study that same year revealed that a quarter of physician residents interviewed at New York City hospitals thought it was not unethical to refuse care for AIDS patients [4].

As a brand new doctor, I was stunned by the powerful sense of agency those medical colleagues assumed in excluding anyone from an identity as "patient." I knew that, as a profession, we had done this before—excluding African Americans from white hospitals, excluding the impoverished from general medical care. But I had attended medical school in the 1970s, and, informed by the civil rights and women's movements, I was expecting our profession to carry more, not less, of the suffering public body.

In my disillusionment, I also realized that whenever doctors narrowed the definition of "patient," they also narrowed the definition of "doctor," putting qualifiers around the humanitarian virtues and fiduciary obligations of medical practitioners. In disqualifying groups of people from medicine's embrace, they diminished the scope and signification of the social covenant between the medical profession and society. Always, the narrowing and diminishing were emphatically substantive, because they always constituted value judgments about the worth or nature of particular human beings.

Struggles within the profession over the right to establish the meanings carried by words like "patient" and "doctor" and "social covenant" provided convincing evidence that such words were bendable, breakable, amenable to reconstructions that were shaped around physicians' political positions, religious beliefs, professional sentiments, and social ethics. It mattered profoundly who controlled the language. The consequences were critical for anyone hoping to be regarded as a patient, wholly contingent upon where he or she landed in the newly reconstructed field of meanings.

While these reconstructions of meaning evolved in the medical clinic, they evolved simultaneously within a larger social context—one that both reflected and configured the medical profession. Within the public sector, AIDS activists and gay rights groups were particularly effective social participants, insisting that doctors and the medical system become entities that carry people with AIDS as patients.

One of the critical lessons I learned from the early AIDS epidemic was this: medicine is a profoundly human enterprise, pushed and pulled and tugged and shaped by many human hands, a collective handiwork of patients, doctors, and public interests that highlights strong interdependencies among the personal, professional, cultural, and political realms. It's an evolving social process in which we are all connected by a live-wire dialectic in mutually affecting arrangements—sometimes increasing polarization, but at other times energizing new social and political liaisons, vitalizing fresh collective consciousness.

Wounded by the Paradigm of Cure

Unable to cure these men or prolong their lives, some doctors felt useless and left the scene. But many doctors held on and stayed within the picture—like the 6 young women in the drawing who stay in relation to Temma, if only to hold her. For me, making the decision to stay required that I figure out how to think and feel and behave outside the margins of the conventional text of what it meant to be a "good doctor"—one who aggressively stalked disease with a bold armamentarium of skills and pills. Facing a population of patients who would die, regardless of what I could offer, presented enormous challenges to my perceived professional identity, an identity already challenged by my personal identifications with gender, sexuality, and class.

No single professional organization exerted compelling and unified leadership on the question of whether a person with AIDS ought to be treated and recognized empathically by his surrounding world as someone who should be carried. Our profession faltered in its initial ambivalence regarding both doctors who refused to render medical care and the manifest failure of the cure paradigm to encompass the experiences of dying people as "patients." We fumbled a critical, historic opportunity to exert strong moral authority and reaffirm a social covenant with the public that explicitly embraced respect and compassion for all suffering persons as our patients.

For a doctor at the beginning of the epidemic, simply to have included an AIDS patient in her medical practice often challenged formidable professional norms and ideology. It often constituted a radical social act, insisting on the repatriation of people with AIDS into identities as "patients" who deserved our medical care. And always situated in the center of the picture was a person with AIDS who was then, most often, a person of frightening physical "brokenness," someone facing a mysterious illness and imminent death.

AIDS Memoirs as Claims of Patient and Doctor Identity

I cannot speak for the many other physician-memoirists who have written about the early AIDS epidemic, but I discern one common subtext in our collective writings: the desire not only to bear witness to patients and their suffering, but also to assert that people with AIDS must be included as "patients" within our medical and social systems of care. They were written into the text of a doctor's work, identified as patients without qualification, situated squarely within conventional patient-physician relationships. At the same time, these memoirists also made claims about the identities of doctors, about the practice of medicine, about new paradigms of medical care. They spoke to the serious responsibilities a doctor always had as a co-constructionist of the health care system. They reminded us that, at a personal level, each physician had to decide how to live his or her own life in medicine; that you could not then—as you cannot now—isolate the personal from the professional and from the political.

Over the years, the profound iterative relationships between the personal, professional, and sociopolitical ultimately worked in this country to reshape our social ethics and public perceptions regarding persons with AIDS. Gradually, they were recognized empathically as those among us who evidenced our common human brokenness, and

they were carried regularly by our profession and society. Housing and job discrimination were banned. The media began rendering sympathetic portrayals of HIV-infected persons.

