Tuberculosis

Resurgence in the 1990s

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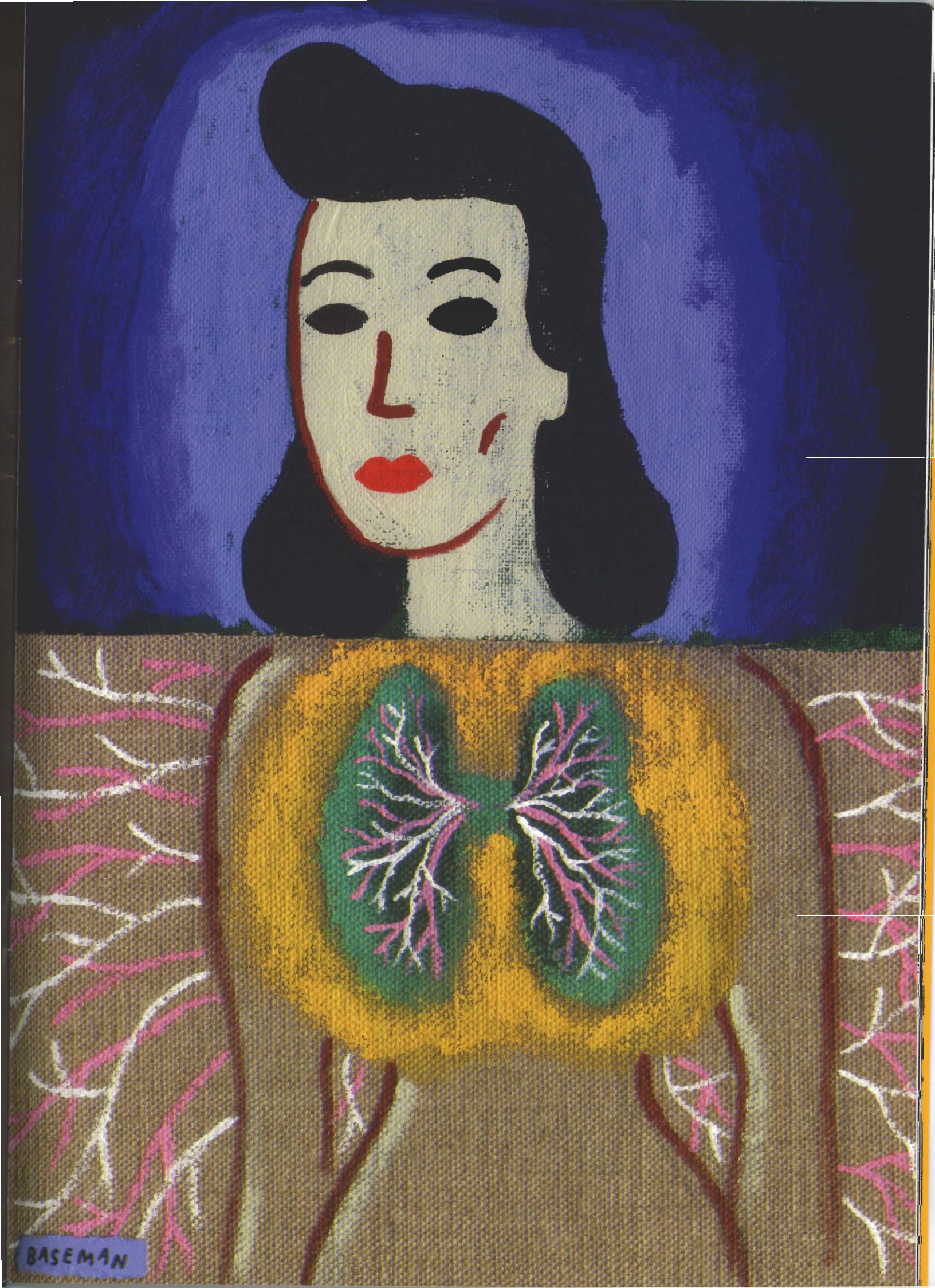
BASEMAN

It is a pleasure and opportunity to be here with you today. After spending time over the last several weeks reflecting about what I could bring to this conference, I found a copy of *The Journal of Collegium Aesculapium* published in 1985. Dr. James Parkin, with whom I was an undergraduate, made the comment that preparation for his talk for this conference was a unique experience. He had never used the scriptures to help prepare a medical talk. I have prepared a few church talks utilizing the scriptures but have always been accused of giving them like a medical talk, so it will be interesting to see how this one comes out.

