John Mahoney and the Introduction of Penicillin to Treat Syphilis

by John Parascandola*

When the German scientist Paul Ehrlich introduced Salvarsan for the treatment of syphilis in 1910, it was hailed as a wonder drug. For centuries physicians had used mercury and a variety of other compounds to treat syphilis without great success. Salvarsan and other arsenical drugs indeed represented a significant advance in syphilis therapy and became the standard treatment for the disease.[1] But although the arsenicals could produce a cure, at least in the early stages of syphilis, there were significant drawbacks to their use. The drugs were complicated to administer and could have toxic side effects.[2] In addition, success depended upon prolonged treatment. A standard course of therapy might involve the patient visiting his or her doctor weekly for a year or more to receive injections of arsenic and bismuth drugs. Under these circumstances, it is not surprising that there was a high rate of noncompliance. By the early 1940s, so-called rapid treatment methods requiring from five days to several weeks had been developed, with the drug being administered by intravenous drip or multiple injections. This intense treatment had to be carefully monitored and involved an increased risk of untoward reactions. The intravenous drip method required hospitalization of the patient. Clearly a better therapeutic agent was needed, and that agent turned out to be penicillin.[3]

Penicillin Enters Therapeutics

As is well known, penicillin was discovered by Alexander Fleming, whose paper on the subject was published in 1929. It was not until penicillin was taken up by Howard Florey, Ernst

Chain, and their colleagues at Oxford University a decade later, however, that it was developed into a successful therapeutic agent. In animal studies and some ten clinical cases conducted by the Oxford team, penicillin showed extraordinary promise as an antimicrobial drug.[4]

Substantial amounts of penicillin were needed for the extensive clinical trials required to confirm the promise of these early results, and to provide adequate supplies of the drug for therapeutic use if it did live up to its potential. Florey recognized that large-scale production of penicillin was probably out of the question in Britain, whose chemical industry was fully absorbed in the war effort. So Florey and his colleague Norman Heatley traveled to the United States in the summer of 1941 to see if they could interest the Americans in the effort to produce penicillin on a large scale.[5]

Most important among the institutions visited by Florey and Heatley was the Department of Agriculture's Northern Regional Research Laboratory (NRRL) in Peoria, Illinois, of interest largely because of the expertise of its Fermentation Division. This contact proved to be crucial to the success of the project, as the NRRL was a key contributor of innovations that made large-scale production of penicillin possible.

Orville May, Director of the NRRL, agreed to have the Laboratory undertake a vigorous program to increase penicillin yields. Within a few weeks, Andrew Moyer found that he could significantly increase the yield of penicillin by substituting lactose for the sucrose used by the Oxford team in their culture medium. Shortly thereafter, Moyer made the even more important discovery that the addition of corn-steep liquor to the fermentation medium produced a ten-fold increase in yield. Corn-steep liquor was a by-product of the corn wet-milling process, and the NRRL, in an attempt to find a use for it, tried it in essentially all of their fermentation work.

Later, the Peoria laboratory increased the yield of penicillin still further by the addition of penicillin precursors, such as phenylacetic acid, to the fermentation medium.

It was recognized that the Oxford group's method of growing the mold on the surface of a nutrient medium was inefficient, and that growth in submerged culture would be a superior process. Florey's *Penicillium* culture, however, produced only traces of penicillin when grown in submerged culture. Under the direction of Kenneth Raper, staff at the NRRL screened various *Penicillium* strains and found one that produced acceptable yields of penicillin in submerged culture. Soon a global search was underway for better penicillin-producing strains, with soil samples being sent to the NRRL from around the world. Ironically, the most productive strain came from a moldy cantaloupe from a Peoria fruit market. A more productive mutant of the so-called cantaloupe strain was produced with the use of X-rays at the Carnegie Institution. When this strain was exposed to ultraviolet radiation at the University of Wisconsin, its productivity was increased still further.[6]

While Heatley remained in Peoria helping the NRRL staff get the penicillin work started, Florey visited various pharmaceutical companies to try to interest them in the drug. Although Florey was disappointed in the immediate results of his trip, three of the companies (Merck, Squibb, and Lilly) had actually conducted some penicillin research before Florey's arrival, and Pfizer seemed on the verge of investigating the drug as well. At this time, however, the promise of penicillin was still based on only limited clinical trials.

