Chapter Nine

Miracle Drugs?

On 23 November 1941, twenty-one-year-old Margaret E. "Midge" Wall and her good friend Iris Garrard swore their commitment to the Army Nurse Corps. They had graduated from Mount Sinai Hospital Nursing School that May, passed their licensing exams, and were working at the hospital. But now the young women were looking for something else, perhaps an adventure. As Wall later wrote, "On 6 November 1941, election day in Chicago, Iris and I were feeling very patriotic. We had just voted for the first time." They had the day off, and went down to the nurses' recruiting station to get information on the Army Nurse Corps. "By the end of the day," she said, "not only had we filled our applications for admission into the Army Nurse Corps, but we had our complete physical examination as well."[1]

Both from North Carolina, the young women had chosen nursing school in Chicago to see the world. Now, when offered assignments in either South Carolina or in Vancouver, Washington, "the latter struck our fancy. This would be a chance to go West, to travel." The night of their swearing-in they boarded a train for Vancouver and three days later were at the Vancouver Barracks Army camp. Wall remembered the American flag flying. "There was a beautiful green lawn, and this together with the neat rows of white buildings was a beautiful and peaceful site. Already we were in love with that place before we had actually driven through the gate." Wall was assigned to Ward No. 13, the contagious disease ward devoted to tuberculosis patients, in Barnes Hospital and immediately went to work. Most of her patients had been evacuated from Alaska. Some of them were Inuits, but most were American soldiers, "typical of the G. I. patients I have come to know so well and love." Many patients were very sick and confined to bed, so her duties involved feeding and bathing them, and assisting in performing and refilling pneumothoraces. Neither she nor the other nurses wore protective clothing or masks while caring for patients. On 7 December, a fellow nurse ran into her room with news of the Japanese bombing of Pearl Harbor. Listening to the radio, they

realized that war was now upon them. "Yes, it was now here, and I had been in the Army only fifteen days." Wall would serve in the Army Nurse Corps for four-and-one-half years.

Wall asked for foreign duty but waited for two-and-one-half years for an overseas assignment. A diary she later wrote for *Stars & Stripes* about her life in the Army reveals that in addition to Ward No. 13, she worked in orthopedics and gastrointestinal wards during the years 1941 through 1943. Finally, in May 1943, she got her new assignment and after several months of training, boarded a ship out of San Francisco for the South Pacific theater. Her first post was the 27th Station Hospital in New Caledonia, where she contracted dengue fever, a serious disease transmitted by mosquitoes. But, more happily, she also met a "tall and handsome officer," Lieutenant (Lt.) John Gaule, an infantry officer with the Sixth Replacement Depot. The two became engaged and when they learned that her unit would be transferred out of New Caledonia, asked for permission to marry. (The War Department had lifted the prohibition on marriage for members of the Army Nurse Corps in 1943.) They wed on 3 January 1945 and after three months of married life, Midge, now Margaret Gaule, departed for the front lines and the Battle of Okinawa, one of the deadliest encounters of World War II. "I could hardly wait to get ashore and care for these wounded men of ours.... Now I finally had a chance to do the nursing I had wanted for so long to do," she later wrote. Assigned to the shock ward of the 74th Field Hospital on Buckner Bay, Okinawa, Gaule was able to give newly developed and life-saving whole blood and blood plasma units to severely wounded men. It was an experience that would stay with her for life. The War Department gave Gaule a commendation for her war service and discharged her on 25 March 1946 (Figure 9-1).

John and Margaret Gaule began their postwar life in John's hometown of Omaha, Nebraska, where he worked in the insurance business. By 1956, they had three sons. One Sunday evening in August of that year, returning from a trip to North Carolina to visit her family, Gaule was feeling tired and then had a "massive oral hemorrhage." Her husband rushed her to an Omaha hospital where several physicians examined her, including P. James Connor, M.D., just out of medical school.[2] Diagnosed with "chronic pulmonary tuberculosis, far advanced, active," Gaule entered the veterans' hospital in Omaha. When she wrote of her illness to Jean Greer, who had been the assistant chief nurse at Barnes Hospital, Greer responded, "I cannot tell you how shocked and sorry I was to receive the news that your letter brought yesterday.... Do not kid yourself—it is going to be a long and tedious battle." She knew, because she, too, had had tuberculosis, and had spent eighteen months in the hospital and more than eight years with a pneumothorax. She told Gaule that three other nurses from the Barnes tuberculosis ward—Cecilia Smith, Frances Van Hoomissen, and Gladys Larkin—had also developed tuberculosis. This meant that five of twenty-five nurses—20 percent—in tuberculosis Ward No. 13 at Barnes during the early war years developed active tuberculosis. Remembering that kiss under the mistletoe from a patient, Gaule later said, "I should have known there'd be a problem with Ward 13."[3]

Figure 9-1. Margaret E. Gaule, nurse with the 74th Field Hospital on Buckner Bay, Okinawa, who participated in the Battle of Okinawa in 1945.
Photograph courtesy of the family of Margaret E. Gaule.

Although seriously ill, Gaule was fortunate to be in the first generation of tuberculosis patients during the era of effective treatment—but it was not a quick or miracle cure. Gaule spent eight months in the Omaha veterans' hospital on rest therapy and new antibiotic medications. Her physicians at the Veterans Administration (VA) considered surgery, but she and her husband got a second opinion at the Mayo Clinic, which recommended against it, so she refused surgical intervention.[4] Once she was discharged from the hospital, Gaule continued to take antibiotics for a year. Given the hardship, and the cost of care for her three young children while she was in the hospital, Gaule filed for veterans' compensation. In January 1958, however, the VA Board of Veterans' Appeals denied her claim because she had not developed active tuberculosis within three years of her termination of service in the Army Nurse Corps, and therefore fell outside of the presumptive period for benefits.[5] Unlike so many Army nurses over the years, Gaule was able to recover her health and had another baby boy. But her scarred lungs remained a lifelong reminder of the costs of being a tuberculosis nurse—and of the fact that the government had refused to recognize her sacrifice.