Modern-Day Epidemics and Reconstructions of American Medicine

The social construction of medical practice and patient-physician identities remains as operative today as it was in the early AIDS epidemic. To me, this means that, as doctors, we need to stay mindful about all interrelationships that determine how it is that we actually practice medicine and who is included in or excluded from the big picture.

Many modern-day examples resonate with remarkable tensions born of the traditional interdependencies among the personal, professional, and societal realms that we experienced during the early AIDS epidemic. Perhaps the most robust example centers around our country's modern epidemic of uninsured citizenry. Currently, about 45 million Americans do not own health insurance. As such, they are medically disenfranchised people ejected from enduring and solid identities as patients within a coherent and reliable health care system.

Another example of the defining power of these interdependencies is demonstrated by the profound influence of the pharmaceutical and device industries upon the face of American medicine. We can think about industry's forceful hand in defining huge new categories of patients around new constructions of illness and about the corollary expansions of physician duties which that process newly creates.

Finally, in the burgeoning field of medical enhancement, biodiverse human traits—height, muscular strength, or intelligence—are increasingly medicalized or pathologized, and new "patients" are created with new "diseases" that impose new obligations on the "medical profession" and its "doctors."

These modern examples raise the same old questions: Who holds the pen that draws the dividing lines between patients and nonpatients, between health and disease? Who composes the picture of American medicine?

The longer I practice, the more I respect the power of the dialectical relationships among doctors, the medical profession, and society to determine the nature of American medicine and the covenant between doctors and patients. I have learned that to ignore those relationships is to practice medicine incompletely and inefficiently. I have come to understand that practicing medicine always expresses a philosophical and political position, and that doctoring—with a pen or a stethoscope—can be a radical social act. I believe that each of us makes a mark, in our own small way, in the small corners of the world where we work and live as doctors, always deciding how medicine ought to look, and who it should carry.

References

1. ArtsceneCal. Announcements Page. Available at: http://artscenecal.com/Announcements/1105/LagunaMsm1105.html. Accessed

March 21, 2006.
2. Fugile G. A broken beauty and its artists. In: Prescott TL, ed. *A Broken Beauty*. Grand Rapids, MI: William B. Eerdmans Publishing Company; 2005:97.
3. IM-Internal Medicine. What internists think about AIDS. IM—Internal Medicine. 1987;8:53-60.
4. Staver S. MDs wary of treating AIDS patients. *American Medical News*. June 19, 1987; 35:59-60.

Acknowledgments
I am grateful to Timothy Grubbs Lowly for producing his affecting artwork with the collaborative assistance of Robin Spencer, Yoonhee Kim, Amanda Hasse, Michelle Ness, Heather Yanul, Krissa Harwood, and Temma Lowly. I thank Stuart Byer of the Laguna Art Museum for facilitating reproduction of the artwork for this essay, and Howard Brody, MD, PhD, and the Department of Medical Humanities at Michigan State University for inviting me last year to speak about many of the issues developed in this essay.

Kate Scannell, MD, is an internist and geriatrician in Oakland, California, with Kaiser Permanente Northern California, where she also directs the Department of Medical Ethics.

Virtual Mentor
Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 277-288.

Suggested Readings and Resources

ABC News Primetime. *Are We Ready for the Bird Flu?* Laurie Garrett segment. Available at: http://www.abcnews.go.com/Primetime/Flu/story?id=1170177&page=1. Accessed February 3, 2006.

American Medical Association Council on Ethical and Judicial Affairs. Ethical considerations in the allocation of organs and other scarce medical resources among patients. *Arch Intern Med.* 1995;155:29-40.

American Medical Association. Opinion 8.115 Termination of the patient-physician relationship. *Code of Medical Ethics.* Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=browse&doc=policyfiles/HnE/E-8.115.HTM&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-7.05.HTM&nxt_pol=policyfiles/HnE/E-8.01.HTM& Accessed March 15, 2006.

American Medical Association. Opinion 9.031 Reporting impaired, incompetent, or unethical colleagues. *Code of Medical Ethics.* Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=browse&doc=policyfiles/HnE/E-9.031.HTM&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-8.21.HTM&nxt_pol=policyfiles/HnE/E-9.01.HTM& Accessed March 7, 2006.

American Medical Association. Opinion 9.067 Physician obligation in disaster preparedness and response. *Code of Medical Ethics.* Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=browse&doc=policyfiles/HnE/E-9.067.HTM&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-8.21.HTM&nxt_pol=policyfiles/HnE/E-9.01.HTM& Accessed March 2, 2006.

American Medical Association. Opinion 10.01 Fundamental elements of the patient-physician relationship. *Code of Medical Ethics.* Available at: http://www.ama-assn.org/apps/pf_new/pf_online?f_n=browse&p_p=T&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-10.01.HTM&nxt_pol=policyfiles/HnE/E-10.017.HTM& Accessed March 7, 2006.