Florey next visited his old friend Alfred Newton Richards, then vice president for medical affairs at the University of Pennsylvania. More importantly, Richards was chair of the Committee on Medical Research (CMR) of the Office of Scientific Research and Development

(OSRD). The OSRD had been created in June, 1941 to assure that adequate attention was given to research on scientific and medical problems relating to national defense. Richards had great respect for Florey and trusted his judgement about the potential value of penicillin. He approached the four drug firms that Florey indicated had shown some interest in the drug (Merck, Squibb, Lilly, and Pfizer) and informed them that they would be serving the national interest if they undertook penicillin production and that there might be support from the federal government. It was agreed that although the companies would pursue their research activities independently, they would keep the CMR apprised of developments, and the Committee could make the information more widely available (with the permission of the company involved) if that were deemed in the public interest.

Although there was some concern that investments in fermentation processes might be wasted if a commercially-viable synthesis of penicillin were developed, other companies also began to show an interest in the drug. Some firms worked out collaborative agreements of their own (e.g., Merck and Squibb, later joined by Pfizer). Pharmaceutical and chemical companies played an especially important role in solving the engineering and scientific problems inherent in scaling up submerged fermentation from a pilot plant to a manufacturing scale. On March 1, 1944, Pfizer opened the first commercial plant for large-scale production of penicillin by submerged culture in Brooklyn, New York.

Meanwhile, clinical studies in the military and civilian sectors were confirming the therapeutic promise of penicillin. The drug was shown to be effective in the treatment of a wide variety of infections, including streptococcal and staphylococcal infections. The United States Army established the value of penicillin in the treatment of surgical and wound infections.

The increasingly obvious value of penicillin in the war effort led the War Production Board (WPB) in 1943 to take responsibility for increased production of the drug. The WPB investigated more than 175 companies before selecting 21 to participate in a penicillin program under the direction of Albert Elder. These firms received top priority on construction materials and other supplies necessary to meet the production goals. The WPB controlled the disposition of all of the penicillin produced. One of the major goals was to have an adequate supply of the drug on hand for the proposed D-Day invasion of Europe.[7]

Venereal Disease in Wartime

Venereal disease has typically been a cause of concern in wartime, and the Second World War was no exception. Governments feared that soldiers indulging in sex with prostitutes or so-called "promiscuous" women were in danger of contracting a venereal disease and becoming incapacitated. The concern over the rate of venereal disease infection in American military recruits in the First World War I had in fact been a major factor in the establishment of a Division of Venereal Diseases in the United States Public Health Service through the Chamberlain-Kahn Act in 1918.

Although the support for venereal disease work waned after the war ended, the Public Health Service (PHS) initiated a reinvigorated campaign against venereal disease after Thomas Parran became Surgeon General of the PHS in 1936. Parran had earlier been head of the Venereal Disease Division, and was strongly committed to fighting venereal diseases. Through his speeches and publications, he helped to break the taboo on discussing syphilis and other venereal diseases in the popular press. He also played a key role in the passage of the National

Venereal Disease Control Act in 1938. The act provided federal funding through the PHS to the states for venereal disease control programs, as well as supporting research into the treatment and prevention of venereal disease.[8]

With the outbreak of the Second World War in Europe, Parran's educational campaign against venereal disease was intensified. As a part of its efforts to combat venereal disease, the PHS issued posters, brochures, and other publications on the subject. Motion picture films were also a part of the campaign to educate the military and the public about syphilis and gonorrhea. The PHS even collaborated with Warner Brothers Studios in 1943 to produce a 30-minute version, known as "Magic Bullets," of the 1940 feature film "Dr. Ehrlich's Magic Bullet." (On the negative side, PHS was also conducting the now-infamous Tuskegee syphilis experiment in Alabama at this time.) [9]

It should also be noted that the PHS viewed the pharmacist as an important player in venereal disease education and control. In 1942, the Surgeon General sent a letter to the editors of pharmaceutical and medical journals, enclosing a press release on "The Pharmacist and VD Control." The release pointed out that the pharmacist was in a good position to educate the public about venereal disease because people with such infections often go to him/her for advice and medicine. Using his/her personal influence, the pharmacist can direct patients who have not sought medical attention for their condition to see a doctor , and steer them away from patent medicines advertised to cure syphilis and gonorrhea. The pharmacist could also distribute pamphlets and display posters on the subject in his/her store. As a good citizen, the pharmacist should also support community efforts to control venereal disease. The press release concluded:

"By participating actively in the venereal disease control program being promoted

by the United States Public Health Service and State health authorities, and by the Joint Committee of the American Social Hygiene Association and the American Pharmaceutical Association, pharmacists of the country will strengthen public confidence in their profession. At the same time they will know personally that their best efforts are being given toward the elimination of the venereal disease scourge, both for the best interests of the civilian population and for the greater fighting efficiency of the armed forces of the Nation."[10]

John Mahoney and the Venereal Disease Research Laboratory

In addition to its prevention and treatment programs, the Public Health Service also contributed to research efforts on venereal disease. One of the responsibilities assigned to the Division of Venereal Diseases by the 1918 Chamberlain-Kahn Act was "to study and investigate the cause, treatment, and prevention of venereal diseases."[11] Over the following years, the Division provided funding to universities such as the University of Pennsylvania and Johns Hopkins University to support research on venereal disease. In addition, the Division itself carried out its own research, especially clinical studies at the clinic at Hot Springs, Arkansas maintained by the PHS in cooperation with the National Park Service and the Arkansas State Board of Health, which was intended primarily for the treatment of indigent cases of venereal disease. In addition, investigations of rabbit syphilis were carried out at the PHS Hygienic Laboratory (forerunner of the National Institutes of Health) in the 1920s.[12]

In 1927, while Thomas Parran headed the Division of Venereal Diseases, arrangements were made for an experienced PHS commissioned officer to be detailed for venereal disease

work to the marine hospital operated by the PHS in Staten Island, New York. One of the primary functions of the PHS, dating back to its origins, had been the operation of hospitals for the care of merchant seamen. The physician-officer assigned to the Staten Island facility in 1927 was asked to study methods of treating syphilis and gonorrhea, with a special emphasis on efforts to shorten the period necessary for cure of these diseases. The *Annual Report* of the PHS for 1927 commented:

> "Since a considerable percentage of the work in the marine hospitals is on account of venereal diseases, any success in the prevention and improved treatment of these diseases would effect a very direct saving to the Government."[13]

A small research laboratory was set up, and additional staff were soon assigned to the work. In addition to the laboratory experiments, clinical studies were also undertaken with the cooperation of hospital staff. In 1929, Dr. John F. Mahoney assumed direction of this laboratory, which was later named the Venereal Disease Research Laboratory.[14]

John Mahoney was born on August 1, 1889 in Fond du Lac, Wisconsin. He graduated from Marquette Medical College in Milwaukee in 1914, and then undertook internships at the Milwaukee County Hospital and the Chicago Lying-in Hospital. In October, 1917, he joined the Public Health Service as a scientific assistant. The following March he was commissioned as an Assistant Surgeon in the Public Health Service Commissioned Corps.

Mahoney followed a pattern that was typical of many young officers of the Service at that time, serving for relatively short periods of time at various quarantine stations and marine hospitals. He also served for a time at the Ellis Island Immigration Station. From late 1925 to

early 1929, Mahoney was assigned to work abroad on the medical aspects of immigration in Ireland, England, and Germany. He took advantage of his service in Europe to visit laboratories and clinics to study syphilis, a disease which interested him. When Mahoney returned to the United States in 1929, he was assigned to the Staten Island Marine Hospital.[15]

Mahoney and his colleagues at the Venereal Disease Research Laboratory carried out both laboratory and clinical studies on venereal disease. Their studies led to an enhanced knowledge of the mechanism and rate of penetration into tissues by the spirochete, the microorganism that causes syphilis. Mahoney's group also significantly improved the serologic tests used in diagnosing the disease. When the sulfonamides were introduced in the 1930s, the Venereal Disease Research Laboratory investigated and helped to demonstrate the efficiency of these drugs in the treatment of gonorrhea.[16]