I have entitled the talk "Tuberculosis Resurgence in the 1990s." I thought it would be useful from a historical point of view to see just how long and what we've known about tuberculosis. I was intrigued to find in Chinese history that about 3000 B.C. there was a book written called *Nei Ching,* which means "The Book of Medicine." These writings had a fairly interesting description of a disease that had been observed. There may be something lost in the translation, but it reads as follows: "Generally the disease gives rise to high fever, sweating, asthenia, unlocalized pain making all positions difficult and slowly bringing about consumption and death; after which the disease is transmitted to all relations until the whole family has been wiped out." So, apparently as early as 3000 years B.C. there was some understanding of the transmissibility of tuberculosis. There are more objective findings that would clearly indicate that tuberculosis existed during the Shang dynasty from 1650 to 1027 B.C. Analysis of bones taken from this period has shown evidence of tuberculosis, manifested as Pott's disease.

Evidence for the existence of tuberculosis in Egypt was first discovered by Elliott Smith in 1907. He described the mummy of Nesperehan, an Egyptian civic dignitary of the 21st Dynasty, that had classic Pott's disease and a large psoas abscess that had drained into the pelvis. Since that discovery many Egyptian mummies have been found that have vertebral deformities consistent with Pott's disease, some of which date back as early as 3400 B.C.

In India there is a writing called "Rig Veda," which means knowledge, containing a group of hymns and incantations that the Indians used to treat various kinds of maladies. One of these hymns, written about 1500 B.C., is clearly written for the treatment of tuberculosis.

The next obvious source was to go to the Bible and see if I could find some references to tuberculosis there. Leprosy is referred to frequently, but nothing that clearly suggests tuberculosis. It is interesting to speculate why that might be, since tuberculosis certainly existed at the time of the Old Testament. There is not much room for the physician in Hebrew philosophy. God was the healer. He was the source of life and health and sent disease and disaster to mankind as a punishment for sin, healing only if man were worthy of cure. In Exodus 15:26 it says, "If thou will diligently harken to the voice of the Lord God and will do that which is right in his sight and will give ear to his statutes, I will put none of these diseases upon thee, which I have brought upon the Egyptians, for I am the Lord that healeth thee." So we are to understand that the Hebrew philosophy was that disease was a divine punishment and therefore a mark of sin. There are a couple of other things I did find about physicians in the Old Testament. For example, "When thou feelest sick, call upon God and bring the physician, for the prudent man scorneth not the remedies of the earth." So apparently, if you talked and asked for God's help first, then you could call the physician. But compare that to the words that were given to King Asa recorded in Chronicles II in the 16th chapter, where it says, "And Asa in the thirty and ninth year of his reign was diseased in his feet until his disease was exceedingly great [remember he was a righteous king], yet in his disease he sought not to the Lord but to the physicians." The next line says, "And Asa slept with his fathers." He died. So you talked to God first, and then you could call on your physician, but if you went directly to the physician, it didn't work.

Since nothing was written about tuberculosis in the Old Testament, I went to the next time frame in which I could find something recorded. This was in the Cuneiform Text that described the transmission of tuberculosis by expectoration. This was a fact accepted by Hippocrates, who lived 460–377 B.C.

We have to get almost to modern times to get additional information. In the 17th century there was a French physician whose name was Franciscus Sylvius. In 1679, while doing an autopsy, he discovered nodular formations in the lungs, intestine, and liver of a patient, and he gave them the name of tubercula. Nearly two centuries later, in 1865, a man named Villian was able to transfer pus from patients with tuberculosis to rabbits and produce a similar disease. Interestingly, that didn't cause much interest, and many history books don't even mention his name. It was not until later in that century, when Robert Koch did his famous experiments, that the cause of tuberculosis was established in the eyes of the world. He took pus from humans with tuberculosis, isolated the bacillus in pure culture, stained it, and then inoculated experimental animals, thus reproducing the disease. He received the Nobel Prize in 1905 for his work. Unfortunately, there was no effective treatment for the disease for the next 60 years after this extraordinary discovery.

The public perception of tuberculosis has not always been as it is today. This is a part of history that I was not really familiar with. Early in the 1800s, tuberculosis was perceived to be what we would call today a "designer disease." It was still very much a lethal disease, but it

involved a lot of very well-known and wealthy people. Lord Byron described in some of his writings about how pale he looked. Many of the female population who enjoyed his writings said, "I should like to die of consumption; look at poor Byron, how exquisite he looks in dying." Isn't that an interesting observation? Consumption apparently was an expression of character, physical refinement, and artistic purity. If you weren't that way before you got consumption, the disease would confer those qualities upon you. Such was the belief at that time. Many famous people died of tuberculosis. The one that intrigued me the most was Molière, who suffered a fatal pulmonary hemorrhage during the performance of a play entitled "The Imaginary Malady." He was highly critical of all the treatments physicians offered. Other famous people who died of pulmonary tuberculosis included St. Francis, Emperor Joseph II, Calvin the Reformer, Chopin, Carl Maria von Weber, and Laënnec.

