## From Mercury to Miracle Drugs: Syphilis Therapy Over the Centuries John Parascandola

Shortly after Columbus had arrived in the New World, as the fifteenth century drew to a close, a terrible new disease which we now call syphilis appeared in Europe. A controversy developed over whether or not the disease had been imported to Europe from the Americas, beginning with Columbus and his crew, or had existed in Europe earlier, perhaps in a different form. The question of the origin of syphilis is still not firmly resolved today, but at present the evidence seems to be pointing against the American origin theory. The venereal nature of syphilis was recognized relatively early.

Once the venereal nature of syphilis was understood, people could be (and were) warned against having intimate relations with individuals who were infected, assuming they could identify the infected. But once one had contracted the disease, what remedies were available to alleviate, if not cure, the malady? Some of those who believed that the pox was the just rewards of immoral behavior questioned whether or not those afflicted with the disease even deserved to be treated.<sup>1</sup>

Not surprisingly, when this terrible new disease first appeared, all sorts of remedies were recommended for dealing with it. For example, Torella advised such strange treatments as applying a cock or pigeon flayed alive, or a live frog cut in two, to an infected penis.<sup>2</sup> A major aim of most treatment was to remove the morbid matter causing the disease from the patient. This could be done in various ways, for example, by blood-letting or the use of laxatives. An alternative method involved having the patient

bathe in a mixture of wine and herbs, or in olive oil. Syphilitics could also be placed in an enclosed heated space, causing them to sweat, another mechanism for eliminating corrupt matter from the body.<sup>3</sup>

The two remedies that eventually came to be by far the most popular, however, were mercury and guaiacum. Mercury had long been used, especially by the Arabs, in the treatment of skin diseases and even leprosy. Therefore it seemed reasonable to try it against syphilis, which generally involved skin lesions and was thought to resemble leprosy. Numerous physicians in the early sixteenth century advocated the use of mercury in the forms of ointments or rubs. Even anti-venereal underpants, coated on the inside with a mercurial ointment, were available in Italy. It was recognized, however, that excess mercury could be harmful. Overdosing with mercury could lead to such toxic side effects as shaking, paralysis, and the loosening and loss of teeth. Sometimes the mercury was applied to the body and the patient was then placed in a heated area for long periods of time. This introduced the possibility of mercury vapors entering the respiratory tract, which could be very dangerous.<sup>4</sup>

At first mercury was only given externally, for example, in the form of an ointment. The internal administration of mercury seemed to be too dangerous. At the end of the eighteenth century, however, the internal administration of mercury began to overtake the external methods. The mercury could be administered in the form of enemas, or taken orally in a gum form or as calomel (the salt mercurous chloride). Van Swieten's liquor, consisting of grains of corrosive sublimate (mercuric chloride) dissolved in a solution of water and alcohol, became popular in the late eighteenth

century. Mercury poisoning was probably not uncommon, but side effects that were probably due to the treatment were often attributed to the disease itself. Mercury remained the preferred treatment for syphilis up into the twentieth century.<sup>5</sup>

The principal challenger to mercury in the early history of syphilis was guaiacum (or guaiac) wood. The guaiacum tree was native to the Indies, and the Spanish and the Portuguese began using the wood to treat syphilis by the early fifteenth century. At the time, it was widely believed that God often placed remedies for a disease in the areas where that disease flourished. Since many Europeans began to ascribe the origins of syphilis to the Americas, it did not seem unreasonable that a cure for the disease might exist in that part of the world.<sup>6</sup>

The wood was administered by grinding it into a powder and then boiling it in water. The resulting decoction (the liquid remaining when the wood is removed) was then ingested by the patient. But typically treatment with guaiacum involved much more than simply drinking a decoction made from the wood. The patient was generally placed in a warm room and put on a strict diet with limited food intake. He or she was also given mild laxatives. The patient then drank a large dose of the decoction daily, after which he or she was wrapped in blankets to induce sweating. This regimen was carried out for thirty days, and was undoubtedly quite debilitating to the patient. A 1519 book by the German humanist and religious reformer Ulrich von Hutten on guaiacum, which was translated into several languages, helped to popularize the drug. Hutten himself suffered from syphilis and was convinced that he had been cured by guaiacum (although he appears to have eventually died of syphilis). As someone who was opposed to the

medical establishment, he was delighted to recommend an empirical remedy that came from a "barbarian" land with no doctors.<sup>7</sup>