Airborne Transmission

While Gaule and other tuberculosis nurses were caring for patients without gloves or masks, the debate about airborne transmission and immunity continued in both military and civilian medical circles. In 1943 Army medical reserve officer Colonel (Col.) John Wakeman Turner reprised Bushnell's epidemiology of tuberculosis in *Military Surgeon*, lamenting the fact that many people "do not believe in the laws of tuberculous immunization," and that "such a state of mind is unfortunate and is not helpful in practical prophylaxis."[6] In 1948 a civilian physician similarly wrote, "It is estimated that about one half of the population of the United States is tuberculin positive.... Most doctors feel that a positive tuberculin indicates a greater resistance to a reinfection of the disease."[7] Others continued to worry, however, about high rates of tuberculosis among nurses. An *American Journal of Nursing* author said that tuberculosis should be considered an occupational disease for the nursing profession, but that "tuberculosis control among nurses is lagging far behind the control of silicosis in industry."[8]

Predictably, the issue of tuberculosis transmission transcended medical circles and entered the courts. In the 1940s some people began to make workers' compensation claims for contracting tuberculosis in the workplace and patients began to sue hospitals for developing tuberculosis while being treated for something else.[9] Two New York City physicians were frustrated that although "contagiousness is not a definite fixed characteristic of tuberculosis," in the courts "claims for compensation are granted daily by judges, referees and juries on the lay belief that tuberculosis is always a contagious disease."[10] In 1951 the journal *Chest* noted a study that found that only 247 of 4,539 general hospitals had "satisfactory programs" to prevent the transmission of tuberculosis in their institutions, and warned that "no hospital can afford to have contagious tuberculosis exist among its patients or personnel unless they are under rigid isolation technique."[11] Many hospitals had been

compelled to compensate their employees and, *Chest* observed, "[C]ourts have granted awards to persons, who, as patients, were exposed to contagious cases of tuberculosis and later fell ill from this disease." This judicial involvement was regrettable, the editors believed, because when "rigid isolation technique was instituted…the fear of having tuberculosis patients in general hospitals because of contagion is unfounded."[12]

Several efforts, however, suggested the need for continued education and advocacy to encourage general adherence to the procedures. In 1955 the National Tuberculosis Association issued a fifty-page document on tuberculosis control procedures with rigorous contagious disease precautions, and the American College of Chest Physicians assembled a series of scientific papers on the issue for wide distribution. Some people called for more legal authority. Two physicians suggested that because some patients simply would not practice hygienic measures, "It appears that successful management can never be completely attained without the aid of a compulsory hospitalization law."[13] Others agreed that "tuberculosis is a serious communicable disease that should require isolation, enforceable by law."[14]

After the war, in addition to periodic tuberculin and X-ray examinations of its staff, Fitzsimons did gradually institute more stringent protective practices. In 1947, the hospital medical service reported that "a real effort has been made to establish good standard measures of aseptic technique."[15] Measures included special lectures, training on the wards, and the inevitable circulation of memoranda on the subject. The next year the construction of a "gown room" allowed medical personnel to scrub before and after entering the tuberculosis wards.[16] In 1949, Fitzsimons constructed a new administration building and a separate receiving ward for the tuberculosis section that provided additional isolation, and by 1950 nurses were attending a four-day orientation course on tuberculosis that included instruction on "protective technique, conducted by an especially trained Army nurse assigned permanently to the Chest Disease Section."[17] Out of step with these changes, a 1956 Army lesson plan on "The Fundamentals of Tuberculosis Nursing," by nurse Florence Bankhead, continued to emphasize the role of sputum rather than airborne infection in tuberculosis transmission. "Tuberculosis germs are carried from the mouths of people who have active tuberculosis to the mouths of well people," she wrote. "These germs are spread by kissing, coughing, spitting, sneezing, and also by putting things like pencils, pens, forks, spoons, or cups into one's mouth after they have first come into contact with germs from a person with active tuberculosis."[18]

Researchers continued to investigate tuberculosis transmission exploring routes such as skin punctures or abrasions, the alimentary tract, cigarettes and smoking, dust, and animal secretions.[19] Some scientists also began to uncover evidence of the power of tuberculosis bacteria to persist and travel in the air. In the 1930s, W. F. Wells, of the University of Pennsylvania's Department of Pathology, demonstrated that droplet nuclei could be suspended in the air for long periods of time. Citing this and other studies, Max B. Lurie, of the University of Pennsylvania and the Henry Phipps Institute in Philadelphia (Esmond Long's institution), stated

in 1946 that "pulmonary tuberculosis is largely an airborne disease. It originates from the inhalation of invisible droplet nuclei or microscopic dust particles carrying tuberculosis bacilli."[20] In 1949 Esta McNett, a nurse and a consistent advocate of protective technique, urged the use of facemasks, stating the "modern medical opinion inclines strongly toward inhalation infection as the most important mechanism in the transmission of tuberculosis."[21] But the issue was still not settled.

In the mid-1950s Richard L. Riley, a student and colleague of W. F. Wells, theorized that tuberculosis bacteria could exist on these droplet nuclei and therefore travel far from a patient to be inhaled by other people.[22] To test this theory and to see if ultraviolet light could disinfect air containing tuberculosis bacilli, he installed two chambers with cages of guinea pigs in the air ducts above the rooms of patients with advanced tuberculosis in a Baltimore VA hospital. In one chamber, air from the patients' rooms was exposed to ultraviolet light before reaching the guinea pigs and in the other chamber it was not. After two years Riley found that none of the guinea pigs in the chamber using ultraviolet light had been infected with tuberculosis, but 71 of 156 guinea pigs in the other chamber had become infected. Besides proving the salutary effect of ultraviolet light, the latter finding also, even more strikingly, proved that tuberculosis bacteria could be airborne. After eliminating other sources of tuberculosis, that is, ensuring that the workers who cared for the animals had never been infected with tuberculosis and that the animals had not infected one another, Riley and his team asserted that their evidence "justifies the conclusion that all seventy-one guinea pigs were infected by aerial contamination produced by patients occupying a tuberculosis ward."[23]

In its 1959 article, "Aerial Dissemination of Pulmonary Tuberculosis: A Two-Year Study of Contagion in a Tuberculosis Ward," Riley's team was able "to demonstrate beyond question the fact of aerial dissemination and the probability of its predominant importance in the transmission of pulmonary tuberculosis." The air did not contain a large quantity of tuberculosis bacteria, but, team members argued, their work demonstrated that even a small number of bacilli could cause an infection. Given that epidemiological studies had shown that it took a tuberculin-negative nurse about a year to convert to positive, the Riley team could argue that "the amount of airborne tuberculosis in the vicinity of patients, though small, appears to be enough to account for the observed rate of infection, at least in nurses." Pulmonary tuberculosis, the team concluded, "is a classic example of air-borne contagion."[24] This theory was widely disseminated in a textbook by Riley and F. O'Grady, *Airborne Infection*, first published in 1961.[25] The National Tuberculosis Association awarded Riley its Trudeau Medal, given annually for the most meritorious contribution to increased understanding of the cause, prevention, and treatment of tuberculosis. The National Tuberculosis Association said that Riley's work "has shaped modern thinking about transmissibility, the uselessness of many traditional isolationist strictures, scientifically valid cautionary measures, and the place for air disinfection with ultraviolet radiation."[26]

This, finally, was the scientific proof needed to end the debate on transmission and protect tuberculosis workers, patients' families, and the public from infection. When the American Epidemiological Society reprinted the article as a classic in

1995, Dr. Michael B. Iseman, tuberculosis expert at the National Jewish Center for Immunology and Respiratory Medicine in Denver, wrote that "because of these findings, urgent steps have been taken to lessen the risks of institutional transmission of tuberculosis."[27] In a bittersweet irony, however, those precautions would become increasingly less urgent because researchers finally were able to devise a cure.

