

“Normal Exposure” and Inoculation  
Syphilis: A PHS “Tuskegee” Doctor in  
Guatemala, 1946-48

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Susan M. Reverby  
Marion Butler McLean Professor in the History  
of Ideas and Professor of Women’s and Gender  
Studies, Wellesley College  
Wellesley MA  
781 283 2535  
sreverby@wellesley.edu

Policy is often made based on historical understandings of particular events, and the story of the “Tuskegee” Syphilis Study (the Study) has, more than any other medical research experiment, shaped policy surrounding human subjects.<sup>1</sup> The forty-year study of “untreated syphilis in the male Negro” sparked outrage in 1972 after it became widely known, and inspired requirements for informed consent, the protection of vulnerable subjects, and oversight by institutional review boards.<sup>2</sup>

When the story of the Study circulates, however, it often becomes mythical. In truth the United States Public Health Service (PHS) doctors who ran the Study observed the course of the already acquired and untreated late latent disease in hundreds of African American men in Macon County, Alabama. They provided a little treatment in the first few months in 1932 and then neither extensive heavy metals treatment nor penicillin after it proved a cure for the late latent stage of the disease in the 1950s.<sup>3</sup> Yet much folklore asserts that the doctors went beyond this neglect, and that they *secretly infected* the men by injecting them with the bacteria that causes syphilis. This virally spread belief about the PHS’s intentional infecting appears almost daily in books, articles, talks, letters, websites, tweets, news broadcasts, political rhetoric, and above all in whispers and conversations. It is reinforced when photographs of the Study’s blood draws circulate, especially when they are cropped to show prominently a black arm and a white hand on a syringe that could, to an unknowing eye, be seen as an injection.

Historians of the Study have spent decades now trying to correct the misunderstandings in the public and the academy, and to make the facts as

knowable as possible.<sup>4</sup> The story is horrific enough, it is argued, without perpetuating misunderstanding over what really did happen and how many knew about it.<sup>5</sup> What if, however, the PHS did conduct a somewhat secret study whose subjects were infected with syphilis by one of the PHS doctors who also worked in “Tuskegee?” How should this be acknowledged and affect how we discuss historical understandings that drive the need for human subject protection?

### Rumors and Realities

Scholars who wish to debunk the myth of deliberate infection in the Study can acknowledge that myths do express some basic realities. As the oral historian Alessandro Portelli argues, “The wrong tales allow us to recognize the interests of the tellers and the dreams and desires beneath them”<sup>6</sup> “A rumor,” other folklorists suggest, “is a ‘form of communication though which men [and women] caught together in an ambiguous situation attempt to construct a meaningful interpretation of it by pooling their intellectual resources.’”<sup>7</sup> In a highly racialized and racist country, the idea that government scientists—drunk on their power over trusting sharecroppers in need of care—would deliberately and secretly infect black men with a debilitating and sometimes deadly disease seems possible.

Yet those scholars may also argue that people who believe in such deliberate infection are confusing the Study with other American 1960s and 1970s horror tales about overzealous medical researchers who injected cancer cells into elderly Jewish patients and provided live hepatitis cells through oral and injecting means to young children with mental retardation. The conflating also comes when the Study is referred to as “America’s Nuremberg” (to equate

its affect on ethics) and to link it to the horrors of the monstrous Nazi medical experiments. In addition, to think the men were infected taps deep into our cultural collective consciences' fears of experimentation. It avoids considering the Study's unwitting participants' sexual activities, or those of their parents, since syphilis is primarily, of course, a sexually transmitted disease. To assume the men in the Study were infected, rather than watched for decades, appears to make the racism worse, although it is the very ordinariness of the withholding of treatment that ought to frighten us more.<sup>8</sup>

Historians and other scholars have also argued that there were debates over whether the heavy metals treatments were appropriate for those in the late latent stage of the disease and that public health's mission was to stop contagion, not focus on chronic illness. Others have claimed, too, that the concern with the dangers of penicillin limited some of its usefulness, especially for patients who were at least two decades out from initial syphilitic infection.<sup>9</sup>

Historians may also emphasize medical understandings of syphilis's stages and transmission. These explanations require discussing the multiple stages of the disease and when and how decisions about treating those in latency were made. More importantly, even if the government doctors had wanted to give the men syphilis, it is very difficult to pass on syphilis outside of sexual contact, breast-feeding, or congenitally from a still infectious mother to her newborn. To explain this is also to confront pre-20<sup>th</sup> century understandings of the disease as hereditary, not just congenital, since syphilis cannot be just passed down in genes or somehow through a bloodline. It demands explaining the doctors could not just inject the spirochetal bacteria that causes syphilis easily from the blood of one person to another, and that centuries of research efforts

had demonstrated the difficulties of finding ways experimentally to recreate the disease in the healthy.<sup>10</sup> The *Treponema pallidum*, the spirochete-shaped bacteria that causes syphilis, cannot be cultured and grown *in vitro* in a laboratory (unlike *N. gonorrhoea*, which can be cultured).