American Thoracic Society. Fair allocation of intensive care unit resources. *Am J Respir Crit Care Med.* 1997;156:1282-1301. Erratum in: *Am J Respir Crit Care Med.* 1998;157:671.

ArtsceneCal. Announcements Page. Available at: http://artscenecal.com/Announcements/1105/LagunaMsm1105.html. Accessed March 21, 2006.

Astin JA. Why patients use alternative medicine. *JAMA.* 1998;279:1548-1553.

Atun RA, Samyshkin YA, Drobniewski F, et al. Barriers to sustainable tuberculosis control in the Russian Federation health system. *Bull World Health Organ.* 2005;83:217-223.

Barbera J, Macintyre A, Gostin L, et al. Large-scale quarantine following biological terrorism in the United States: scientific examination, logistic and legal limits, and possible consequences. *JAMA.* 2001;286:2711-2717.

Barroso L, Treanor J, Gubareva L, Hayden FG. Efficacy and tolerability of the oral neuraminidase inhibitor peramivir in experimental human influenza: randomized, controlled trials for prophylaxis and treatment. *Antivir Ther.* 2005;10:901-910.

Barry J. *The Great Influenza: The Epic Story of the Deadliest Plague in History.* New York, NY: Penguin Books; 2004:251.

Bartlett AC, Bestul TH. *Cultures of Piety: Medieval English Devotional Literature in Translation.* Ithaca, NY: Cornell University Press; 1999:19-40.

Becker A. Momentum builds for cell-culture flu vaccines. *CIDRAP News.* June 27, 2005. Available at: http://www.cidrap.umn.edu/cidrap/content/influenza/general/news/june2705cell.html. Accessed February 4, 2006.

Bioterrorism Preparedness and Response Act, 42 USC 247d-6(h)(4) (2002).

Black HC, Garner BA, eds. *Black's Law Dictionary.* 2nd pocket ed. St Paul, Minn: West Publishing Co.; 2001:661.

Calandrillo SP. Vanishing vaccinations: why are so many Americans opting out of vaccinating their children? *Univ Mich J Law Reform.* 2004;37:353-440.

Camus A. *The Plague.* 1st international ed. New York, NY: Vintage Books; 1991.

Canada's high-tech cancer fight. *Toronto Star.* March 20, 2004:F04.

Cava MA, Fay KE, Beanlands HJ, McCay EA, Wignall R. The experience of quarantine for individuals affected by SARS in Toronto. *Public Health Nurs.* 2005;22:398-406.

Cello J, Paul AV, Wimmer E. Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template. *Science*. 2002;297:1016-1018.

Center for Law and the Public's Health at Georgetown and Johns Hopkins Universities. *Model State Public Health Laws*. Available at: http://www.publichealthlaw.net/Resources/Modellaws.htm#MSEHPA. Accessed February 27, 2006.

Centers for Disease Control and Prevention. Select Agent Program. Available at: http://www.cdc.gov/od/sap/. Accessed March 16, 2006.

Centers for Disease Control and Prevention. Tiered use of inactivated influenza vaccine in the event of a vaccine shortage. *MMWR Weekly*. 2005;54:749-750. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5430a4.htm. Accessed on February 26, 2006.

Centers for Disease Control and Prevention. Updated guidelines for evaluating public health surveillance systems: recommendations from the guidelines working group. *MMWR*. 2001;50(No. RR-13):1-31.

Clayton RA, White O, Fraser CM. Findings emerging from complete microbial genome sequences. *Curr Opin Microbiol.* 1998;1:562-566.

Council for International Organizations of Medical Sciences. *CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects. Geneva 2002*. Available at: http://www.cioms.ch/frame_guidelines_nov_2002.htm. Accessed March 30, 2006.

Council of State and Territorial Epidemiologists. *Position Statements for 2005*. Available at: http://www.cste.org/position%20statements/searchbyyear2005.asp. Accessed March 3, 2006.

de Jong MD, Tran TT, Truong HK, et al. Oseltamivir resistance during treatment of influenza A (H5N1) infection. *N Engl J Med.* 2005;353:2667-2672.

Dwyer J, Global health and justice. *Bioethics*. 2005;19:460-475.

Dwyer J. Teaching global bioethics. *Bioethics*. 2003;17:432-446.

Dye C, Watt CJ, Bleed DM, Hosseini SM, Raviglione MC. Evolution of tuberculosis control and prospects for reducing tuberculosis incidence, prevalence, and deaths globally. *JAMA*. 2005;293:2767-2775.

Einstein A. *Ideas and Opinions*. New York, NY: Three Rivers Press; 1954.

Emanuel E, Wendler D, Grady C. What makes clinical research ethical? *JAMA*. 2000;283:2701-2711.