Historian Sheldon Watts has suggested that the Spaniard Oviedo, whom we have already encountered as the first person to ascribe the origins of syphilis to the New World, helped to popularize guaiacum for financial reasons. While in the Indies, Oviedo learned that the wood was a reputed cure for syphilis. According to Watts, Oviedo knew that the public accepted the doctrine that for every disease or poison God had placed a cure nearby, and so he claimed that the people of the Indies had long suffered from syphilis but were able to cure the disease with guaiacum. He arranged for his partners, the Fugger family of bankers, to obtain monopoly rights from the King of Spain to import and market the wood throughout the Spanish Empire. This arrangement resulted in handsome profits for Oviedo and the Fuggers.

Mercury and guaiacum were also not infrequently used together in the treatment of syphilitics by doctors anxious to cover all bases. In the sixteenth century, the efficacy of guaiacum was challenged by Paracelsus, and its use began to progressively decline. Sometimes it was replaced by other woods and roots, included sarsaparilla, another American import. Mercury temporarily lost some of its credibility around the beginning of the nineteenth century, but made a comeback by the 1860s. Although there were certain new treatments that were employed in the nineteenth century, such as potassium iodide and certain preparations of arsenic, Quétel has concluded that other forms of treatment had a hard time competing with mercury. Mercury remained king in the

treatment of syphilis until the twentieth century, although it left much to be desired as a remedy.<sup>9</sup>

While Mercury continued to dominate the treatment of syphilis, and, in desperation, physicians tried a host of other methods as well. The chancres or ulcers of syphilis victims were sometimes cauterized (burned with a heated instrument or caustic substance). Steam baths were combined with mercury vapor. One doctor even tried using smallpox vaccination as a treatment for syphilis. Thomas Lowry wrote about the case of one poor soldier in the Union Army during the American Civil War in the 1860s as follows:

"Surgeon E. A. Tomkins of Fort Yamhill, Oregon, described an unfortunate soldier with syphilis who, over a period of about four month, was treated with potassium iodide in sarsaparilla, corrosive sublimate, lunar caustic, calomel, black draught, emetics, blistering, iron, quinine, and external chloroform. At the end of the treatment, he was in severe pain, with one leg badly swollen and cold, barely able to walk." <sup>10</sup>

In the early years of the twentieth century the cause of syphilis was uncovered and a diagnostic test for its detection became available. Soon another major advance occurred that was to transform the treatment of the disease. Paul Ehrlich, who had been devoting much of his research in the 1890s to immunology, returned in the first decade of the twentieth century to a subject that had interested him earlier, the development of chemical agents to treat infectious disease. Ehrlich and his coworkers in Frankfurt began a search for chemical substances that would attack disease-causing microorganisms

within the body. The hope was to find chemical drugs that acted like "magic bullets" that would specifically destroy the microorganisms without injury to human cells. His work initially focused on a group of microorganism called trypanosomes, which caused such diseases as sleeping sickness.

Ehrlich learned in 1905 that two British researchers had found that the arsenic-containing organic compound atoxyl could eliminate trypanosomes from the blood of infected animals. Unfortunately, it was soon found that relapses commonly occurred and that that the large therapeutic doses required could damage the optic nerve and produce blindness. Ehrlich reasoned, however, that he might be able to modify the structure of atoxyl in a way that reduced or eliminated its effect on the optic nerve while still retaining its toxicity towards trypanosomes. Over the next few years, hundreds of arsenic compounds were synthesized and tested in his laboratory.

After the discovery of the spirochete that caused syphilis in 1905, Ehrlich began trying arsenical drugs against syphilis as well because there appeared to be a similarity between trypanosomes and spirochetes. In 1909, the Japanese scientist Sahachiro Hata, working in Ehrlich's laboratory, discovered that compound number 606 was effective in treating syphilis infections in rabbits. After extensive animal tests, Ehrlich arranged for the drug to be distributed to selected medical specialists for human clinical trials. The results were promising, and in 1910 Ehrlich announced the new drug to the world.