With the onset of the industrial revolution, the demographics of tuberculosis began to rapidly change, with the urban poor becoming a primary target. Malnutrition and overcrowding, which was suffered primarily by this class, created the greatest risk. Tuberculosis became a disease of the poor and disenfranchised.

So when you don't have a treatment or cure for a problem, what do you do? You get organized, protest, and march. It was no different in the 1800s. In 1892 a group called the Penn Society for the Prevention of Tuberculosis organized and went nationwide to promote better hygiene, but in addition, to improve the moral behavior of the working classes. Those were their twin goals. To quote Ellen La Motte, an antituberculosis crusader, "It is primarily and essentially a disease of the poor.... People of this class are by nature weak, shiftless, and lacking in initiative and perseverance. They have neither inherited nor acquired moral strength...and are often vicious, besides." By the turn of the century, tuberculosis was seen as a menace to society. Poverty itself was considered a measure of sinfulness, hearkening back to the Hebrew philosophy of the Old Testament that if you were ill it was a direct punishment from God for sinful living. So we see the transformation in less than a century of the sick person, who was once considered intelligent, spiritual, and physically beautiful, to a creature of weakness, ignorance, and immorality. Stereotypes linked with racism were common as well because of the higher incidence of this disease in African Americans and in American Indians.

Other interesting events occurred during the early 1900s. A group of ladies decided that expectoration was the major cause of the spread of tuberculosis. Since they couldn't get men to quit spitting on the sidewalks, they put together large brigades of women with mops and disinfectants in Syracuse, New York, to disinfect the sidewalks. None of these efforts really were very helpful in reducing the spread of tuberculosis. The appearance of sanitoria in 1905 did not cure many people of tuberculosis, but it may have helped in reducing its spread.

In 1943 a major breakthrough occurred when a poultry farmer in New Jersey got very frustrated because his chickens were all dying, and he was convinced that it was something to do with the barnyard dirt. He gathered up some samples and took them to a microbiologist named Selman Waksmann at Rutgers University, who proceeded to identify a fungus that was causing his chickens to be sick. He fortuitously discovered that this fungus, *Streptomyces gresius,* produced a substance that we now know as streptomycin. For that work and its discovered effect on the tuberculosis bacillus, he won the Nobel Prize in 1952. That same year, INH was essentially rediscovered. It had been known about before but had been sitting on the shelf for quite some time. With the introduction of INH, the death rate from tuberculosis was markedly reduced. In 1970 another major breakthrough occurred with the discovery of rifampin, which allowed shortened treatment periods for tuberculosis. The victory over the greatest killer of modern times seemed absolute in the early 1980s. We live in the age of science where science triumphs. We look to science to solve all of our problems, much like the Hebrews looked to God to solve theirs. I would suggest that maybe we ought to incorporate the approach of the Hebrews in trying to solve the problem of tuberculosis.

Tuberculosis worldwide is a major problem. Thirty to 60 percent of adults in developing countries are affected. Each year there are eight million cases of and at least three million deaths from the disease.

The incidence of tuberculosis nationally, as well as in the state of Utah, has diminished over a 30-year period at a predictable rate of 6 percent per year since records were first kept in 1953. There were over 84,000 cases reported in the United States in 1953, which decreased to a low of 22,201 in 1985. The rate remained steady for the next three years and then increased, so that by 1991 over 26,000 cases were reported, an increase of 18 percent from the low in 1985. The Center for Disease Control (CDC) estimates that in the past seven years there have been 39,000 more cases than would have been expected if the 6 percent reduction in cases per year had continued. Some additional interesting observations having to do with the incidence of tuberculosis relate to race and ethnic groups. Seventy percent of tuberculosis cases in the United States are in racial/ethnic minority populations. The case rates by ethnic origin are 10 times higher among Asian and Pacific Islanders than with non-Hispanic whites, eight times higher among African Americans, and five times higher among Hispanics and American Indians. Overall, the percentage change in the number of cases between 1985 and 1991 has increased in

every group. Asian and Pacific Islanders have gone up 24 percent, whites up 30 percent, African Americans up 60 percent, and Hispanics up 96 percent. Utah doesn't have large numbers of tuberculosis cases, fortunately, but the pattern is similar. The low in the state of Utah was in 1987, when there were 29 cases. In 1992, 78 cases were reported, compared to 59 the year before.