Emanuel E, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? The benchmarks of ethical research. *J Infect Dis.* 2004;189:930-937.

Emanuel EJ. Do physicians have an obligation to treat patients with AIDS? *N Engl J Med.* 1988;318:1686-1690.

Etheridge EW. *Sentinel for Health: a History of the Centers for Disease Control.* Berkeley: University of California Press; 1992.

Farmer P, Campos NG. Rethinking medical ethics: a view from below. *Developing World Bioeth.* 2004;4:17-41.

Farmer P. *Pathologies of Power: Health, Human Rights And The New War On the Poor.* Berkeley: University of California Press; 2004.

Fauci A. International health and tropical disease research: an NIAID perspective. Paper presented at: American Society of Tropical Medicine and Hygiene Washington Annual Meeting; Dec 11, 2005; Washington, DC.

Fauci AS. Emerging and reemerging infectious diseases: the perpetual challenge. *Acad Med.* 2005;80:1079-1085.

Folch E, Hernandez I, Barragan M, Franco-Paredes C. Infectious diseases, non-zero-sum thinking, and the developing world. *Am J Med Sci.* 2003;326:66-72.

Freedman B. Health professions, codes, and the right to refuse HIV-infectious patients. *Hastings Cent Rep.*1988;18:S20-25.

Fugile G. A broken beauty and its artists. In: Prescott TL, ed. *A Broken Beauty.* Grand Rapids, MI: William B. Eerdmans Publishing Company; 2005

Gallup JL, Sachs JD. The economic burden of malaria. *Am J Trop Med Hyg.* 2001;64:85-96.

Gao W, Soloff AC, Lu X, et al. Protection of mice from lethal H5N1 avian influenza virus through adenovirus-based immunization. *J Virol.* 2006;80:1959-1964.

Garrett L. *The Coming Plague.* New York, NY: Penguin Books; 1995.

Garrett L. The next pandemic? *Foreign Affairs.* Available at: http://www.foreignaffairs.org/20050701faessay84401-p10/laurie-garrett/the-next-pandemic.html. Accessed February 12, 2006.

Gates Foundation, The Bill and Melinda. Global Health. Available at: http://www.gatesfoundation.org/MediaCenter/FactSheet/. Accessed February 20, 2006.

Getz K. A swift predominance of ex-US sites. *Applied Clinical Trials*. Available at: http://www.actmagazine.com/appliedclinicaltrials/article/articleDetail.jsp?id=261633. Accessed March 7, 2006.

Gostin LO. Influenza pandemic preparedness: legal and ethical dimensions. *Hastings Cent Rep*. 2004;34:10-11.

Gostin LO, Bayer R, Fairchild AL. Ethical and legal challenges posed by severe acute respiratory syndrome. *JAMA*. 2003;290:3229-3227.

Gostin LO, Gravely SD, Shakman S, Markel H. Quarantine: voluntary or not? *J Law Med Ethics*. 2004;32(4 Suppl):83-86.

Gostin LO, Sapsin JW, Teret SP, et al. The Model State Emergency Health Powers Act: planning for and response to bioterrorism and naturally occurring infectious diseases. *JAMA*. 2002;288:622-628.

Grady D. Odds of bird flu pandemic proving difficult to calculate. *Deseret News*. Available at: http://deseretnews.com/dn/view/0,1249,615156470,00.html. Accessed February 3, 2006.

Guerrant RL. Why America must care about tropical medicine: threats to global health and security from tropical infectious diseases. *Am J Trop Med Hyg*. 1998;59:3-16.

Gupta R, Irwin A, Raviglione MC, Kim JY. Scaling-up treatment for HIV/AIDS: lessons learned from multidrug-resistant tuberculosis. *Lancet*. 2004;363:320-324.

Gwatkin DR. Global burden of disease [letter; comment]. *Lancet*. 1997;350:141-145.

Hanley M. *Medieval Themes and Topics*. Available at: http://www.wsu.edu/~hanly/chaucer/coursematerials/humours.html. Accessed March 27, 2006.

Henry of Lancaster. *Le Livre de Seyntz Medicines (The Book of Holy Medicine)*. Arnould, EJ, ed. Oxford, UK: Anglo-Norman Text Society; 1940.

Hoelscher M, Garg S, Bangari DS, et al. Development of adenoviral-vector-based pandemic influenza vaccine against antigenically distinct human H5N1 strains in mice. *Lancet*. 2006;367:475-481.

Hubbard R. Flu drug put on fast track. *Birmingham News*. January 18, 2006. Available at: http://www.al.com/business/birminghamnews/index.ssf?/base/business/1137579737 11140.xml&coll=2. Accessed February 3, 2006.

Huber SJ, Wynia MK. When pestilence prevails: physician responsibilities in epidemics. *Am J Bioeth*. 2004;4:W5-W11.