Antibiotics

The discovery of penicillin and its wonderful wartime success in curing a wide range of infections spurred increased research—indeed a race—to find additional antibiotic agents. In the spirit of this hunt, Rutgers University soil scientist Selman Waksman and his assistant Albert Schatz discovered in 1943 that streptomycin inhibited the growth of tuberculosis bacilli in the laboratory. There was little interest in their work, however, until 1945, when researchers at the Mayo Clinic showed streptomycin's effectiveness in treating patients with advanced cases of tuberculosis.[28] Then, as curiosity about the new drug surged, the National Research Council convened representatives of the Army, Navy, VA, and Public Health Service in mid-1946 to structure trials for streptomycin therapy and determine how to distribute the limited supply of the drug. The ubiquitous Esmond Long served as the acting chair and Fitzsimons became one of the leading institutions in the project. The process to develop an effective cure, however, took almost a decade during which time physicians continued to prescribe bed rest, lung collapse treatments, and surgery—in addition to antibiotics—to help their patients.

Military and VA hospitals were attractive research venues because of the often-large numbers of similar patients (young men) with the same disease or injury. Medical officers would identify patients whose condition and symptoms they believed would make them appropriate for new, experimental procedures or medicines, and then seek the patient's voluntary consent. (The power relationship between officers and enlisted men, physicians and patients, however, raises the question of the extent to which consent was indeed voluntary.[29]) The streptomycin trials also indicated that experimentation in military and veteran populations was becoming increasingly politically sensitive. Historian Harry Marks has described how streptomycin experiments on tuberculosis patients helped usher in a new era in scientific research using double-blind randomized drug testing that has become the standard today. The new procedures enabled scientists to compare results for patients receiving a new drug with results from a control group receiving placebos, and the randomized selection of subjects avoided biasing the test cohort and prevented physicians and patients from knowing which they were receiving.[30] Military and VA investigators were reluctant to use this protocol, however, due to concerns about fairness, physician control, and public relations.

Streptomycin seemed to be so promising, in fact, that the National Research Council committee decided against using placebos, believing the practice would not be fair to its patients. The committee instead agreed that the first

cases on which to test the new drug should be those where the tuberculosis diagnosis was clear, and "moderately advanced in extent, with evidence of recent progression."[31] Long preferred to leave the choice of patient subjects to the research staff. He told Larry B. McAfee at Bruns Hospital, who participated in the trials, that medical officers at Fitzsimons were concerned about public relations because "[i]f the word gets around that some men have been selected for a 'Miracle Drug,' the press may seize the opportunity, and the Army may be accused of partiality." Therefore, he told McAfee "this office would rather leave the problem to your own judgment in this respect."[32] The VA representative on the committee was also reluctant to use a control group, and objected to the word "experiment," for the trials, preferring "investigation" or "observations" to avoid public censure.[33] The Public Health Service did not participate in the initial National Research Council studies due to lack of funding at the time, but rather conducted its own, smaller investigation and, in contrast to the Army, Navy, and VA researchers, did use control groups. Harry Marks argues that although "both studies testified favorably on behalf of streptomycin, it was the Public Health Service studies, properly randomized, that received credit for demonstrating the new drug's benefits in treating tuberculosis." Moreover, he concludes, the Public Health Service's work "served as an example of scientific progress in therapeutics."[34]

The first National Research Council trials began in June 1946, with groups of ten patients at a time receiving streptomycin, with a prescribed dosage of 1.8 grams per day for four months. Researchers were advised to watch for signs of toxicity. The National Research Council also appointed an outside review board to evaluate the results of the trials. In December researchers convened what would be the first of fourteen "Streptomycin Conferences," held from 1946 to 1955, to evaluate the results, coordinate the studies, and discuss clinical and laboratory issues.[35] At that meeting they found that streptomycin was effective in reversing the course of many cases of tuberculosis, and in particular was able to stop the progression of the usually lethal miliary and meninginal tuberculosis. Researchers also immediately recognized several limitations to streptomycin: (*a*) the drug reduced tuberculosis bacteria reproduction but did not kill them; (*b*) prolonged treatment allowed resistant bacteria to develop; (*c*) the drug could damage a cranial nerve responsible for hearing and balance; and (*d*) because the body did not absorb streptomycin well it needed to be administered by numerous, often painful injections.[36]

Patients' improvement was dramatic, nevertheless. Captains Stanley H. Hoffman and George A. Hyman at Fitzsimons reported on a "rather typical" patient whose progression showed the results of the combination of streptomycin and collapse therapy. The twenty-one-year-old white male arrived in April 1947 with "severe constitutional symptoms," including a cough, three-quarters cup of sputum a day, positive smear, and advanced tuberculosis with cavities in both the lungs. They collapsed his right lung and put him on streptomycin, two grams per day given in five injections, from 25 April to 25 August. The patient's temperature returned to normal after three weeks, his cough improved, and his sputum

was negative by July. X-ray films in August "showed remarkable clearing with no definite evidence of cavitation visible," and the improvement continued even after the streptomycin injections were stopped.[37] Because of results such as these, institutions clamored to participate in the National Research Council trials. Torn between conducting careful, scientific studies on the effects of a possible miracle drug on a small number of patients, or making the drug available to a wide range of desperately ill patients, the Army, Navy, and VA researchers opted for the latter. By 1947 the oversight group had lost control over many of the protocols.

The treatment regime was rigorous at the start: large doses (up to two grams) of streptomycin divided into five or six injections daily, for three or four months, which could amount to 450 to 720 shots (this, before the advent of tiny, disposable needles). Many patients also underwent surgery in addition to the drug regime. Fitzsimons' researchers reported on twelve patients who each had from five to ten ribs removed in thoracoplasty, and then received streptomycin for four to eight months with a total dose ranging from 64 to 470 grams. All of the patients improved, losing their fever, gaining weight, and producing negative sputum tests. The fact that one of the twelve left the hospital against medical advice, though, and two others presented "severe disciplinary" problems is not surprising given the invasiveness of the surgery and multiple daily hypodermics.[38] Because some patients had trouble with their balance or hearing or even became deaf after several months of therapy, physicians at Fitzsimons confirmed that "streptomycin is definitely toxic to the great majority of patients." But so many patients responded well that "at present, it would seem folly to withhold the drug when indicated." They cautioned, however, that streptomycin should be used as a complement to and not a substitute for other types of treatment.[39]

Fitzsimons had a strong team guiding the introduction of antibiotic therapies during this time of transition. Col. James H. Forsee, chief of surgery from 1946 to 1953, and Col. Carl W. Tempel, chief of medical services from 1950 to 1955, led efforts to test various combinations of rest, antibiotics (which they called "chemotherapy"), and surgery to find the safest and most effective protocol for their patients. Forsee and Tempel followed similar career paths. Both graduated from medical school in St. Louis in 1929, Forsee from Washington University and Tempel from the St. Louis University Medical School, and then received their Army commissions immediately after graduation. Forsee's first Army assignment was at Fitzsimons General Hospital where he served until 1934, during which time he studied the tuberculin testing of staff and the question of tubercularization.[40] His subsequent assignments included service in Hawaii and at Walter Reed General Hospital. During World War II Forsee earned the Legion of Merit for his service as commander of the Second Auxiliary Surgical Group in Italy. After the war, he returned to Fitzsimons as chief of surgery, and wrote an extensive and widely read report on the front-line surgical treatment of the severely wounded.[41] After Fitzsimons, Forsee (Figure 9-2) served as a surgical consultant at Army posts in Asia and Walter Reed. Promoted to major general in 1962, he held the position of special assistant to the Surgeon General in Washington until his death in 1963 at the age of fifty-nine.