In sum, it takes time and a commitment to learning the medical science, understanding standard public health practices, and considering cultural beliefs in both the public and health care communities to explain why the men in Alabama were not, and could not easily have been, infected by the PHS, and yet why this is believed. Telling a quick black and white story makes for a better rhetorical media or political sound bite, or a brief historical introduction in a glossed over bioethics lesson.

Ironically, though, the mythic version of the “Tuskegee” Study may offer a better picture of mid-century PHS ethics than the seemingly more informed accounts. For Public Health Service researchers did, in fact, deliberately infect poor and vulnerable men and women with syphilis in order to study the disease. The mistake of the myth is to set that story in Alabama, when it took place further south, in Guatemala.

The Guatemala story emerges from the records of work done by the PHS’s Dr. John C. Cutler between 1946 and 1948, now in the University of Pittsburgh archives. An internationally known public health researcher-administrator and expert on sexually transmitted diseases and reproductive health, Cutler had been an assistant surgeon general in the PHS and the deputy director of the Pan American Sanitary Bureau (a precursor to the Pan American Health Organization).<sup>11</sup> He worked in Guatemala, India and West Africa and ended his career as, his obituary in 2003 read, “a much beloved professor both at the

graduate school of Public Health and the Graduate School of Public and International Affairs” at Pitt.<sup>12</sup>

Cutler was dedicated to researching and conquering sexually transmitted (then known as venereal) diseases and providing usable and effective contraception to women. He published more than fifty articles on varying venereal diseases, the prophylaxis of disease with chemical contraceptives, and the lessons for ending the AIDS epidemic.<sup>13</sup> Those who know about the “Tuskegee” Study will recognize his name as a key researcher of that work during the 1960s and one of its staunchest defenders on PBS’s 1993 *Nova* film about it called “The Deadly Deception,” produced more than twenty years after the Study closed.<sup>14</sup>

Almost two decades *before* his involvement with the Study in Alabama, the PHS put Cutler in charge of a two-year research project in Guatemala. This experiment in the global, rather than the American South, differed from the Study in Alabama in two major ways: government doctors *did infect* people with syphilis and then *did treat* them with penicillin. In this research program of a series of carefully delineated experiments, PHS doctors exposed their subjects to syphilis or gonorrhea through the use of infectious prostitutes or directly through inoculum made from tissue from human and animal syphilitic gummas and chancres, or pus of gonorrhea filed sores. After learning what they wished from each exposure, they used penicillin presumably to cure the infection.

Exploring why these experiments in Guatemala were so different from those in Alabama provides insight into the ethical concerns of the PHS researchers, the powerful pull of the need for scientific knowledge, and the difficulty of analyzing the inter-relationship and movement of research between

what has been called the “imperial periphery” and “metropolitan transformations.”<sup>15</sup>

### Penicillin Cure or Chemical Prophylaxis?

By the end of World War II, penicillin became more widely available and had begun to demonstrate its effectiveness as a cure with early and secondary syphilis and numerous other diseases.<sup>16</sup> Much of the drug’s doses and limitations still remained to be tested. Looking out at the future, 1940s syphilologists began to realize, however, as Johns Hopkins’s Joseph Earle Moore would lament a decade later, “the biologically minded clinician regrets... that syphilis seems to be vanishing with most of its fascinating and more fundamental riddles still unsolved.”<sup>17</sup>

One of these remaining questions had to do with if, in addition to condoms, there was a need for a better chemical prophylaxis against the disease that a man could apply directly to his penis right after possible exposure, or whether just relying upon penicillin as cure from a health professional after the syphilis was diagnosed would be sufficient.<sup>18</sup> Syphilologists were well aware of the problems with many of the serologies done to determine syphilis, the inability to translate animal research studies (primarily done with rabbits and sometimes with chimpanzees) to humans, the complicated chronicity of the disease, and the wiliness of the syphilitic spirochete that had fascinated them for decades.