Demand for 606 soon outgrew the ability of Ehrlich's laboratory to produce it, and he arranged with a German chemical company to produce the drug under the tradename Salvarsan. 

Salvarsan. 

11

Salvarsan represented the first effective treatment for syphilis, and hence was hailed as a major medical breakthrough. Although the drug was indeed a major advance in the treatment of the disease, it was by no means an ideal therapeutic agent. Salvarsan, as an arsenical compound, had serious side effects. It also had to be administered by injection, and treatment was prolonged, sometimes involving an injection a week for a year or more. Ehrlich did introduce a somewhat improved form of the drug, Neosalvarsan, within a few years, and other arsenicals were introduced later. In spite of the problems with arsenical therapy, it remained the primary form of treatment of syphilis from its introduction until the discovery of the effectiveness of penicillin against the disease in the 1940s.

Initially the length of treatment with arsenical drugs generally extended from several weeks to perhaps two months. Treatment regimens varied, however, and the high cost of the drug meant that there was a tendency to stop its use once the Wasserman test, measuring the presence in the blood of the spirochete that caused syphilis, was negative. As a result of experience during the First World War and immediately thereafter, however, it became clear that it was necessary to continue treatment for a significantly longer period of time in order to avoid relapse.

In 1921, the use of bismuth to enhance the efficacy of the arsenicals was introduced. Like arsenic and mercury, however, bismuth had certain toxic side effects. During the 1920s, the standard therapy for syphilis involved weekly injections of arsenic preparations, frequently rotated with mercury and bismuth compounds, for a period of one to two years. In the United States, the most widely accepted schedule was that

developed by the Cooperative Clinical Group, organized in 1928 by five large American syphilis clinics. Their protocol for acute syphilis involved weekly injections of Neosalvarsan and bismuth, on an alternating schedule, for a period of 68 weeks. This regimen was complicated to administer, expensive, prolonged, and potentially dangerous, and patients did not always complete the full course of therapy.<sup>12</sup>

Although this therapy was reasonably effective in the treatment of primary and secondary syphilis, side effects ranged from relatively minor ones, such as nausea and headache, to serious problems such as necrosis (death of skin cells) at the site of injection, kidney failure, and acute hepatitis, occasionally resulting in death. In addition, arsenical therapy had little or no effect in cases of advanced neurosyphilis, a late stage of the disease affecting the nervous system. This was especially true in patients who had developed general paresis, involving brain damage and characterized by dementia and paralysis.<sup>13</sup>

In 1917, however, an Austrian physician began experimenting with a form of therapy for paresis that became widespread in the 1920s and after. A medical graduate of the University of Vienna, Julius Wagner-Jauregg accepted an appointment in a psychiatric clinic in 1883. Although he had no formal training in psychiatry, which was still in its infancy as a discipline, he became professor of psychiatry at the University of Graz in 1893. He also continued clinical research in mental health in his hospital practice. Early in his career, he developed an interest in investigating the effects of inducing fevers in patients with psychoses, based on empirical observations from early

times that patients with mental illness sometimes seemed to improve when attacked by a fever.

In 1917, Wagner-Jauregg decided to try using malaria as a form of fever therapy in patients with paresis. He injected nine patients suffering from this condition with tertian malaria, a form of the disease which was relatively innocuous and could generally be cured by drug therapy with quinine. He found that six of the cases showed significant remission, and in three of these cases the remission proved to be enduring. In 1919, he began this experimental treatment on a large scale. Others also began to carry out clinical trials with malaria therapy, which proved to be far more successful than any previous treatment for paresis. In 1922, the treatment was used on the first American patient at St. Elizabeths Hospital in Washington, DC. The method was soon widely accepted and Warner-Jauregg received the Nobel Prize in Physiology or Medicine in 1927 for his discovery of the therapeutic value of malaria inoculation in the treatment of paresis. <sup>14</sup>

Joel Braslow has argued that we cannot answer the question of whether malaria fever therapy actually worked with any degree of certainty. No randomized clinical trails of the sort that would be accepted as evidence today were ever performed on the method. With the discovery of the effectiveness of penicillin against syphilis in 1943, malaria therapy was eventually phased out, although it remained the treatment of choice until the late 1940s and early 1950s, and continued to find some use even after that time. In its heyday, it was certainly widely believed to be effective. In addition, Braslow has pointed out that it resulted in a decided improvement in the relationship between physicians and paresis patients. Whereas previously, both the patients and their doctors had viewed the

condition of the patients as hopeless, there was now some cause for optimism. Braslow wrote:

"The advent of malaria therapy restructured patients' and physicians' perceptions of themselves and each other. Irrespective of whether the treatment worked, not only did these physicians believe that they could act decisively against the syphilitic spirochete, but their belief in its efficacy allowed them to write more sympathetically about their patients and, perhaps, to care for them in a less objectified and more humane way. Furthermore, this new technology not only allowed patients to seek hospitalization voluntarily but permitted even those who were there against their will to become active participants in their treatment."

Developments in the 1930s resulted in some modifications in the treatment of syphilis in its earlier stages. As Kampmeier has pointed out, the stumbling block to adequate treatment with arsenicals continued to be the issue of compliance on the part of the patients. A course of weekly injections for over a year was too much of a burden for many patients, and so often the full treatment was not carried out. Experiments reported by Harold Hyman at Mount Sinai Hospital in New York in 1933 demonstrated that active medications could be delivered relatively safely by means of slow intravenous drip. This work led Hyman's colleague Louis Chargin to speculate that the intravenous drip procedure might be applied to arsenic therapy, with the possible result of curing syphilis in a matter of days or weeks, instead of a year or more. However, the procedure required hospitalization of the patients.

Chargin, Hyman and their coworkers began clinical testing of the intravenous drip method of Neoarsphenamine therapy for syphilis at Mount Sinai Hospital in 1933.

Although the results were promising, the death of a patient led the team to look for a drug that might be less toxic and more stable. At about this time, other investigators had shown that Mapharsen (arsenoxide) was much less toxic than Neoarsphenamine but equally as effective. The Mount Sinai group switched to Mapharsen and continued their studies with good results and a substantial decrease in toxic effects in a five-day treatment regimen. Large-scale clinical trials at a number of institutions confirmed these early results, demonstrating that at the most effective dose intravenous Mapharsen therapy yielded satisfactory results in 85 to 90 percent of cases of primary syphilis and 70 percent of cases of secondary syphilis. <sup>16</sup>

Of course, there was also no shortage of quack doctors and patent medicines supposedly able to cure syphilis, as had been the case for centuries. In nineteenth century America such nostrums as Swaim's Panacea and Helmbold's Extract of Buchu had been advertised as cures for syphilis. So-called medical or anatomy museums, generally aimed at men, also were often fronts for quacks who claimed to treat venereal disease and sexual dysfunctions. Brooks McNamara described a typical American museum of this type as follows:

"Once inside the main room, the assault on the patron's nerves began in earnest. Everywhere about him were glass cases filled with hideously diseased organs modeled in death-like wax or luridly painted papier-mâché. The lights were low, the atmosphere hushed and funereal. Case

after case displayed gaping sores and hideous deformities attributed to syphilis, gonorrhea, or that nameless terror of the nineteenth century, the "secret vice," masturbation...At this point a solicitous "floor man" would appear from nowhere and begin to talk to the frightened patient. If it appeared that the customer was in need of medical aid – or could be convinced that he was – he was steered upstairs to the 'medical institute' run by an "eminent specialist" in the various secret diseases."

In the twentieth century, as regulation of the advertising and labeling of medicines increased in the United States and other countries, the marketers of syphilis remedies turned to using euphemisms for the disease in an attempt to disguise their claims.

Everyone knew, for example, that "blood poisoning" in an advertisement meant syphilis. Products sold as "blood purifiers" had been used by some people as remedies for syphilis in the nineteenth century. Sarsaparilla tonics, such as Ayers and Hoods, were popular in this regard, as this plant (as we have seen) was originally thought to be a remedy for syphilis. Such products continued to be used in the 1920s and beyond. For example, Compound Syrup of Sarsaparilla and Burdock with Iodide of Potassium was being sold as a treatment for "blood poisoning resulting from syphilis" in the 1930s. <sup>19</sup>