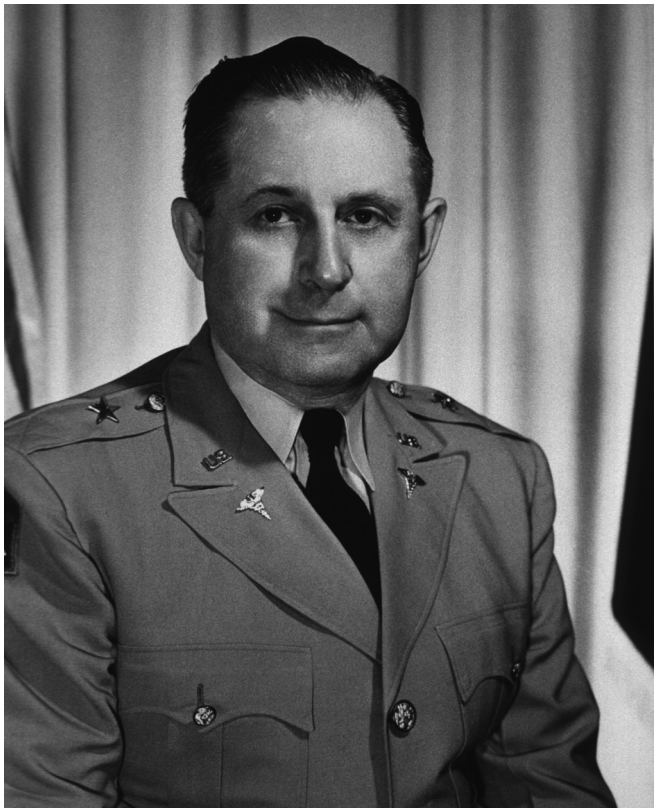


Figure 9-2. James H. Forsee, tuberculosis specialist at Fitzsimons General Hospital, in 1957. Photograph courtesy of the National Library of Medicine, Image #B012074

Carl Tempel's first assignment was at William Beaumont Army Hospital, after which he served at a number of Army hospitals, including Fitzsimons from 1937 to 1940. During the war he was assigned to Walter Reed and then commanded a general hospital in the Asia-Pacific Theater. After the war, he commanded the 42nd General Hospital in Tokyo, and returned to Fitzsimons in 1947, becoming chief of medical services in 1950. After another tour of duty in the Far East, Tempel (Figure 9-3) returned to Fitzsimons in 1960 as its nineteenth commander. Like Forsee, he attained the rank of major general. Tempel retired in 1962 and joined the administration of the Webb-Waring Institute for Medical Research at the University of Colorado Medical Center in Denver.[42] He died in 1979 and was buried at Fort Logan Cemetery in Denver.[43]

Forsee and Tempel were colleagues and friends at Fitzsimons. Their families lived next to each other on "Colonel's Row," and during their years of overlap in Denver they coauthored several articles on tuberculosis treatment, including "The

Figure 9-3. Carl W. Tempel, tuberculosis specialist at Fitzsimons General Hospital, in 1957. Photograph courtesy of the National Library of Medicine, Image #B024680.

Definitive Treatment of Pulmonary Tuberculosis," in *Military Surgeon*, 1950.[44] An example of their leadership includes Forsee's textbook, *The Surgery of Pulmonary Tuberculosis* (1954), based on his experience with the surgical treatment of patients at Fitzsimons. The Association of Military Surgeons of the United States Army also recognized Tempel with the Stitt Award in 1957 for his outstanding medical research with streptomycin.[45]

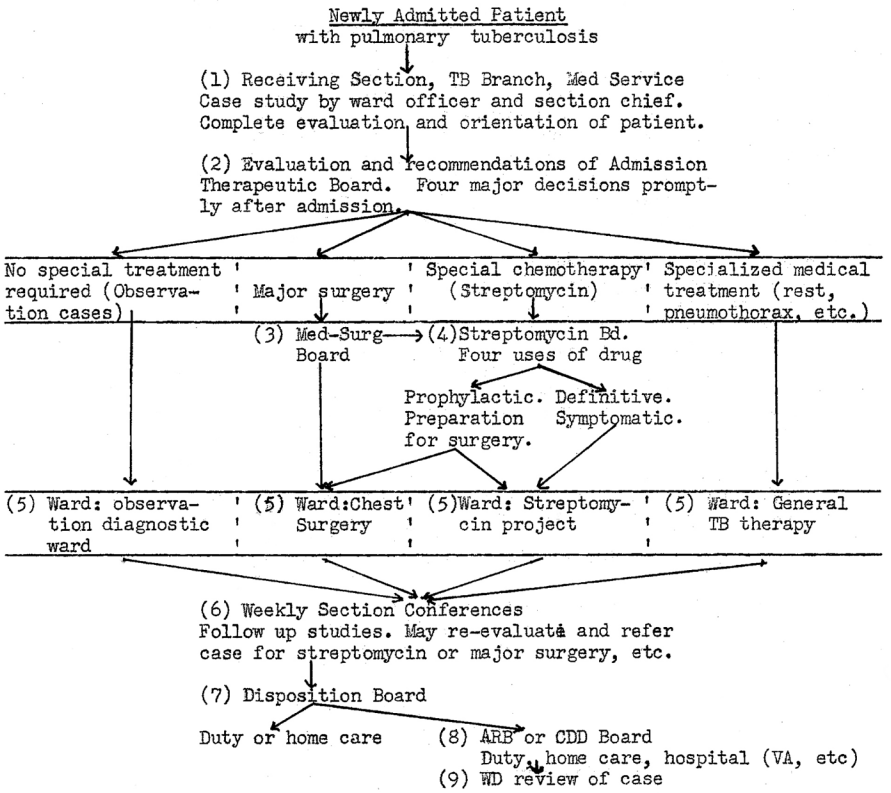
The challenge facing Forsee and Tempel in the late 1940s and early 1950s was to harness streptomycin's power against tuberculosis while minimizing the development of antibiotic resistance and the drug's toxicity to patients.They used all the tools at their disposal—bed rest, collapse therapy, surgery, and the new drugs. Forsee began to administer streptomycin prior to surgery, with the aim of "either improving the operability of the patient or for aiding in the conversion of an unsuitable operative risk in need of surgery to a reasonable surgical risk."[46] Fitzsimons' surgeons also tried resection or removal of diseased lung tissue followed by antibiotics

with good results and found that reducing the streptomycin dosage reduced toxicity and bacterial resistance.[47] Tempel and his colleagues developed elaborate tables of treatment regimens according to the nature, location, and extent of the patient's infection. In 1947, for example, he prescribed seventeen possible treatment plans (Figure 9-4) combining bed rest, temporary or permanent lung collapse, surgical removal of lung tissue, and streptomycin injections.[48] Tempel also found that bacterial resistance to streptomycin increased with the length of time it was administered. Only 3.9 percent of patients treated for 60 days developed resistance, but fully one-third of patients did after 120 days of streptomycin.[49] Tempel concluded in 1949, therefore, that "streptomycin is only an adjunct to conventional methods of therapy,… chemotherapy will never replace surgical and other measures of therapy."[50]