Huhn GD, Austin C, Langkop C, et al. The emergence of West Nile virus during a large outbreak— Illinois, 2002. *Am J Trop Med Hyg.* 2005;72:768-776.

Iftikhar SA, Roistacher K. Indigenous Plasmodium falciparum malaria in Queens, NY. *Arch Intern Med.* 1995;155:1099-1101.

IM-Internal Medicine. What internists think about AIDS. *IM—Internal Medicine.* 1987;8:53-60.

Jacobson v Massachusetts, 197 US 11, 25 S Ct 358 (1905).

Joffe H. *Risk and "the Other."* Port Chester, NY: Cambridge University Press; 1999:37-55.

Kass N, Hyder A. Attitudes and experiences of U.S. and developing country investigators regarding human subjects regulations. In: *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries.* Volume II. Washington, DC: National Bioethics Advisory Commission; 2001:B-38-B-39.

Kim JY, Shakow A, Mate K, Vanderwarker C, Gupta R, Farmer P. Limited good and limited vision: multidrug-resistant tuberculosis and global health policy. *Soc Sci Med.* 2005;61:847-859.

Knox N. WHO: "Matter of time" before pandemic strikes. *USA Today.* November 7, 2005. Available at: http://www.usatoday.com/news/world/2005-11-07-who-flu_x.htm. Accessed February 3, 2006.

Koo D, Caldwell B. The role of providers and health plans in infectious disease surveillance. *Eff Clin Pract.* 1999;2:247-252.

Kotalik J. Preparing for an influenza pandemic: ethical issues. *Bioethics.* 2005;19:422-431.

Langmuir AD, Andrews JM. Biological warfare defense: 2. The Epidemic Intelligence Service of the Communicable Disease Center. *Am J Public Health.* 1952;42:235-238.

Langmuir AD. The Epidemic Intelligence Service of the Center for Disease Control. *Public Health Rep.* 1980;95:470–477.

Lee J. Science and the health of the poor [editorial]. *Bull World Health Org.* 2003;81:473.

Lo B, Katz MH. Clinical decision making during public health emergencies: ethical considerations. *Ann Intern Med.* 2005;143:493-498.

London A. Justice and the human development approach to international research. *Hastings Cent Rep.* 2005;35:24-37.

Mackenzie D, Choo K. Bird flu: kick-start vaccination or face the consequences. *New Sci*. Available at: http://www.newscientist.com/channel/health/mg18825215.900 Accessed February 4, 2006.

MacKenzie D. SARS much more deadly than first estimated. *New Sci*. Available at: http://www.newscientist.com/article.ns?id=dn3662. Accessed February 4, 2006.

Macklin R. After Helsinki: unresolved issues in international research. *Kennedy Inst Ethics J*. 2001; 11:17-36.

Macklin R. Avoiding exploitation. In: *Double Standards in Medical Research in Developing Countries*. Cambridge, UK: Cambridge University Press; 2004:99-129.

Macklin R. *Double Standards in Medical Research in Developing Countries*. Cambridge, UK: Cambridge University Press; 2004.

Marra MA, Jones SJ, Astell CR, et al. The genome sequence of the SARS-associated coronavirus. *Science*. 2003;300:1399-1404.

Masur H, Emanuel E, Lane HC. Severe acute respiratory syndrome: providing care in the face of uncertainty. *JAMA*. 2003;289:2861-2863.

McDaniel v Paty, 435 US 618, 698 S Ct 1322 (1978).

Mills A, Shillcutt S. Communicable diseases. In: Lomborg B, ed. *Global Crises, Global Solutions*. New York, NY: Cambridge University Press; 2004: 62-114.

Mukherjee JS, Rich ML, Socci AR, et al. Programmes and principles in treatment of multidrug resistant tuberculosis. *Lancet*. 2004;363:474-481.

Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet*. 1997;349:1269-1276.

Murray JF. A century of tuberculosis. *Am J Respir Crit Care Med*. 2004;169:1181-1187.

National Academy of Sciences. Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology. *Biotechnology Research in an Age of Terrorism: Confronting the "Dual-use" Dilemma*. Washington, DC: National Academies Press; 2004. Available at: http://fermat.nap.edu/books/0309089778/html. Accessed March 16, 2006.

National Bioethics Advisory Commission. *Ethical and Policy Issues in International Research: Clinical trials in Developing Countries*. Vol. I. Bethesda, Md: National Bioethics Advisory Commission; 2001. Available at: http://www.bioethics.gov/reports/past_commissions/nbac_international.pdf Accessed March 2, 2006.

National Science Advisory Board for Biosecurity (NSABB). Available at: http://www.biosecurityboard.gov/. Accessed March 30, 2006.

Nicolson C, Major D, Wood JM, Robertson JS. Generation of influenza vaccine viruses on Vero cells by reverse genetics: an H5N1 candidate vaccine strain produced under a quality system. *Vaccine.* 2005;23:2943-2952.