By the late nineteenth century, however, sarsaparilla had largely fallen into disuse for this purpose in orthodox medicine, although syrup of sarsaparilla was still being used as a vehicle for delivering drugs such as mercury and iodine (which were used to treat syphilis). Textbooks of pharmacology of the early twentieth century generally dismiss the value of sarsaparilla as a remedy for syphilis. Arthur Cushny's popular textbook of

pharmacology, for example, stated that the drug "has some reputation in the treatment of syphilis, but there is no reason to believe that it is of any service here."<sup>20</sup>

Patent medicine quacks were not hesitant to don the mantle of science to sell their wares. Not long after Ehrlich discovered Salvarsan, for example, a New York charlatan marketed a cure for "blood poison" (syphilis) in which he used both Ehrlich's name and the number 606 (a term by which Salvarsan was also known). In the 1930s, a practitioner opened the "606 Medical Laboratory" in Chicago for the treatment of "men's disease" – a euphemism for syphilis and gonorrhea. The advertisement for this establishment could easily have given one the impression that Dr. Ehrlich himself was in charge. Another twentieth century "cure" for syphilis was named Ricord's Specific, drawing on the name of a famous nineteenth-century syphilologist. <sup>21</sup>

Dr. Sayman's Wonder Herbs was another patent medicine of the twentieth century that supposedly cured syphilitic "taints." The remedy consisted of a mixture of various plant products, such as ginger, rhubarb, licorice and senna, along with sodium bicarbonate or sodium carbonate. The Chief of Drug Control of the United States Food and Drug Administration noted in 1933 that while the medicine might be of some value in relieving gas in the stomach and bowel, it was worthless in the treatment of syphilis. Furthermore, he added:

"Yet this concoction was recommended for syphilitic 'taints,' as if you could have just a little bit of this dread disease! But when you have syphilis you have it. It is as impossible to have a mere taint of it as it would be to fire off a cannon a little bit at a time."<sup>22</sup>

Quack devices were also used for the supposed diagnosis and cure of syphilis. Albert Abrams, "the dean of twentieth century charlatans" in the United States, built a series of machines which he claimed could diagnose the disease of a patient from a sample of dried blood, even if the patient were miles away. In time, Abrams stated that the patient's autograph would work just as well, which enabled him to diagnose syphilis in famous persons of the past such as Henry Wordsworth Longfellow and Edgar Allan Poe. A New York "clinic" used an electrical device to treat young men who had been led to believe that they might be infected with syphilis. The patient sat naked on a kind of toilet throne with his back against a metal plate and his scrotum suspended in a whirling pool of liquid. Both the liquid and the metal plate were hooked to a battery, and the patient received a shock, presumably convincing him that the treatment was working.<sup>23</sup>

The introduction of penicillin as a therapeutic agent in the 1940s revolutionized the treatment of syphilis. Alexander Fleming had accidentally discovered the antibacterial properties of the *Penicillium* mold in 1928, and realized that a substance produced by the mold (which he called penicillin) might have therapeutic value as a topical agent against disease-causing bacteria. It was not until the early 1940s, however, that researchers at Oxford University in England isolated a relatively pure form of Fleming's penicillin and were able to demonstrate its therapeutic efficacy in animals and then in human clinical trials. The United States government gave high priority to the development of penicillin on a large-scale for use in the war effort, as the drug was proving to be the most potent anti-bacterial substance known to date. At first supplies were limited and mostly reserved for military use, but by 1944 innovations introduced in

American government, university and industry laboratories had greatly increased the yield and available supply of penicillin. In April 1945, all restrictions on its distribution in the United States were removed.<sup>24</sup>

In 1943, investigators at the Mayo Clinic showed that penicillin was effective against gonorrhea bacilli that were resistant to the sulfa drugs, thus giving physicians another weapon against this venereal disease. PHS physician John Mahoney and his colleagues at the Venereal Disease Research Laboratory in the PHS hospital at Staten Island, New York, soon confirmed these results. But Mahoney also decided to divert a small amount of his limited supply of the drug from the gonorrhea research to test it against syphilis. According to a coworker of Mahoney, the drug was first tried against the spirochetes that cause syphilis *in vitro* (i.e., outside of the body in a test tube or other apparatus) and failed to show any activity. Fortunately, the Staten Island investigators proceeded to the next step in trying penicillin *in vivo* (i.e., in the living body) in syphilitic rabbits.<sup>25</sup>