Physicians soon had another weapon, however, because in 1949 Danish scientist Jorgen Lehman discovered the antibiotic properties of para-aminosalicylate (PAS). Daily doses of PAS given orally in combination with lower doses of streptomycin every other day effectively controlled tuberculosis and reduced the chances of side effects and bacterial resistance. Assessing the results at forty-two hospitals that treated 7,000 cases with streptomycin and PAS (2,000 of them at Fitzsimons), tuberculosis specialists at the 1949 Eighth Streptomycin Conference recommended against using streptomycin alone, due to the problems of toxicity and resistance and the availability of PAS.[51]

But the optimal treatment was not yet clear. The British journal *Tubercle* editorialized in 1950 that "for a long time clinicians have been feeling their way towards the best way of using the many therapeutic measures at their disposal in the treatment of pulmonary tuberculosis.… There is no settled technique of dosage or length of [the] course of treatment and no agreement as to which sorts of cases should or should not have them."[52] Perhaps in response to such pleas, Tempel, Forsee, and their colleagues published numerous articles outlining tuberculosis treatment, considering factors such as therapeutic effectiveness, lack of toxicity, bacterial resistance, ease of administration, patient acceptance, sustainability for prolonged use, and relative costs of various protocols.[53] As chemotherapy became more effective and less toxic, they also eased the bed rest requirements that were difficult for so many patients. Tempel began to prescribe bed rest only during the early months of hospitalization or in case of serious illness. Thereafter, patients on drug therapy had four hours out of bed daily for "self-care and limited educational and recreational pursuits on the ward." When patients' sputum was negative, chest X-rays were improved, and they had been free of symptoms for a period of six months, they could begin ambulatory outpatient care.[54]

Finally, in 1952, scientists at three different drug companies—Bayer, LaRoche, and Squib—identified a third drug, isoniazid, as effective against tuberculosis bacteria. Gerhard Domagk, a German scientist at Bayer who had won the 1939 Nobel Prize for developing a powerful sulfa drug, pioneered this work. Barred from leaving the country to accept his Nobel award, and despite Allied bombing raids and the Nazi harassment and seizure of his Jewish wife (who survived



From the above it is evident that many staff members contribute to the care of our patients or review the findings, including the following (See reference numbers above)

(1) Admission ward examination
(2) Admission therapeutic Board
(3) Medical-Surgical Board
(4) Streptomycin Board
(5) Specialized Rx on wards
(6) Section conferences, civilian consultations
(7) Disposition Board
(8) ARB, CDD Board (Military only)
(9) WD Boards (Military only)

Figure 9-4. Table of treatment regimes for tuberculosis patients in "Annual Report of Fitzsimons General Hospital, Denver, Colorado, calendar year ending 31 December 1947," 76–77, FGH, Box 5, RG 112, National Archives and Records Administration, College Park, Maryland.

the war), Domagk continued his work on a tuberculosis cure. After the war, Allied scientists gained access to German research laboratories and discovered Domagk's work. Thus researchers at the three companies found isoniazid almost simultaneously.[55] At Fitzsimons, Tempel's team immediately tried isoniazid with streptomycin on sixty-one patients and found that they responded favorably.[56] In 1954 other researchers found that the three drugs together—streptomycin, PAS, and isoniazid—had greater therapeutic value and created fewer resistant strains than

any previous combination.[57] Isoniazid therefore provided the final weapon that, in combination with PAS and/or streptomycin, safely and effectively cured tuberculosis. The treatment was not quick and easy—it involved taking two or three powerful drugs for several months, and sometimes even undergoing surgery—but for most individuals, it was a cure. Thus, as tuberculosis expert Michael Iseman explains, by 1954, "it was recognized that combining isoniazid, streptomycin, and PAS afforded nearly universal, lifetime cures of a scourge that had ravaged humankind like no other."[58]

Tuberculosis rates had already been steadily declining throughout the twentieth century in many countries, but with effective antibiotics the ability to save the lives of the very sick and to actually cure many tuberculosis cases marked a qualitative change in the fight against the disease and the status of tuberculosis medicine. The effect was—finally, thankfully—dramatic. In 1955, George J. Drolet and Anthony M. Lowell assessed "The First Seven Years of the Antimicrobial Era, 1947–1953," tracking the trajectory of tuberculosis death rates in the VA, Army, and Navy hospitals. They found that before streptomycin, the annual death rate for tuberculosis hospital patients was 20 percent to 23 percent; streptomycin reduced that to 17 percent, PAS and streptomycin brought it to about 10 percent, and the addition of isoniazid brought it down to 7.5 percent of VA and military tuberculosis patients, a two-thirds decrease in the death rate in less than a decade. The national trend was similar, with tuberculosis deaths in the United States falling 60 percent from 48,064 in 1947 to 19,393 in 1953. Other countries experienced declines ranging from a 38 percent drop in Mexico to an 83 percent reduction in Iceland. Drolet and Lowell believed that the shift from bed rest and collapse therapy to the "antimicrobial era" of chemotherapy and excisional surgery marked "the most rapid decline in tuberculosis mortality the world has ever seen."[59]

Others were equally elated. One writer said the trends vindicated Public Health Service epidemiologist Wade Hampton Frost's prediction that tuberculosis would one day be eradicated.[60] Louis Dublin, who had excoriated the VA's tuberculosis program for releasing infectious veterans, was ebullient. "The balance between the tubercle bacillus and man has finally given way in favor of man," he wrote. "We cannot say exactly when control will be complete, but there is every indication that it will be some time in the course of the next 20 years."[61] Most of the celebrants knew tuberculosis too well, however, to be sanguine. As the *American Journal of Public Health* observed in 1956, "While great gains against tuberculosis mortality have been achieved,…far more extensive measures are needed to eradicate infection from millions of adults who still harbor tubercle bacilli."[62] This would prove to be only too true.