Nuffield Council on Bioethics. *The Ethics of Research Related to Healthcare in Developing Countries.* London, UK: Nuffield Council on Bioethics; 2002. Available at: http://www.nuffieldbioethics.org/go/print/ourwork/developingcountries/introduction. Accessed February 28, 2006.

Osterholm M. Preparing for the next pandemic. *N Engl J Med.* 2005;352:1839-1842.

Palese P. Influenza: old and new threats. *Nat Med.* 2004;10:S82-87.

Pang X, Zhu Z, Xu F, et al. Evaluation of control measures implemented in the severe acute respiratory syndrome outbreak in Beijing, 2003. *JAMA.* 2003;290:3215-3221.

Paolo WF Jr, Nosanchuk JD. Tuberculosis in New York City: recent lessons and a look ahead. *Lancet Infect Dis.* 2004;4:287-293.

Participants in the 2001 Conference on Ethical Issues of Research in Developing Countries. Fair benefits for research in developing countries. *Science.* 2002;298:2133-2134.

Participants in the 2001 Conference on Ethical Issues of Research in Developing Countries. Moral standards for research in developing countries: from reasonable availability to fair benefits. *Hastings Cent Rep.* 2004;34:17-27.

Perez D, Sorrell E, Donis R. Avian influenza: An omnipresent pandemic threat. *Pediatr Infect Dis J.* 2005;24:S208-S216.

Petro JB, Relman DA. Understanding threats to scientific openness. *Science.* 2003;302:1898.

Porter R. *The Greatest Benefit to Mankind: A Medical History of Humanity from Antiquity to the Present.* London, UK: Fontana Press; 1997.

Powell JH. *Bring Out Your Dead: The Great Plague of Yellow Fever in Philadelphia in 1793.* Philadelphia: University of Pennsylvania Press; 1993.

Public Engagement Pilot Project on Pandemic Influenza. *Citizen Voices on Pandemic Flu Choices.* Washington, DC: National Academy Press; 2005. Available at: http://ppc.unl.edu/publications/documents/PEPPPI_FINALREPORT_DEC_2005.pdf. Accessed February 26, 2006.

Rawcliffe C. *Medicine and Society in Later Medieval England*. London, UK: Sandpiper Books Ltd; 1995.

Rawls J, *The Law of Peoples*. Cambridge, Mass: Harvard University Press; 1999.

Rosenberg CE. *The Cholera Years: the United States in 1832, 1849, and 1866*. Chicago, Ill: University of Chicago Press; 1987.

Ross R. *Memoirs, With a Full Account of The Great Malaria Problem and Its Solution*. London, UK: J. Murray; 1923:226.

Sachs J. *The End of Poverty: Economic Possibilities for Our Time*. New York, NY: Penguin Group; 2005.

Sandman P, Lanard J. Pandemic influenza risk communication: the teachable moment. December 4, 2004. Available at: http://www.psandman.com/col/pandemic.htm. Accessed February 3, 2006.

Schultz J. Bird flu vaccine won't precede pandemic. Quoting Daniel Lucey, co-director of the Biohazardous Threats and Emerging Diseases graduate program at Georgetown University: "There is no H5N1 pandemic so there can be no pandemic vaccine." *United Press International* Web site. Available at: www.upi.com/ConsumerHealthDaily/view.php?StoryID=20051128-054641-9412r. Accessed February 4, 2006.

Selgelid MJ. Ethics and infectious disease. *Bioethics*. 2005;19:272-289.

Sencer DJ, Millar JD. Reflections on the 1976 Swine Flu Vaccination Program. *Emerg Infect Dis*. 2006;12:29-33.

Shapiro H, Meslin E. Ethical issues in the design and conduct of clinical trials in developing countries. *N Engl J Med*. 2001;345:139-142.

Shortridge KF. Pandemic influenza: a zoonosis? *Semin Respir Infect*. 1992;7:11-25.

Singer PA, Benetar SR, Bernstein M, et al. Ethics and SARS: lessons from Toronto. *BMJ*. 2003;327:1342-1344.

Small PM, Fujiwara PI. Management of tuberculosis in the United States. *N Engl J Med*. 2001;345:189-200.

Southeast Regional Center of Excellence for Biodefense and Emerging Infections. The dual-use dilemma in biological research. In: *Core I. Policy, Ethics, and Law Core of the Southeast Regional Center of Excellence for Biodefense and Emerging Infections*. Available at: http://www.serceb.org/modules/serceb_cores/index.php?id=3. Accessed March 2, 2006.

Stanford Program in Human Biology Web site. *The Medical and Scientific Conceptions of Influenza.* Available at: http://www.stanford.edu/group/virus/uda/fluscimed.html. Accessed February 4, 2006.