Penicillin and Syphilis

Thus when penicillin was introduced as a therapeutic agent during World War II, Mahoney already had substantial experience with syphilis and its treatment. He also became aware of a paper by Wallace Herrell and his colleagues at the Mayo Clinic, published in the *Journal of the American Medical Association* in May of 1943, which showed that penicillin was effective against sulfonamide-resistant gonorrhea.[17] In a paper published in 1956, Mahoney recalled that he received his initial supply of penicillin through the National Research Council, and that the drug was earmarked for further development of a therapy for male gonorrhea (presumably as a follow-up to the initial observations of the Mayo Clinic investigators).[18] The emphasis on male gonorrhea no doubt reflected the priority of the military with respect to the

supply of penicillin. Mahoney's recollections are supported by a note in the first paper from his laboratory on penicillin, which credits the federal program, involving the National Research Council and the Office of Scientific Research and Development, as the source of the penicillin.[19] Two other accounts of the initial source of Mahoney's penicillin exist, but I have not been able to corroborate either one. Ralph Williams, who undoubtedly knew Mahoney, stated in his history of the PHS that at first Mahoney and his colleagues actually grew the *Penicillium* mold themselves to produce penicillin for their work because it was in such short supply.[20] In his history of venereal disease in America, historian Allan Brandt states that Mahoney received his first penicillin in early 1943 from investigators in Oxford, England.[21]

However Mahoney came by his initial supply of penicillin, he and his coworkers did confirm the observations of the Mayo Clinic researchers on the efficacy of penicillin in the treatment of sulfonamide-resistant gonorrhea.[22] But Mahoney also decided to divert a small amount of the drug from the gonorrhea research to test it against syphilis. He later noted that it had long been a rule in the Venereal Disease Research Laboratory to test any preparation that it worked with for therapeutic activity against experimental syphilis in rabbits.[23] According to Mahoney's coworker R. C. Arnold, the drug was first tried against spirochetes (the microorganisms that cause the disease) *in vitro,* and failed to show any activity.[24] Fortunately, the Staten Island investigators proceeded to the next step of trying the drug *in vivo* in syphilitic rabbits. The results of limited animal tests were so encouraging that Mahoney decided to move ahead quickly to clinical experiments. He justified this early move to human use because penicillin appeared to be generally non-toxic and no harm would be done to the patients if the drug did not work and he had to return to arsenic therapy.[25] In 1943, it had not yet been

recognized that penicillin could produce serious toxic effects in some patients.[26]

On the basis of their initial animal results, Mahoney and his colleagues were provided with additional penicillin through the government program so that they could try the drug in humans as well as expand the animal studies. In June, 1943, Mahoney, Arnold, and serologist Ad Harris began their study with four patients. A preliminary report on these first four cases was presented at the meeting of the American Public Health Association in New York on October 14, 1943 and published in December of that year.[27] The four syphilis patients were given six intramuscular injections of penicillin a day for eight days, for a total of 1,200,000 units of the drug. No significant toxic side effects were observed. The investigators reported that:

"The results of the blood studies indicate that the therapy was responsible for a more or less rapid and complete disappearance from the blood stream of the reacting substance which is measured by the various tests and which is usually associated with activity in early syphilis."[28]

Four cases, of course, were not enough to base any definitive conclusions on, and there was always a danger that the patients might relapse after a time. Mahoney therefore intended to continue observation of the patients for as long as possible. The Staten Island researchers were willing to make only a rather cautious statement about the effectiveness of penicillin against syphilis in this preliminary paper.

> "Should the more extensive and prolonged experience confirm the impression which is to be gained by the pilot study, a rebuilding of the structure of syphilis therapy may become necessary. This development of an optimal therapy will require carefully controlled studies designed to determine the most effective relationship between the amount of the drug and the duration of the treatment

> period. Also, the role of the treatment in latent disease and visceral and central nervous system syphilis will require careful scrutiny before the reasonably effective measures which are available at present may be replaced by a therapy based upon penicillin. Because of the long post treatment period of observation which is a requisite for the evaluation of a syphilis therapy, the progress toward the adoption of a new mode of treatment must, of necessity, be deliberate."[29]

Microbiologist Gladys Hobby later recalled the excitement created by Mahoney's presentation of the penicillin paper at the American Public Health Association meeting.