Drug therapy did pose new problems. Because of the long duration of the treatment and antibiotics' side effects, some patients declined to complete the course of therapy. This enabled some bacteria to become resistant, and if the patient's tuberculosis resurged, made it more difficult to fight. By 1963, one study found that 8 percent of all new cases of tuberculosis in the country were resistant to streptomycin, PAS, or isoniazid.[63] Other issues emerged with regard to public health and tuberculosis

that continue to be debated today. For example, if early cases of tuberculosis were the easiest to cure, Trudeau medalist James J. Waring at the University of Colorado Medical School asked, "just how minimal does tuberculosis have to be before one would not treat it with chemotherapy?"[64] Should public health officials treat people who had positive tuberculin tests but no other symptoms? Who should be in charge of tuberculosis treatment? Some believed that with effective chemotherapy and fewer patients, tuberculosis treatment could be returned to general practice medicine. But editors at the journal *Chest* countered that not all physicians and medical institutions understood the importance of educating patients about self-care and ensuring that they completed the full drug regimen. This, they cautioned, increased the chance of noncompliance, the development of bacterial resistance, and the spread of tuberculosis. They therefore advocated continuing to send tuberculosis patients to specialists who could provide comprehensive education and care.[65] Carl Tempel, in civilian life at the Webb-Waring Institute in Denver, cautioned in 1964 against "complacency in tuberculosis control," noting that one-quarter of the U.S. population was still infected with tuberculosis bacilli, and that many cases were not discovered until they were far advanced. He counseled continued vigilance and community education on tuberculosis to identify new cases and prevent strains from developing drug resistance.[66]

The new therapies did enable the Army to eliminate most tuberculosis from the ranks by screening out tuberculous recruits and then carefully overseeing the comprehensive application of the new treatments on any military patients. A study of VA and military patients successfully treated with chemotherapy from 1951 through 1954 reported that 86 percent returned to duty, work, or school. The researchers happily found that "working does not cause relapse, even when the work requires a high degree of physical exertion, even when pulmonary tuberculosis has been far advanced—if there has been definitive treatment of the disease."[67] By 1955 only 4.4 percent of veterans receiving disability payments had tuberculosis (91,000 of more than 2 million).[68]

This trend raised policy questions. After World War II, the U.S. Congress and the VA again struggled to define clear and equitable benefits for tuberculous veterans; the emergence of effective chemotherapy for the disease further complicated the issue. Postwar benefits provided disability compensation from 0 percent to 100 percent depending on the degree of a veteran's impairment. World War II tuberculosis veterans also had access to vocational rehabilitation and "G. I. Bill" education benefits and loans, and some of their survivors were eligible for Social Security benefits.[69] In the late 1940s, Congress authorized a three-year presumptive period for service-connected tuberculosis—the policy that denied Margaret Gaule's request for compensation. To the congressional mandate, the VA added additional coverage periods of six months for minimal tuberculosis, nine months for moderate tuberculosis, and twelve months for advanced tuberculosis. The government also continued to periodically revise the definition of service-connected tuberculosis as well as the level of disability and range of benefits to keep up with the evolving treatment regimes.[70]

A 1955 VA survey of civilian and military medical specialists' views on the validity of the disability rating system indicated the impact of antibiotics. One-fourth of the 153 respondents believed that tuberculosis benefits had become too liberal because diagnostic techniques and antibiotics often enabled the cure or arrest of the disease obviating the need for compensation.[71] One physician noted that "the arrested tuberculosis awards are in excess nowadays, with the new drugs and ambulatory therapy practiced and especially in those cases which have been operated on and for all practical purposes, cured."[72] The VA also became increasingly confident in its ability to treat tuberculosis. During one round of disability benefit adjustments in the 1970s, VA officials observed that "due to the impact of programs dealing with case-finding, diagnostic refinements, and improved chemotherapy, tuberculosis can now be quickly identified and up to 95% of new cases of tuberculosis can be quickly cured." They concluded that the relapse rate after effective treatment was so low as to be "virtually meaningless."[73]

Given such confidence and the fact that drug therapy shortened the bed rest requirements and hospital stays, hospitals across the country converted their tuberculosis wards to outpatient clinics, and sanatoriums slowly emptied; the last patient left Lake Saranac Sanatorium in New York in 1954. During the 1950s and 1960s tuberculosis institutions either had to adapt or close. Some, like the National Jewish Hospital in Denver, established programs for other respiratory diseases such as emphysema, cystic fibrosis, and asthma. In the early 1950s, the Army Medical Department's tuberculosis program at Fitzsimons reported a 55 percent reduction in occupied tuberculosis beds and an increasing number of outpatient visits; the hospital consequently took on new responsibilities.[74] In 1947 the Medical Department had designated Fitzsimons as an Army X-ray center for the treatment of malignant tumors, so that as tuberculosis rates fell and cancer rates increased, Fitzsimons' thoracic surgeons turned their skills to lung cancer and other diseases of the chest, and radiologists adapted their technology to therapeutic as well as diagnostic measures.[75] Fitzsimons also supported the postwar baby boom with a growing pediatrics program that cared for military dependents, and treated battle casualties from the Korean War in the 1950s, and Vietnam War in the 1960s and 1970s, specializing in chest wounds.[76] In 1955, the hospital found itself once again in the national spotlight, when, after a fishing trip in the Rocky Mountains, President Dwight D. Eisenhower suffered a heart attack and was rushed to Fitzsimons.[77] Seriously ill, the president stayed at the hospital in a special suite from 24 September to 11 November, and upon his departure commended the Fitzsimons staff for their medical care and extended his "very grateful thanks."[78]

With the end of the Cold War, however, and the contraction of Department of Defense facilities, Fitzsimons again faced the chopping block. Colorado's elected officials and Fitzsimons' partisans fought off several closure attempts, but in 1990 Congress passed the Defense Base Realignment and Closure Act that resulted in the closure of Fitzsimons in 1996 and the transfer of its health-care responsibilities to the U.S. Army Medical Department Center and School at Fort Sam Houston, Texas. The Department of Defense then transferred the

physical structures and land to what is now called the Fitzsimons Life Science District, which houses the University of Colorado Health Sciences Program and the Colorado Science and Technology Park for private enterprise. The District retained the Fitzsimons name for the campus but sought to "demilitarize" the post by converting the street names honoring military personnel to Denver city street names. Thus, names such as Bruns and Bushnell Avenues, Hutton and Halloran Circles, Moncrief Road, Quade Drive, Van Valzah Street, and Wright Loop are now gone.

But not all traces of the Army's "good tuberculosis men" have disappeared. If in the twenty-first century tuberculosis has become a minor, if not forgotten, presence at Fitzsimons, it remains nonetheless commemorated in the tall main hospital building that Lawrence Lewis dedicated in 1941. It is now called Building 500, but a new generation of medical personnel meets to discuss today's medical challenges in the Bushnell Auditorium and the Bruns Conference Room.