The results of limited animal tests were so encouraging that Mahoney decided to move ahead to clinical experiments. He justified this early move to testing on humans because penicillin appeared to be generally non-toxic and no harm would be done if the drug did not work and he had to return to arsenic therapy. In 1943, it has not yet been recognized that penicillin could produce serious allergic side effects in some patients.<sup>26</sup>

In June 1943, Mahoney and his colleagues began their clinical study with four patients. The results were very promising, and the Staten Island group gave a preliminary report of the work at a national meeting. Although they were cautious in their report of

the results, especially since the study had involved only four patients, their paper created great excitement. Microbiologist Gladys Hobby, who heard the presentation of the paper, later recalled:

"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."<sup>27</sup>

The story was picked up by the popular press as well. In an article headed "New Magic Bullet," *Time* discussed how Mahoney, in a "jam-packed session" of the meeting, announced that "penicillin had apparently cured four cases of early penicillin." Dr. Mahoney, according to the story, was "stunned" by the results. The magazine 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, but even given the limitations of the study, the results generated high hopes for this new drug against an old disease. One doctor who took to the floor to comment on the paper at the meeting was carried away by his enthusiasm to exult: "This is probably the most significant paper ever presented in the medical field." <sup>28</sup> At another conference a

month later, a PHS physician referred to the work of Mahoney and his colleagues as "overshadowing anything that has happened in syphilis control since the days of Ehrlich."<sup>29</sup>

The results of the limited study at Staten Island were promising enough to lead to the organization of a large-scale, national clinical trial of penicillin in the treatment of syphilis. Initially, eight civilian venereal disease clinics, along with one each from the Army, Navy and Public Health Service, participated in the study, but additional facilities were later included. Not surprisingly, the Staten Island PHS hospital, where Mahoney and his colleagues were located, was one of the original sites for the study. In September 1944, Mahoney and other participants in the study published papers describing their results with over 1400 cases. They were able to demonstrate that penicillin treatment led to the disappearance of the spirochete from open lesions, the healing of those lesions, and a reversal of the blood serologic response from positive to negative (presumably due to the elimination of spirochetes from the blood). Further clinical trials confirmed the place of penicillin as the treatment of choice for syphilis.<sup>30</sup>

On 26 June 1944, the U. S. Army adopted penicillin as the routine treatment for syphilis. Penicillin allowed military physicians to get men suffering from venereal disease back to being available for combat quickly. The infected men remained ambulatory and began to convalesce almost immediately after treatment was begun, so they could be kept close to the front lines and returned to combat as soon as the therapy was completed. At first, however, there was not enough penicillin available to treat all cases that might potentially benefit from it. Penicillin of course had therapeutic value of

the treatment of war wounds and various infections diseases other than syphilis and gonorrhea.<sup>31</sup> Physician-ethicist Henry Beecher called attention in a 1969 paper to the problem that military surgeons faced in this situation:

"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, a decision had to be made between using it for 'sulfa-fast' [sulfa-resistant] gonorrhea or for infected war wounds [its effectiveness against syphilis had not been fully established at the time]. Colonel Edward D. Churchill, Chief Surgical Consultant for that Theatre, 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."

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 had 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. A graduate student in social work, who completed a research project at a rapid treatment center 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 sexual behavior." A number of public health officials suggested that the quicker and less arduous penicillin treatment could actually lead to an increase in venereal disease. Johns Hopkins bacteriologist Thomas B. Turner, for example, gave a talk at the 1948 ASHA meeting entitled "Penicillin: Help or Hindrance?," in which he discussed the successes of the drug against venereal disease, but also cited the loss of fear as a deterrent to exposure. Similar concerns about the undermining of standards of morality had been voiced when Ehrlich's Salvarsan had been introduced to treat syphilis in the early twentieth century.<sup>33</sup>

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, did the advent of this more effective drug therapy eliminate these diseases or the social and moral issues surrounding them.