Staver S. MDs wary of treating AIDS patients. *American Medical News*. June 19, 1987; 35:59-60.

Tambyah PA. SARS: responding to an unknown virus. *Eur J Clin Microbiol Infect Dis.* 2004;23:589-595.

Teutsch SM, Churchill RE, eds. *Principles and Practice of Public Health Surveillance.* New York, NY: Oxford University Press, Inc.; 2000.

Thacker SB, Berkelman RL. Public health surveillance in the United States. *Epidemiol Rev.* 1988;10:164-190.

Thacker SB, Dannenberg AL, Hamilton DH. Epidemic Intelligence Service of the Centers for Disease Control and Prevention: 50 years of training and service in applied epidemiology. *Am J Epidemiol.* 2001;154:985–992.

Thorson A, Petzold M, Nguyen TK, Ekdahl K. Is exposure to sick or dead poultry associated with flu-like illness?: Population-based study from a rural area in Vietnam with outbreaks of highly pathogenic avian influenza. *Arch Intern Med.* 2006;166:119-123.

Tiruviluamala P, Reichman LB. Tuberculosis. *Annu Rev Public Health.* 2002;23:403-426.

Trouiller P. Drug development outcomes for tropical diseases: 1975-1997. Paper presented at: Médecins sans Frontières/World Health Organization Workshop. Drugs for Communicable Diseases, Stimulating Development and Securing Availability; October 1999; Paris, France. Available at: http://www.accessmed-msf.org/prod/publications.asp?scntid=592001159122&contenttype=PARA&). Accessed February 28, 2006.

United States Central Intelligence Agency. *The Global Infectious Disease Threat and its Implications for the United States. NIE-99-17D.* Available at: http://www.cia.gov/cia/reports/nie/report/nie99-17d.html. Accessed February 28, 2006.

University of Toronto Joint Centre for Bioethics, Pandemic Influenza Working Group. *Stand on Guard for Thee: Ethical Considerations in Preparedness*. November, 2005. Available at: http://www.utoronto.ca/jcb/home/ documents/pandemic.pdf. Accessed on March 14, 2006.

Upshur RE. Principles for the justification of public health intervention. *Can J Public Health.* 2002;93:101-103.

US Code of Federal Regulations. Agricultural Bioterrorism Act of 2002. *7 CFR Part 331* (2005); Possession use and transfer of select agents and toxins, *9 CFR Part 121* (2005); and HHS Final rule. Office of Inspector General. *42 CFR Part 73* (2005).

US Code of Federal Regulations. Public welfare. Protection of human subjects. 45 CFR 46 (1991).

US Constitution. Amendment XIV, §1.

Veatch RM. Disaster preparedness and triage: justice and the common good. *Mt Sinai J Med*. 2005;72:236-241. Available at: http://www.mssm.edu/msjournal/72/72_4_pages_236_241.pdf. Accessed on February 26, 2006.

Vila-Corcoles A, Ochoa-Gondar O, Llor C, Hospital I, Rodriguez T, Gomez A. Protective effect of pneumococcal vaccine against death by pneumonia in elderly subjects. *Eur Respir J*. 2005;26:1086-1091.

von Leeuwenhoek A. Excerpt from a letter dated September 17, 1683, to the Royal Society of London, and printed in the Philosophical Transactions of the Royal Society. Available at: http://www.ucmp.berkeley.edu/history/leeuwenhoek.html. Accessed March 20, 2006.

Wertheimer A. *Exploitation*. Princeton, NJ: Princeton University Press; 1996.

World Health Organization. *Avian Influenza A(H5N1)—Update 31: Situation (poultry) in Asia: Need for a Long-term Response, Comparison with Previous Outbreaks*. March 2, 2004. Available at: http://www.who.int/csr/don/2004_03_02/en. Accessed February 3, 2006.

World Health Organization. *Summary of Probable SARS Cases with Onset of Illness from 1 November 2002 to 31 July 2003*. Available at: http://www.who.int/csr/sars/country/table2004_04_21/en/index.html. Accessed on February 4, 2006.

World Health Organization, *WHO checklist for influenza pandemic preparedness planning, 2005*. Available at: http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_4/en/index.html. Accessed on February 26, 2006.

World Medical Association. *Declaration of Helsinki, Ethical Principles for Medical Research involving Human Subjects*. Principle 19. Available at: http://www.wma.net/e/ethicsunit/helsinki.htm. Accessed February 20, 2006.

Yardley J. After its epidemic arrival, SARS vanishes. *New York Times*. May 15, 2005. Available at:

http://www.nytimes.com/2005/05/15/health/15sars.html?ex=1143349200&en=220b704e741d344c&ei=5070. Accessed March 24, 2006.