The Twenty-First Century

Despite the advent of antibiotic therapy, tuberculosis never submitted to significant control in those parts of the world lacking good housing, sanitation, nutrition, and robust medical and public health systems. In the 1980s, a new virus, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), took hold in the country, lowering infected individuals' resistance, and thereby allowing myriad infections, including latent tuberculosis, to flourish. Tuberculosis therefore resurged in the United States, surprising a public health system that had lowered its guard and surveillance activities against the disease. Immigration from countries with high tuberculosis rates also contributed to American rate increases, as did persistent poverty, homelessness, and alcohol and drug abuse.[79] Fitzsimons felt the impact of HIV/AIDS with an average of 14 admissions a week, or 12 percent of inpatient admissions in 1986.[80] The hospital installed negative air pressure rooms, double air lock doors, and staff started using disposable gowns when treating infectious patients. Originally aimed at HIV/AIDS, these precautions soon became critical in the care of tuberculosis patients as well. Tuberculosis cases increased alarmingly in the nation, peaking in 1992 with 26,673 cases or 10.4 per 100,000 population. Rates thereafter declined annually, however, to 15,078, or 5.2 per 100,000 in 2001 and 10,528 cases or 3.4 per 100,000 people in 2011 in the United States.[81]

Tuberculosis never completely receded from Gaule's life. In 2004, eighty-four years of age and widowed, she reflected on her war experience, and resubmitted her request for veterans' benefits. This time the VA Board of Veterans' Appeals agreed to hear her appeal because "new and material evidence has been received to reopen the claim of service connection or residuals of pulmonary tuberculosis."[82] What was new? In the petition to the Board of Veterans' Appeals requesting a review of the case, Gaule's attorney William J. Lindsay Jr., stated that "evidence received subsequent to the January 1958 board determination raises a reasonable possibility of substantiating the claim of entitlement to service connection for pulmonary

tuberculosis."[83] He attached a statement from Dr. P. James Connor, who, as a young physician had examined Gaule in Omaha in 1956 after her first lung hemorrhage. Connor, Lindsay explained, was "one of the few physicians in the United States who is still practicing who has had substantial experience with tuberculosis patients," and was also the Gaule's family physician.[84] Connor's letter stated that it was not unusual for active tuberculosis to turn up in people who had been exposed years before and cited his experience treating such patients between the 1940s and the 1960s. "Tuberculosis is an airborne disease and…Mrs. Gaule was exposed to it while in the service," he asserted, therefore "her chance of acquiring her tuberculosis was over 95% during her period of work as a nurse in the service of the United States government."[85] The appeals board concluded that "Dr. Connor's medical report clearly provides a potential nexus between pulmonary tuberculosis and military service which was not previously shown." Gaule's VA medical history also showed her scarred lungs, and that "substantial medical authority, including Internet research was submitted in support of the claim." It therefore agreed to reopen Gaule's application for service-connected benefits.[86]

On 15 February 2008, almost sixty-two years after she left the Army Nurse Corps, the VA granted Gaule's claim of disability noting "it is at least as likely as not that the pulmonary tuberculosis contracted in 1956 is related to your military service when you worked on Ward 13 at Barnes Hospital." The board assigned her a disability of "0%," however, because "medical evidence does not show that you have significantly disabling residuals to warrant a higher evaluation."[87] But in October 2009, after she was hospitalized with pulmonary hypertension, a condition that can be a result of tuberculosis, the VA recognized the connection and awarded Gaule $300 a month disability payments and $5,000 in retroactive compensation. The decision letter noted that "residuals of pulmonary tuberculosis, service connected, World War II, incurred static disability, 0% from 09/29/2003, 100% from 07/23/2009."[88] Gaule died on 20 February 2011 from complications following a stroke. She was ninety-one-years old.

The particulars of Gaule's case were no doubt central to the VA ruling, but the point here is that more than sixty years after World War II, the federal government was still negotiating policies concerning tuberculosis disability benefits. Today, although the Medical Department can exclude most tuberculosis from the Army, some troops will develop active disease while in service overseas or in the United States.[89] The Army Medical Department therefore continues to conduct tuberculosis surveillance in the ranks and to employ careful and rigorous protective measures when caring for confirmed or suspected tuberculosis patients.[90] This ancient, deadly disease, however, continues to elude understanding, and the search for improved diagnostics and treatments and an effective vaccine continues. According to the World Health Organization, tuberculosis ranks second behind HIV/AIDS as the most deadly single infectious agent for humans, and the combination of the two diseases is especially lethal: tuberculosis is the greatest single killer of people infected with HIV[91] (Figure 9-5). Equally troubling, tuberculosis bacteria continue to develop resistance to antibiotics, threatening decades of progress in disease control. Tuberculosis experts define multi-drug resistant tuberculosis (MDR-TB) bacteria

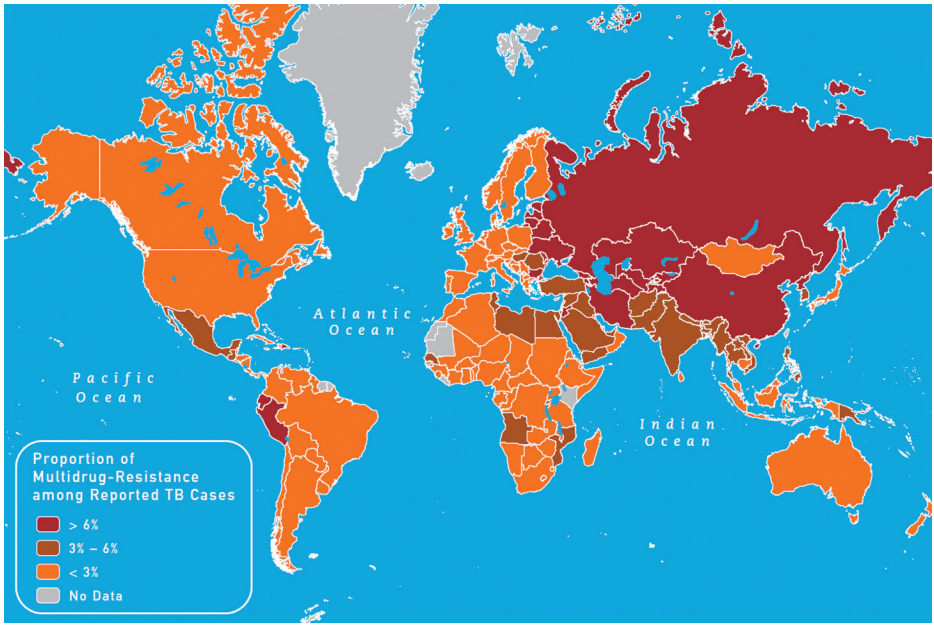


Figure 9-5. Map showing the infection rates of tuberculosis bacilli in the world population, from the Centers for Disease Control and Prevention Yellow Book, 2010. Available at http://wwwnc.cdc.gov/travel/images/map3-16-mdr-tb-large.png.

as those that do not respond to isoniazid and rifampicin, the two most powerful, first-line tuberculosis drugs, and extensively drug resistant tuberculosis (XDR-TB) bacteria as those resistant to isoniazid, rifampicin, and the most effective second-line drugs. Public health officials are now on guard for totally resistant strains that may have developed in patients in several countries in recent years.[92] The severity of these MDR and XDR tuberculosis infections has caused physicians to return to old methods of surgical excision and lung collapse to battle the disease, and to redouble research on *Mycobacterium tuberculosis*. In South Africa, for example, scientists have reproduced Richard Riley's studies on the airborne transmission of tuberculosis to better understand the transmissibility of XDR-TB.[93] As scientific knowledge of tuberculosis evolves, so will Army Medical Department tuberculosis policies and practice, continually redefining the disease experience as well as the hopes and fears of military and veteran patients and their families, doctors, and nurses who struggle with tuberculosis in the twenty-first century.