## **Notes**

- 1. Kevin Siena, "The Clean and the Foul: Paupers and the Pox in London Hospitals, c. 1550 c. 1700," in Kevin Siena, ed., *Sins of the Flesh: Responding to Sexual Disease in Early Modern Europe* (Toronto: Centre for Reformation and Renaissance Studies, 2005), pp. 261-84.
- 2. Claude Quétel, *History of Syphilis*, translated into English by Judith Braddock and Brian Pike (Baltimore: Johns Hopkins University Press, 1990), p. 23.
- 3. Jon Arrizabalaga, John Henderson, and Roger French, *The Great Pox: The French Disease in Renaissance Europe* (New Haven, CT: Yale University Press, 1997), pp. 29-30.
- 4. Quétel, *History of Syphilis*, pp. 30-32, 84; Owsei Temkin, "Therapeutic Trends and the Treatment of Syphilis before 1900," *Bulletin of the History of Medicine* 29 (1955): 309-16.
- 5. Quétel, History of Syphilis, pp. 85-86.
- 6. Deborah Hayden, *Pox: Genius, Madness, and the Mysteries of Syphilis* (New York: Basic Books, 2003), pp. 48-49.
- 7. Quétel, *History of Syphilis*, pp. 27-30; Arrizabalaga, et. al., *Great Pox*, pp. 99-103.
- 8. Sheldon Watts, *Epidemics in History: Disease, Power and Imperialism* (New Haven, CT: Yale Unviersity Press, 1997), p. 130.
- 9. Quétel, *History of Syphilis*, pp. 63, 83-86, 116-17.
- 10. Thomas P. Lowry, *The Story the Soliders Wouldn't Tell: Sex in the Civil War*, pp. 105-06.

- 11. John Parascandola, "The Theoretical Basis of Paul Ehrlich's Chemotherapy," *Journal of the History of Medicine* 36 (1981): 19-43.
- 12. Janice Dickin McGinnis, "From Salvarsan to Penicillin: Medical Science and VD Control in Canada," in *Essays in the History of Canadian Medicine*, ed. Wendy Mitchinson and Janice Dicken McGinnis (Toronto: McClelland and Stewart, 1988), pp. 126-47; R. H. Kampmeier, "Syphilis Therapy: An Historical Perspective," *Journal of the American Venereal Disease Association* 3 (1976): 99-108; *Milestones in Venereal Disease Control: Highlights of a Half-Century* (Washington, DC: U. S. Department of Health, Education, and Welfare, 1957); Jay Casell, *The Secret Plague: Venereal Disease in Canada 1838-1939* (Toronto: University of Toronto Press, 1987), p. 56.
- 13. Jeffrey S. Sartin and Harold O. Perry, "From Mercury to Malaria to Penicillin: The History of the Treatment of Syphilis at the Mayo Clinic 1916-1955," *Journal of the American Academy of Dermatology* 32 (1995): 255-61.
- 14. Nobel Lectures, Physiology or Medicine 1922-1941 (Amsterdam: Elsevier, 1965; Paul Weindling, "Julius Wagner-Jauregg," in Nobel Laureates in Medicine or Physiology: A Biographical Dictionary, ed. Daniel M. Fox, Marcia Meldrum, and Ira Rezak (New York: Garland Publishing, 1990), pp. 545-48; Sartin and Perry, "From Mercury;" Joel Braslow, "The Influence of a Biological Therapy on Physicians' Narratives and Interrogations: The Case of General Paralysis of the Insane and Malaria Fever Therapy, 1910-1950," Bulletin of the History of Medicine 70 (1996): 577-608.