What is the cause of the upsurge? There are a number of factors that play an important role. HIV infection is one of the most important contributors. We know that suppressed immune function in these HIV-infected individuals puts them at great risk for a number of infections, including mycobacterial disease. In addition, of HIV-infected patients who are exposed to tuberculosis, 8 percent per year will develop active tuberculosis. In just five years 40 percent will have active disease. This compares to approximately 5 percent of patients without HIV disease who will develop active disease in the first one or two years after exposure. Only an additional 5 percent will activate their infection over the rest of their lifetime. The statistics represent a tremendous risk to HIV-infected, patients, but they also represent an increased infected pool, which is a risk to others as well.

There are a number of problems diagnosing tuberculosis in HIV-infected patients. Because of the suppressed immune system, false negative tuberculin skin tests are fairly common. We consider a very low level of induration as being significant in these patients, so that even a five-millimeter induration is considered significant. If you have a patient who is HIV infected, has been exposed, and has a negative skin test, they should be tested for anergy before you conclude that the skin test is really negative. Unusual clinical presentations in HIV-infected patients are common. They may have infiltrates in any area of the lung, but no cavities. They may have mediastinal or hilar lymphadenopathy, and, most importantly, they may have a normal chest X ray, in spite of positive smears and cultures. Therefore, the usual radiographic findings we associate with tuberculosis may not be present. The prevalence of extrapulmonary tuberculosis in AIDS patients is much higher than in a population that is not HIV infected.

A second group that contributes to the upsurge in tuberculosis cases are immigrants, who generally come from countries that have a very high prevalence rate for tuberculosis. There are increasing numbers of immigrants to our country and, interestingly, five out of the six countries that have the largest number of immigrants to the United States also have the highest incidence of tuberculosis in their native countries. In 1991 foreign-born individuals represented almost 27 percent of the newly diagnosed cases of tuberculosis, compared to 20 percent in 1985.

A third group with an increasing incidence of tuberculosis includes IV drug abusers and crack cocaine smokers. These seem to be risk factors independent of HIV infection.

Residents of prisons are a fourth group with a striking increase in the incidence of tuberculosis. There are a number of reasons for this increase. Our war on drugs plays an important contributing role, because we take people who are at risk, put them in close contact with each other, and thereby spread the disease. Overrepresentation of ethnic and racial populations with tuberculosis, an increasing number of HIV-infected inmates, injecting-drug behavior, and the crowded prison environment with inadequate ventilation make the prisons a virtual hotbed for transmitting tuberculosis.

Another group, the group I have had the most contact with at our hospital, has been the homeless population. It is estimated from several selected studies that tuberculosis infection in this population is between 18 and 51 percent, and active disease is between 2 and 7 percent. They create some major challenges for us because of our inability to make rapid diagnoses. They are admitted to the hospital, where we begin a workup, but they often leave the hospital before results are available. Our ability to locate them and initiate appropriate therapy has been very limited.

Finally, an increase in the number of people who live in poverty has contributed to the spread of tuberculosis. In the early part of this century, the incidence of tuberculosis actually began to diminish before we had effective chemotherapy. This change was attributed to the increase in the standard of living in this country. Therefore, the development of new drugs will not arrest the spread of tuberculosis unless we solve the social problems that contribute to the increase.

The major new threat that we face today is the development and appearance of multiple-drug-resistant tuberculosis. I would define multiple-drug resistance as *Mycobacterium tuberculosis* resistant to more than one major antituberculosis drug. National surveillance in the first quarter of 1991 revealed that 14.4 percent of *Mycobacterium tuberculosis* isolates were resistant to one drug, and 3.3 percent were resistant to both isoniazid and rifampin. Compare that to a study that looked at all the isolates from New York City for the month of April 1991. Of more than 4,000 isolates, 33 percent were resistant to one or more drugs. Twenty-six percent were resistant to isoniazid, and almost 20 percent were resistant to both isoniazid and rifampin. In patients who had received previous antituberculous therapy, 44 percent of the strains were resistant to isoniazid, and 30 percent were resistant to isoniazid and rifampin. Previous therapy was the strongest predictor for the emergence of a resistant organism.