Notes

1. The following account is taken from Margaret Elizabeth Gaule, "The Diary of an Army Nurse by First Lieutenant Margaret Elizabeth Gaule," unpublished manuscript written in May 1945 on the island of Okinawa, in possession of the author.

2. P. James Connor to William J. Lindsay Jr., 31 July 2006, in possession of the author.

3. Author conversation with Gaule, 12 May 2006.

4. Margaret Gaule to Carol R. Byerly, 2007, in possession of the author.

5. Appeal of Margaret W. Gaule, Docket No. 05-25-216, Department of Veterans Affairs, 17 December 2007. The three-year presumption was approved by Congress in Public Law 573, 23 June 1950. See "The Veterans' Administration Disability Rating Schedule: Historical Development and Medical Appraisal," The President's Commission on Veterans' Pensions, Staff Report No. 8, Part B, 18 July 1956, House Committee Print No. 275, Committee on Veterans' Affairs, 84th Congress, 2nd sess.

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15. *Fitzsimons Annual Report,* 1947 [hereafter cited as *FZAR*, year], 82.

16. *FZAR*, 1948, 83.

17. *FZAR*, 1950, 84; and *FZAR*, 1949, 88.

18. Florence A. Burkhead, "Lesson Plan: The Fundamentals of Tuberculosis Nursing," typescript, 1956, Military History Institute, Carlisle Barracks, PA.

19. For example, Esmond R. Long, "The Hazard of Acquiring Tuberculosis in the Laboratory," *American Journal of Public Health* 41 (July 1951): 782–87.

20. Max B. Lurie, "Control of Airborne Contagion of Tuberculosis," *American Journal of Nursing* 46 (1946): 809.

21. Esta H. McNett, "The Face Mask in Tuberculosis," *American Journal of Nursing* 49 (January 1949): 32–36.

22. For example, W. F. Wells, "Droplets and Droplet Nuclei," *American Journal of Hygiene* 20 (November 1934): 611–27.

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31. Memorandum, "Streptomycin Conference," 18 June 1946, Esmond R. Long Papers, Manuscript Collection 362, National Library of Medicine; and Esmond Long to Surgeon General, "Visit at Fitzsimons General Hospital," 13 July 1946, Record Group 112, Records of the Surgeon General of the Army [hereafter cited as RG 112], Entry 31, 1945–56, Box 1428, National Archives and Records Administration [hereafter cited as NARA].

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33. Marks, *The Progress of Experiment*, 116.

34. Marks, *The Progress of Experiment*, 127 and 115.

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44. Carl W. Tempel and James H. Foresee, "The Definitive Treatment of Pulmonary Tuberculosis: General Therapeutic Principles as They Apply to Various Types of Chest Lesions," *Military Surgeon* 108 (1951): 375–83.

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49. Tempel and Dye, "Selecting the Streptomycin Regimen for Patients with Pulmonary Tuberculosis with Special Reference to the Intermittent Dosage Schedule."

50. Carl W. Tempel, "The Place of Streptomycin in the Treatment of Pulmonary Tuberculosis," *Bulletin of the U.S. Army Medical Department* 9 (January 1949): 25–34.

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69. The President's Commission on Veterans' Pensions, "The Historical Development of Veterans' Benefits in the United States," Staff Report No. 1, 1956, House Committee Print No. 244, Committee on Veterans' Affairs, 84th Cong., 2nd sess.

70. The President's Commission on Veterans' Pensions, "The Historical Development of Veterans' Benefits in the United States."

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84. Attachment to VA Form 9, Gaule, Margaret W., 07 870 022.

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86. In the Appeal of Margaret W. Gaule, C7 870 022, Board of Veterans' Appeals, Department of Veterans Affairs.

87. Department of Veterans Affairs, VA Regional Office, VA file number 07 807 022, Margaret W. Gaule, Rating Decision, 15 February 2008.

88. Department of Veterans Affairs, VA Regional Office, VA file number 07 870 022, Margaret W. Gaule, Decision on Appeal, 21 October 2009; author's phone conversation with Margaret W. Gaule, 3 March 2010; and conversation with Dennis Gaule, 29 November 2012. My thanks to Dennis Gaule, Margaret Gaule's son, for his assistance in documenting this decision.

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90. For the most recent Department of Defense policies regarding tuberculosis see the DoD Deployment Health Clinical Center Web site: http://www.pdhealth.mil/tuberculosis.asp#cg, accessed 24 August 2012. See also Jamie Mancuso, "Tuberculosis in the U.S. Military," presentation at Walter Reed Army Institute of Research, 15 September 2010, available online at: http://wrair-www.army.mil/Documents/TropMed/11-Mancuso-MTb-WRAIRTropMed.pdf, accessed 6 November 2012; James D. Mancuso, Steven K. Tobler, and Lisa W. Keep, "Pseudoepidemics of Tuberculin Skin Test Conversions in the U.S. Army after Recent Deployments," *American Journal of Respiratory and Critical Care Medicine* 177 (2008): 1285–89; and M. Renè Howell, "Screening for Mycobacterium Tuberculosis in the U.S. Military: Considerations for a Cost-Effectiveness Model," Johns Hopkins Medicine, Johns Hopkins University, n.d., available at: http://www.health.mil/dhb/afeb/meeting/021803meeting/TB%20Screening%20US%20Military%20Cost%20Model.pdf, accessed 30 November 2012.

91. WHO tuberculosis fact sheet, available at: http://www.who.int/mediacentre/factsheets/fs104/en/, accessed 30 November 2012.

92. Gwen Huitt, "MDR/XDR-TB," Denver TB Course, 13 October 2012, available at: http://www.nationaljewish.org/pdf/Proed_TB_2012_Huitt_MDR_XDRTB.pdf, accessed 30 November 2012; and Centers for Disease Control and Prevention, Web site on Tuberculosis, available at http://www.cdc.gov/TB/default.htm, accessed 30 November 2012.

93. See for example, Russell R. Kempker, Sergo Vashakidze, Nelly Solominia, Nino Dzidzikashvili, and Henry M. Blumberg, "Surgical Treatment of Drug-Resistant Tuberculosis," *The Lancet Infectious Diseases* 12 (February 2012): 157–66; Edward A. Nardell, "Quantifying Transmission of MDR-TB: Riley Revisited," presentation at Department of Microbiology, Immunology, and Pathology, Colorado State University, 8 April 2008; and Lee B. Reichman and Janice Hopkins Tanne, *Timebomb: The Global Epidemic of Multi-Drug-Resistant Tuberculosis* (New York, NY: McGraw-Hill, 2002).