In 1944 the PHS had done experiments on prophylaxis in gonorrhea at the Terre Haute Federal Penitentiary in the United States. In this prison, the “volunteers” were deliberately injected with gonorrhea, but the PHS had found it difficult to get the men to exhibit infection and the study was abandoned.<sup>19</sup> To

continue that work, and to extend it to syphilis, the PHS looked south beyond American borders.

The PHS had a long history of international work going back to its 19<sup>th</sup> century participation in foreign quarantines and sanitary conferences with a focus on infectious diseases, and then its 1945 establishment of an Office of International Relations to formalize these efforts.<sup>20</sup> To coordinate disease control in the Americas, the PHS had led the organizing in 1901 of the Pan American Sanitary Bureau (the precursor to the Pan American Health Organization) and the American Surgeon Generals, official heads of the PHS, served as directors of the Bureau between 1902 until 1936.<sup>21</sup> Indeed, one historian has argued the Pan American Sanitary Bureau “functioned until the late 1930s...as a virtual branch of the [PHS].”<sup>22</sup> In turn many Central American and Latin American countries sought assistance from the PHS and the Rockefeller Foundation as their funds and surveys assisted in the creation of federal control over health in regional and indigenous areas through the development of a public health infrastructure.

The United Fruit Company owned and controlled much of Guatemala, the quintessential “banana republic,” in the first half of the 20<sup>th</sup> century. When the PHS looked to Guatemala for its research in the immediate post-World War II years, it came into the country during the period known for its relative freedoms; between 1944 and the U.S. led CIA coup of the elected government in 1954, there were efforts made at labor protection laws, land reform, and democratic elections. The PHS was part of the effort to use Guatemala for scientific research as they presumed to transfer laboratory materials, skills, and knowledge to a Guatemalan public health elite.<sup>23</sup>



Guatemala appeared to be a possibility as for an excellent site for study for several reasons. The PHS training of Juan Funes, Guatemala's leading venereal disease public health official, made the forging of close cooperation easier and the building of a public health infrastructure important. Unlike Alabama, where the PHS expected to find a large number of subjects with the late latent stage of the disease already, Guatemala offered subjects who did not yet have syphilis. For in his somewhat haphazard surveys in the 1930s, the Harvard Medical School Tropical Medicine professor George Cheever Shattuck found little syphilis in the Guatemalan highlands and reported little in the army as well. Shattuck shared the belief of Guatemalan health officials that "syphilis is more frequent in Latins [especially in Guatemala City] than in Indians and that, when manifested in an Indian, it appears in mild form."<sup>24</sup> Racialized assumptions about the disease, central to the project in Alabama, also followed it to Guatemala.

With a grant from the National Institute of Health to the Pan American Sanitary Bureau under the direction of the PHS's Venereal Disease Research Laboratory (VDRL), the PHS cooperated with officials at the Guatemala's Ministry of Health, the National Army of the Revolution, the National Mental Health Hospital and Ministry of Justice on what was benignly called "a series of experimental studies on syphilis in man." The focus of the experiments was to understand whether various chemicals, other than the ones then available, could be used as a prophylaxis against syphilis after sexual exposure to the disease, to try and see what caused false positive serologic tests for the disease, and to demonstrate more fully when and how differing dosages of penicillin actually cured infection.<sup>25</sup>

The PHS and the Pan American Sanitary Bureau assigned Cutler, who had been working at the VDRL and on the Terre Haute prison gonorrhea project, to lead this research in Guatemala with the assistance of the PHS-trained Funes. Cutler and Funes had two goals. One was to use what was called “syphilization” to test the human response to “fresh infective material to enhance body response to disease...[to understand] superinfection and reinfection.”<sup>26</sup> The second goal was to find ways to prevent the disease immediately after exposure.<sup>27</sup> During World War II, the United States had provided its troops calomel-sulpha-thiazole ointment in “pro kits.” (prophylaxis kits). But these were painful to use, so the PHS wondered if less noxious chemicals or penicillin could be used instead.<sup>28</sup>

#### “Normal Exposure” and Normal Science

Animal experimentation, especially with rabbits, was long a mainstay in 20<sup>th</sup> century syphilis research, but it could not answer these pressing research questions. The PHS researchers wanted to do an experiment where they knew there would be a good deal of what they politely called “normal exposure” to the disease in humans. As subjects, they chose the usual quartet of the available and contained: prisoners in a national penitentiary, inmates in Guatemala’s only mental hospital, children in the national orphanage, and soldiers in a barracks in the capital.