15. Braslow, "The Influence," pp. 606-07.

- 16. Kampmeier, "Syphilis Therapy," p. 105; Louis Chargin and William Leifer, "Massive Dose Arsenotherapy of Early Syphilis by Intravenous 'Drip Method," *A. M. A. Archives of Dermatology* 73 (1956): 482-84; Harold Thomas Hyman, "Massive Arsenotherapy in Early Therapy by the Continuous Intravenous Drip Method," *Archives of Dermatology and Syphilology* 42 (1940); 253-61; "Massive Arsenotherapy for Syphilis," *Journal of the American Medical Association* 126 (1944): 554-57.
- 17. James Harvey Young, *The Toadstool Millionaires: A Social History of Patent Medicines in America before Federal Regulation* (Princeton, NJ: Princeton University Press, 1961), pp. 58-66, 114-17.
- 18. Brooks McNamara, Step Right Up: An Illustrated History of the American Medical Show (Garden City, NY: Doubleday, 1976), p. 42.
- 19. James Harvey Young, *The Medical Messiahs: A Social History of Health Quackery in Twentieth-Century America* (Princeton, NJ: Princeton University Press, 1967), p. 84; Ruth deforest Lamb, *American Chamber of Horrors: The Truth about Food and Drugs* (New York: Farrar and Rinehart, 1936), p. 71; F. J. Cullan, "Federal Control of Venereal Disease Nostrums Through Proposed Legislation," *Journal of Social Hygiene* 19 (1933): 513-522.
- 20. Arthur Oslo, George E. Farrar, Jr., and Robertson Pratt, *Dispensatory of the United States of America 1960 Edition* (Philadelphia: J. B. Lippincott, 1960), p. 1215; David M. R. Culbreth, *A Manual of Materia Medica and Pharmacology*, sixth edition (Philadelphia: Lea and Febiger, 1917), p. 121; Arthur R. Cushny, *A Textbook of Pharmacology and Therapeutics*, third edition (Philadelphia: Lea Brothers, 1903), p. 355.

- 21. Young, *Toadstool Millionaires*, p. 168; Casell, *Secret Plague*, p. 63; Suzanne Poirier, *Chicago's War on Syphilis*, *1937-1940: The Times*, *the* Trib, *and the Clap Doctor* (Urbana, IL: University of Illinois Press, 1995), pp. 61-63.
- 22. Cullan, "Federal Control," p. 519.
- 23. James Harvey Young, "Device Quackery in America," *Bulletin of the History of Medicine* 39 (1965): 154-162.
- 24. The literature on the history of penicillin is extensive. See, e.g., Robert Bud, *Penicillin: Triumph and Tragedy* (Oxford: Oxford University Press, 2007); Gladys Hobby, *Penicillin: Meeting the Challenge* (New Haven, CT: Yale University Press, 1985); Kevin Brown, *Penicillin Man: Alexander Fleming and the Antibiotic Revolution* (Stroud, UK: Sutton, 2004).
- 25. John Parascandola, "John Mahoney and the Introduction of Penicillin to Treat Syphilis," *Pharmacy in History* 43 (2001): 3-13; Hobby, *Penicillin*, p. 152.
- 26. J. F. Mahoney, R. C. Arnold, and Ad Harris, "Penicillin Treatment of Early Syphilis: A Preliminary Report," *American Journal of Public Health* 33 (1943): 1387-91.
- 27. Ibid.; Hobby, Penicillin, pp. 155-56.
- 28. "New Magic Bullet," *Time* 42 (25 October 1943): 38, 40.
- 29. J. R. Heller, Jr., "Syphilis Control in Wartime," *Southern Medical Journal* 37 (1944): 219-223 (quotation on p. 222).
- 30. A. N. Richards, "Production of Penicillin in the United States (1941-1946)," *Nature*201 (1964): 441-45; 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 (copy at National Library of Medicine); 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; 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.

- 31. Richards, "Production of Penicillin," p. 444; Odin W. Anderson, *Syphilis and Society Problems of Control in the United States, 1912-1964* (Chicago: Center for Health Administration Studies, Health Information Foundation, 1965), pp. 20-21; R. A. Vonderlehr and J. R. Heller, Jr., *The Control of Venereal Disease* (New York: Reynal and Hitchcock, 1946), p. 3.
- 32. Henry K. Beecher, "Scarce Resources and Medical Advancement," *Daedalus* 98 (1969): 275-313 (quotation on pp. 280-81).
- 33. McGinnis, "From Salvarsan to Penicillin," pp. 145-46; 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 (quotation on p. v); Richard A. Koch and Ray Lyman Wilbur, "Promiscuity as a Factor in the Spread of Venereal Disease," *Journal of Social Hygiene* 30 (1944): 517-29; Vonderlehr and Heller, *Control of Venereal Disease*, p. 65; Elizabeth Fee, "Sin vs. Science: Venereal Disease in Baltimore in the Twentieth Century," *Bulletin of the History of Medicine* 43 (1988): 141-64; Allan M. Brandt, *No Magic Bullet: A*

Social History of Venereal Disease in the United States Since 1880, expanded edition (Oxford: Oxford University Press, 1987), p. 46.