Multiple outbreaks have been described, which I will try to summarize. From 1990 through August 1992, the CDC investigated multidrug-resistant tuberculosis outbreaks in seven hospitals in Miami, New York City, New

you from doing something. Sometimes we get cynical or overwhelmed when we can't fix everything. In 1 John 3:17–18 we are told, "But whoso hath this world's good, and seeth his brother have need, and shutteth up his bowels of compassion from him, how dwelleth the love of God in him? My little children, let us not love in word, neither in tongue; but in deed and in truth." No act of love given to another human being is ever wasted, no matter what the circumstances. Maybe it won't solve the problem, but the act is important. However, some things do more good than others.

I had the opportunity 20 years ago to spend two years in East Africa on a research project investigating the causes of fever. We tried to determine the best treatment given the limited resources available. I was in the process of setting up a laboratory, training technicians, negotiating with the government about hospital space, and ordering supplies, all of which seemed pretty far removed from health care at the time. Every day as I drove to work, I saw people along the road who were in desperate need of health caré. I felt guilty that I was driving past these people and going up and doing all these administrative things.

I had a lengthy discussion with the physician with whom I was training. He sat me down and said, "You have not caught the vision of why we are here. You can treat the ulcer and the epilepsy, and improve the health of five or six people you see along the road, but that will have a minimum impact on health care in a country that needs a new approach to provide care to 25 million people." So he again went through the process with me about what we were trying to accomplish and why we were there. We needed to validate a clinical algorithm with appropriate laboratory tests to enable a medical care system to diagnose the causes of fever accurately without much laboratory support and be able to offer effective treatment: In other words, teach them how they can help themselves. It was an analogy of the African story that if you give a man a fish, you feed him for a day, but if you teach him how to fish, he can feed himself for a lifetime. I had to keep telling myself that over and over again to realize there were things I could do that in the long run had a better chance of really helping them help themselves.

I ran across a story quoted in an article from a medical student journal a couple of months ago that related to the message I'm trying to convey. I will read it to you:

> *There is an island where the tides wash thousands of starfish onto the shore, and they are trapped by the receding tide. Thousands of them are dying. A child comes to the beach and sees the starfish dying. He walks down the shore, and one by one, he throws them back into the sea. An old man comes to the shore and watches the child awhile. "Look at all those starfish," he says to the child. "You can't help them all. What you are doing doesn't matter." The child pauses a moment and then says, "It matters to the starfish."*

And I would add, it matters to God.

How many of you have taken the opportunity to go to the homeless shelter? There are all kinds of opportunities that range from going down and helping serve a meal now and again to a project being organized through IHC to get physicians to volunteer time in an evening clinic. There are lots of opportunities if we will just take them. Have you given any talks in your local schools about alcohol or drugs? Have you volunteered at the Odyssey House? Have you talked to your own children and grandchildren about the risks of drugs? Do you care for HIV-infected patients? There is a rumor going around that nobody likes to take care of HIV patients. Some of the reasons include that they have problems that are too complicated and that we don't have adequate training to deal with these problems. I challenge you to learn, educate yourself, and ask for help—be a part of the solution and not part of the problem.

In John 12:8 Christ said, "For the poor always ye have with you." We won't be able to totally resolve this problem, but we need to be actively engaged in efforts to relieve some of their pain. Above all, we need to be caring, loving, and concerned about the children of God. The many opportunities to provide Christian service are what make our profession unique. I hope that each of you will take opportunities each day to give Christlike service to the less fortunate in your community. □

BIBLIOGRAPHY

Bates, Barbara. *Bargaining for Life: A Social History of Tuberculosis, 1876–1938.* University of Pennsylvania Press, 1992.

Bloom, Barry, and Christopher JL Murray. "Tuberculosis: Commentary on a Reemergent Killer." *Science* 257 (1992):1055.

Caldwell, Mark. *The Last Crusade: The War on Consumption, 1862–1954.* Atheneum, 1988.

Chowder, Ken. "How TB Survived Its Own Death to Confront Us Again." *Smithsonian* (November 1992).

Dubos, Rene and Jean. *The White Plague: Tuberculosis, Man and Society.* Rutgers University Press, 1952.

Eklektikos. University of Utah Medical Student Publication, 1992.

Guthrie, Douglas, M.D. *A History of Medicine.* London: JB Lippincott Co., 1946.

HIV-Related Tuberculosis. U.S. Department of Health and Human Services, Center for Disease Control, 1992.

Lyons, Albert, M.D., and R. Joseph Petrucelli II, M.D. *Medicine, An Illustrated History.* New York: Abradale Press, 1987.

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