> "I have a mental image of the room where I first heard Mahoney and his associates describe their results on the use of penicillin in the treatment of syphilis. The room was crowded. Loudspeakers and projection equipment were not as sophisticated then as now. Everyone strained to hear what was said, and the impact was electrifying. By then much had been written on penicillin, but no one had expected that an antibacterial agent would be active against spirochetes as well. Hearing John Mahoney describe the effect of penicillin on the course of syphilitic lesions was overwhelming."[30]

The paper delivered at the meeting was reported on in the popular press as well. In a story headed "New Magic Bullet," *Time* discussed how Mahoney, in a "jam-packed session" of the meeting, has announced that "penicillin had apparently cured four cases of early syphilis." Dr. Mahoney, according to the magazine, was "stunned" by the results. *Time* also reported Mahoney's cautious statement that penicillin would have to be tested in a large number of cases over a long period of time before it could be considered a cure for syphilis, along with his

admission that it was possible that a "reconstruction" of syphilis therapy might be necessary. One doctor who took the floor to comment on the paper was carried away by his enthusiasm to exult: "This is probably the most significant paper ever presented in the medical field."[31]

A month later, PHS physician John Heller, Jr. discussed syphilis control at the annual meeting of the Southern Medical Association in Cincinnati. He referred to the work of Mahoney and his colleagues on the use of penicillin as "overshadowing anything that has happened in syphilis control since the days of Ehrlich."[32]

The results of the clinical tests at the Staten Island hospital, limited as they were, were sufficient to convince Alfred Newton Richards, Chairman of the Medical Research Committee, of the need to move forward with more extensive clinical trials. He later said of the work of Mahoney and colleagues on penicillin and syphilis: "This discovery gave a new and highly important turn to the examination and treatment of that disease."[33]

Under the auspices of the Committee on Medical Research, chaired by Richards, a cooperative clinical trial of penicillin in the treatment of syphilis was organized in the fall of 1943. The project was under the specific direction of the Subcommittee on Venereal Diseases of the National Research Council. The subcommittee appointed a Penicillin Panel, with Mahoney serving as one of the members, to oversee the study.[34]

In October, 1943, the subcommittee organized a conference with representatives from the Public Health Service, the Committee on Medical Research, eight civilian venereal disease clinics, the British Central Scientific Service, and the Canadian Army Medical Corps. At this meeting, which Richards called "the beginning of a revolution in the treatment of syphilis," it was agreed that the eight civilian venereal disease clinics, along with one each from the Army,

the Navy, and the Public Health Service, would participate in the study. It was anticipated that a sufficient supply of penicillin to treat 350 patients a month could be made available for the purposes of the study. The study was later expanded to include other facilities. It remained under the direction of the Penicillin Panel of the Subcommittee on Venereal Disease until the PHS assumed responsibility for its continuation at the beginning of 1946.[35]

As would be expected, the Staten Island Marine Hospital was one of the original sites chosen for the clinical study with Mahoney of course directing the work there. In a paper published in the *Journal of the American Medical Association* in September, 1944, Mahoney and his coworkers reported on the further progress of the original four patients treated, as well as providing some preliminary observations on their results with an additional one hundred patients with early syphilis. Although the results continued to be positive, Mahoney knew that it was too early to be sure that cures had been effected, and he concluded the paper with the following cautious statement:

> "It is desired to recall that the disease syphilis is one which is characterized by chronicity, with long periods of latency and a distinct tendency to clinical and serologic recurrence. The evaluation of any therapy will require a prolonged trial utilizing a wide variety of treatment schedules and a carefully controlled follow-up system. The combined experience available at this time has served to illuminate only a few of the important aspects. The remainder must await the passage of time."[36]

Immediately following this paper in the *Journal* was another paper by Mahoney, Joseph Earle Moore of Johns Hopkins, W. Barry Wood of Washington University, and Walter Schwartz

and Thomas Sternberg of the Army Medical Corps. This paper provided a preliminary report of 1,418 cases involving the penicillin treatment of early syphilis from all of the clinics in the cooperative study. Although the authors continued to exhibit caution, they were able to demonstrate that penicillin treatment led to the disappearance of the spirochete from open lesions, the healing of these lesions, and a reversal of the blood serologic response from positive to negative (presumably due to the elimination of the spirochetes from the blood).[37]