Yerokhin VV, Punga VV, Rybka LN. Tuberculosis in Russia and the problem of multiple drug resistance. *Ann NY Acad Sci.* 2001;953:133-137.

Virtual Mentor

Ethics Journal of the American Medical Association
April 2006, Volume 8, Number 4: 289-291.

Contributors

Alison Bickford is a third-year student in the Medical Scientist Training Program (MD-PhD) at Northwestern University's Feinberg School of Medicine. Her thesis research examines the relationship between dendritic cells and mast cells in infection and autoimmunity. Between graduation from Amherst College and beginning medical school, she spent a year researching tuberculosis with Partners in Health in Siberia.

Mark S. Dworkin, MD, MPHTM, is the state epidemiologist for infectious diseases and team leader for the Rapid Response Team at the Illinois Department of Public Health, Office of Health Protection, Division of Infectious Diseases.

Chris Feudtner, MD, PhD, MPH, is the director of research for the Pediatric Advanced Care Team and the Integrated Care Service at the Children's Hospital of Philadelphia. He is also a senior fellow at the University of Pennsylvania's Center for Bioethics.

Michael Fumento, JD, a senior fellow with the Hudson Institute in Washington DC, is an author, journalist, and attorney specializing in health and science issues. He is a graduate of the University of Illinois College of Law.

Christine Grady, RN, PhD, is head of the Section on Human Subjects Research in the Department of Clinical Bioethics at the National Institutes of Health, Bethesda, Maryland. She is a senior fellow at the Kennedy Institute of Ethics, a fellow of the American Academy of Nursing, and a fellow of the Hastings Center. Her research interests include human subjects recruitment and international research ethics.

Douglas H. Hamilton, MD, PhD, is director of the Epidemic Intelligence Service Program at the Centers for Disease Control and Prevention in Atlanta, Georgia. He received both his medical degree and doctoral degree in microbiology from Vanderbilt University, Nashville, Tennessee.

Maureen Kelley, PhD, is assistant professor in the Philosophy Department and Sparkman Scholar in Global Health in the School of Public Health at the University of Alabama at Birmingham.

Mona Loutfy, MD, MPH, is an assistant professor at the University of Toronto, Ontario, Canada, and an infectious diseases specialist. Her medical degree is from the University of Toronto, and her MPH is from Harvard University's School of Public Health.

Anya Likhacheva is a third-year medical student at the University of Arizona and was the 2003 Outstanding Senior of the Department of Molecular and Cellular Biology.

Jessica Mellinger, MPhil, is a third-year medical student at Northwestern University's Feinberg School of Medicine. Prior to starting medical school, she studied English and the History of Medicine as a Rhodes Scholar at Oxford University.

Sean C. Murphy is an MD-PhD candidate studying malaria at the Northwestern University's Feinberg School of Medicine in Chicago, Illinois.

Parveen Parmar, MD, is a resident in emergency medicine at UCLA. She is a graduate of Stanford University and Northwestern University's Feinberg School of Medicine where she helped found the school's chapter of Physicians for Human Rights.

Kate Scannell, MD, is an internist and geriatrician in Oakland, California, with Kaiser Permanente Northern California, where she also directs the Department of Medical Ethics. She is a graduate of the Michigan State University College of Medicine and author of *Death of the Good Doctor: Lessons from the Heart of the AIDS Epidemic.*

Martin A. Strosberg, PhD, MPH, is professor of healthcare management at the Graduate College of Union University, Schenectady, New York, and professor of bioethics at the Alden March Bioethics Institute at Albany Medical College, Albany, New York.

Sarah Sutton, MD, is a member of the Department of Infectious Disease at Northwestern University's Feinberg School of Medicine. She is a graduate of the Loyola University of Chicago Stritch School of Medicine.

Alison Thompson, PhD, is a post-doctoral fellow at the Centre for Research on Inner City Health at St. Michael's Hospital in Toronto, Ontario, Canada. She has a background in philosophy and applied ethics and is a member of the University of Toronto Joint Centre for Bioethics Pandemic Influenza Working Group.

John Wadleigh, DO, is in private practice in family medicine in Tucson, Arizona. He is a graduate of Western University of Health Sciences, Pomona, California.

Staff Contributor
Sarah Fujiwara is a student at DePaul University's College of Law in Chicago, Illinois, and an intern in the Ethics Group at the American Medical Association, also in Chicago, during the spring 2006 semester.

Theme Issue Editor
Amanda J. Redig, a student in the Medical Scientist Training Program (MD-PhD) at Northwestern University's Feinberg School of Medicine, is conducting her doctoral research at the Robert Lurie Cancer Research Center. Mandy was an intern with the Ethics Standards Group at the American Medical Association in 2003-2004, an experience which helped further her interest in bioethics. She hopes to focus her career on the relationships between clinical oncology, medical research, and science policy.