While the scientific investigators enjoyed the luxury of withholding their final verdict on the effectiveness of penicillin against syphilis, waiting for a definitive answer was not an option for those charged with the medical care of the troops in a wartime situation. By April of 1944, the Chief of the Army's Preventive Medicine Service was requesting advice about the earliest possible time that penicillin treatment of syphilis might be applied in the Army. Just three months later, on June 26, the Army adopted penicillin as the routine treatment for syphilis. Fortunately by that time the supply of penicillin had increased significantly. The British armed forces soon followed their American colleagues in adopting penicillin as the standard treatment for the disease.[38]

Penicillin allowed military physicians to get men suffering from venereal disease back on their feet and available for combat quickly. Raymond Vonderlehr and John Heller of the PHS, summarizing the remarks made by Army Colonel Donald M. Pillsbury at a 1944 conference in St. Louis, reported that:

> "Colonel Pillsbury pointed out that treatment with penicillin makes this possible because most of the patients remained ambulatory and began to convalesce almost immediately after treatment was begun. This arrangement made it possible to

keep the infected men close to the front lines. As soon as penicillin treatment was completed the men were returned to active duty."[39]

As penicillin first became available to military physicians, there was not necessarily enough of the drug to treat all of the cases that might potentially benefit from it. Penicillin of course had therapeutic value in the treatment of war wounds and various infections, as well as in the treatment of syphilis and gonorrhea. Physician-ethicist Henry Beecher called attention to the problem facing military surgeons in a paper published in 1969:

> "Allocation of penicillin within the Military was not without its troubles: When the first sizable shipment arrived at the North African Theatre of Operations, U.S.A., in 1943, decision had to be made between using it for 'sulfa fast' gonorrhea or for infected war wounds. Colonel Edward D. Churchill, Chief Surgical Consultant for that Theatre, opted for use in those wounded in battle. The Theatre Surgeon made the decision to use the available penicillin for those 'wounded' in brothels. Before indignation takes over, one must recall the military manpower shortage of those days. In a week or less, those overcrowding the military hospitals with venereal disease could be restored to health and returned to the battle line."[40]

A moral issue of a different sort was raised by those concerned about the impact of penicillin on sexual mores. As it became more and more obvious that syphilis and gonorrhea could be cured relatively quickly and painlessly with penicillin, some feared that this situation would encourage sexual promiscuity and immorality. One historian has cited a theologian of the period who worried that venereal disease would come to be regarded as strictly a medical

problem, with its sociological and moral implications ignored.[41] A graduate student in social work, who completed a project in a venereal disease rapid treatment center for her M.S. degree in 1947, admitted in her dissertation that she could not answer the question of "whether penicillin will be a help or a hindrance to the control of venereal disease; whether by making the treatment so short and effective patients will lose the fear of contracting the disease and will show more laxness in their sex behavior."[42] A number of public health officials suggested that it was possible that the quicker and less arduous penicillin treatment could actually lead to an increase in venereal disease.[43] It should be noted that similar concerns about the undermining of standards of morality had been voiced when Ehrlich's Salvarsan was introduced to treat syphilis.[44]

Concerns about the impact that penicillin might have on sexual behavior did not materially slow the adoption of the drug for the treatment of syphilis and gonorrhea. Nor, however, has effective drug therapy for sexually-transmitted diseases eliminated the social and moral issues surrounding these diseases.

Conclusion

Further clinical trials with penicillin by Mahoney and others confirmed its place as the treatment of choice for syphilis.[45] Not only did the drug cure the disease, but it quickly rendered patients non-infectious, thereby preventing them from spreading it to others. As Brandt and Jones have noted in their historical chapter in *Sexually Transmitted Diseases*, penicillin led to a dramatic decline in the incidence of syphilis. By the late 1950s, rates of infection in the United States reached an all-time low. Any illusion that the disease was on its way to being eliminated,

however, was shattered by the fact that rates began to climb again in the early 1960s. Changes in sexual mores due to the increasing availability of contraceptives and a decline in funding for public venereal disease programs are two of the factors that may have contributed to this reversal of the downward trend.[46] If penicillin has not eliminated syphilis, however, it has at least provided a safe, quick, easy, and effective treatment for this disease.

In recognition of his contribution to this discovery, John Mahoney received the prestigious Albert Lasker Award for Clinical Research in 1946 for "distinguished service as a pioneer in the treatment of syphilis with penicillin."[47] In December, 1949, he retired from the Public Health Service. That was not to be the end of his career, however, for he went on to become the Health Commissioner of the City of New York, and then the Director of the City Health Department's Bureau of Laboratories until his death in 1957.[48] Although he had a long and distinguished career in public health, during which time he made a number of significant contributions to the field, he will no doubt always be remembered best for his part in revolutionizing the treatment of syphilis.

[captions for photos]

John Mahoney in his Public Health Service uniform (courtesy of the National Library of Medicine).

John Mahoney (lower left) receiving the Albert Lasker Clinical Research Award in 1946 (courtesy of the National Library of Medicine).

The Staten Island Marine Hospital, where Mahoney's venereal disease research laboratory was located (courtesy of the Program Support Center, Department of Health and Human Services).

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15. Biographical information on Mahoney was obtained from Williams, *Public Health Service* (n. 14), pp. 387-390; David E. Price, "John Friend Mahoney," *Dictionary of American Biography*, Supplement Six (New York: Charles Scribner's Sons, 1980), pp. 423-424; official personnel folder of John F. Mahoney, Federal Records Center, National Archives and Records Administration, St. Louis.

16. See, for example, J. F. Mahoney, C. J. Van Slyke, and J. Durward Thayer, "Sulfanilamide Therapy in Hospitalized Gonorrhea," *American Journal of Syphilis Gonorrhea and Venereal Diseases* 22 (1938): 691-698. See also Williams, *Public Health Service* (n. 14), p. 388; Price, "Mahoney"(n. 15), p. 424.

17. Wallace E. Herrell, Edward N. Cook, and Luther Thompson, "Use of Penicillin in Sulfonamide Resistant Gonorrheal Infections," *Journal of the American Medical Association* 122 (1943): 289-292.

18. John F. Mahoney, "Some of the Early Phases of Penicillin Therapy of Syphilis," *A. M. A. Archives of Dermatology* 73 (1956): 485-488. Mahoney refers (p. 485) to penicillin first being made available to him by the National Research Council in 1942, but I think it was more likely in 1943. First of all, Mahoney seems to indicate that he was given the supply after Herrell and his colleagues at the Mayo Clinic had reported their results, which were published in May, 1943 (n. 17), although Mahoney could conceivably have learned of the results before publication. He does, however, cite their published paper. In addition, penicillin supplies were extremely limited throughout 1942. For example, it was apparently not until April 1, 1943 that the first American military casualties were treated by penicillin. Finally, Mahoney indicates that he moved fairly quickly from gonorrhea to syphilis, and the syphilis work was not reported until well into 1943.

19. J. F. Mahoney, Charles Ferguson, M. Bucholtz, and C. J. Van Slyke, "The Use of Penicillin Sodium in the Treatment of Sulfonamide-Resistant Gonorrhea in Men," *American Journal of Syphilis, Gonorrhea, and Venereal Diseases* 27 (1943): 525-528, p.525.

20. Williams, *Public Health Service* (n. 14), p. 388.

21. Brandt, *No Magic Bullet* (n. 8), p. 170.

22. Mahoney, *et. al.*, "Use of Penicillin" (n. 19).

23. Mahoney, "Early Phases" (n. 18), p. 486.

24. Arnold is quoted in Hobby, *Penicillin* (n. 4), p. 152. Hobby also notes on the same page that Harry Eagle of the Johns Hopkins University School of Medicine had also observed that penicillin had no effect on spirochetes *in vitro*.

25. J. F. Mahoney, R. C. Arnold, and Ad Harris, "Penicillin Treatment of Early Syphilis: A Preliminary Report," *Venereal Disease Information* 24 (1943): 355-357, p. 355. The same paper was published in the same month in *American Journal of Public Health* 33 (1943): 1387-1391 (see p. 1387). This paper also indicates that the penicillin was obtained through the National Research Council and the Office of Scientific Research and

Development.

26. On the development of a recognition of the side effects that penicillin could cause in some patients, see James C. Whorton, "'Antibiotic Abandon': The Resurgence of Therapeutic Rationalism," in Parascandola, ed., *History of Antibiotics* (n. 7), pp. 125-136.

27. Mahoney, *et. al.*, "Penicillin Treatment" (n. 25).

28. *Ibid*., p. 356 (in *VDI* paper) and p. 1390 (in *AJPH* paper).

29. *Ibid*., p 356 (in *VDI* paper) and pp. 1390-1391 (in *AJPH* paper).

30. Hobby, *Penicillin* (n. 4), pp. 155-156.

31. "New Magic Bullet," *Time* 42 (October 25, 1943): 38, 40.

32. J. R. Heller, Jr., "Syphilis Control in Wartime," *Southern Medical Journal* 37 (1944): 219-223, p. 222.

33. A. N. Richards, "Production of Penicillin in the United States (1941-1946)," *Nature* 201 (1964): 441-445, p. 444.

34. Joseph Earle Moore, J. F. Mahoney, Walter Schwartz, Thomas Sternberg, and W. Barry Wood, "The Treatment of Early Syphilis With Penicillin: A Preliminary Report of 1,418 Cases," *Journal of the American Medical Association* 126 (1944): 67-72, pp. 67-68; Kampmeier, "Introduction" (n. 3), pp. 260-261; Joseph Earle Moore, *Penicillin in Syphilis* (Springfield, IL: Charles C. Thomas, 1947), p. 4.

35. Richards, "Production" (n. 33), p. 444; J. E. Moore, "Preliminary Statement," in National Research Council - U. S. Public Health Service, *Meeting of Penicillin Investigators*, February 7 and 8, 1946, p. 1 (a copy of this document is at the National Library of Medicine).

36. J. F. Mahoney, R. C. Arnold, Burton L. Sterner, Ad Harris, and M. R. Zwally, "Penicillin Treatment of Early Syphilis: II," *Journal of the American Medical Association* 126 (1944): 63-67, p. 67. This paper was reprinted as a "Landmark Article" in *ibid.*, 251 (1984): 2005-2010.

37. Moore, *et. al.*, "Treatment" (n. 34).

38. Richards, "Production" (n. 33), p. 444; Alexander Fleming, *Penicillin: Its Practical Application* (Blakiston: Philadelphia, 1946), p. 283; Odin W. Anderson, *Syphilis and Society: Problems of Control in the United States, 1912-1964* (Chicago: Center for Health Administration Studies, Research Series 22, 1965), pp. 20-21.

39. R. A. Vonderlehr and J. R. Heller, Jr., *The Control of Venereal Disease* (New York: Reynal and Hitchcock, 1946), p.3.

40. Henry K. Beecher, "Scarce Resources and Medical Advancement," *Daedalus* 98 (1969): 275-313, pp. 280-281.

41. McGinnis, "Salvarsan" (n. 2), p. 145.

42. Judith Torregrosa, "A Study of Forty-Four Syphilitic Patients Under Treatment at the Louisville Rapid Treatment Center from March 1, 1947 to April 15, 1947," M.S. in Social Work dissertation, University of Louisville, 1947 p. v.

43. See, for example, Richard A. Koch and Ray Lyman Wilbur, "Promiscuity as a Factor in the Spread of Venereal Disease," *Journal of Social Hygiene* 30 (1944): 517-529; Vonderlehr and Heller, *Control* (n. 39), p. 65.

44. McGinnis, "Salvarsan"(n. 2), p. 146; Brandt, *No Magic Bullet* (n. 8), p. 46.

45. See, for example, R. C. Arnold, J. F. Mahoney, John C. Cutler, and Sacha Levitan, "Penicillin Therapy in Early Syphilis: III," *Journal of Venereal Disease Information* 28 (1947): 241-244.

46. Allan M. Brandt and David Shumway Jones, "Historical Perspectives on Sexually Transmitted Diseases: Challenges for Prevention and Control," in King K. Holmes, Per-Anders Mardh, P. Frederick Sparling, Stanley M. Lemon, Walter E. Stamm, Peter Piot, and Judith N. Wasserheit, eds., *Sexually Transmitted Diseases*, third edition (New York: McGraw-Hill, 1999), pp. 15-21, p. 18.

47. *Albert Lasker Awards Fortieth Anniversary* (New York: Albert and Mary Lasker Foundation, 1985), p. 23.

48. Price, "Mahoney" (n. 15), p. 424.