Guatemala had legalized prostitution and “allowed prostitutes to pay regular visits to men in penal institutions,” they explained in their reports.<sup>29</sup> With the cooperation of officials at the Ministry of Justice and the warden of Guatemala City’s Central Penitentiary, which housed nearly 1500 inmates, prostitutes who tested positive for either syphilis or gonorrhea were allowed to offer their services to prison inmates, paid for by U.S. taxpayers through the

funds of the PHS. In yet another set of experiments, uninfected prostitutes had inoculum of the diseases placed on their cervixes before the sexual visits began. Serological tests were done on the inmates before the prostitutes were invited to the prison and then afterwards to see if infection had occurred. The men were divided into groups and various chemical and biological prophylaxis techniques were tested after presumed infection. If positive, the men were then provided with enough penicillin to produce a cure.

Rabbits, of course, were much easier to manage and manipulate than human beings, as the doctors soon discovered. Not enough of the sexually well-serviced men (the researchers actually timed how long they spent with the prostitutes and thought they acted “like rabbits”), even when plied with alcohol, seemed to get syphilis.<sup>30</sup> The prostitutes were not easily controlled either, and one researcher lamented, “unfortunately our female donor is leaving her profession for marriage and is no longer available.”<sup>31</sup> The next problem the researchers ran into regarded the blood tests: too many positives even before more “normal exposure” occurred. Since they needed men who either had never had the disease or had already been cured of the disease for their studies, they discovered their pool was too small for statistical significance to be possible. Their first answer then became, not abandoning the research, but rather questioning the tests.

The serology (blood tests) for syphilis had always been a problem, as the balance between sensitivity and specificity created many false positives and false negatives. And as the researchers wrote, “the impression is widespread that in certain tropical and subtropical areas there is a high degree of seropositivity which may not be truly indicative of the prevalence of syphilis.”<sup>32</sup> There had long

been an understanding that the presence of yaws (another treponemal disease) and malaria could affect positive blood tests for syphilis. In Guatemala, while they were getting positive reactions on the tests, they could find no clinical signs or spinal fluid evidence of the disease in the men's bodies.<sup>33</sup> To deal with this the researchers had to do repeat and differing blood tests (drawing 10 cc of blood every week or biweekly) to see if there had spontaneous cure of the disease, or the complex pattern on the blood tests (sometimes negative even when the patient still had the disease) often seen in longstanding syphilis cases.

Even though the inmates were in a prison and there was no mention of any kind of informed consent, the researchers met resistance. As they reported, "the inmates were for the most part uneducated and superstitious. Most of them believed they were being weakened" by the frequent blood withdrawals. Even though penicillin and iron pills were promised, "in their minds there was no connection between the loss of a 'large tube of blood' and possible benefits of a small pill."<sup>34</sup> This resistance and the difficulty of managing the prisoners suggested perhaps the studies on the serologies could be better done elsewhere.

With the cooperation of the Guatemalan government, the researchers turned to 438 children between the ages of 6 and 16 in the National Orphanage to study the blood tests, not to give the children syphilis.<sup>35</sup> Three children who appeared to have signs of congenital syphilis after repeat testing and examination were given penicillin. Yet another 89 gave positive results on their tests but showed no signs of the disease clinically. Finding the problem was not with the antigens used in the tests, the research physicians argued for the use of specific kinds of blood tests with this kind of population to rule out confounding factors they could not identify.<sup>36</sup>

They still, however, had not answered the question of whether penicillin could be used for prophylaxis, not just cure after a definitive positive blood test, in comparison to other chemicals applied directly to the genitalia. Faced with this and continued concerns with the serologies and reinfection after treatment, they turned to experiments with the inmates in the country's only asylum. Here it was not possible to introduce prostitutes, follow the inmates around to watch and time their sexual encounters, or gain acceptance by the female patients for physical examinations. So the researchers planned an inoculation, rather than "sexual exposure," study, though most of the asylum officials at first thought the inoculation was just another kind of drug.<sup>37</sup>

As in Tuskegee and throughout the global South in these years, the cooperation was sought with the institution, not the subject-inmates or their families. And the best way to gain that cooperation was by offering supplies. In a severely under-funded and overcrowded institution, the PHS supplied "much needed anti-convulsant drugs, particularly Dilantin, for the large part of the population which were epileptic." They also "bought a refrigerator for biologicals, a motion picture projector that supplied the sole recreation for the inmates, metal cups, plates and forks to supplement the completely inadequate supply available."<sup>38</sup> Individual subjects were offered cigarettes: an entire packet for inoculation, blood draws or spinal taps and a single cigarette for "clinical observation."<sup>39</sup>

### Creating and Introducing the Inoculum

Making the syphilis inoculum was not easy. One method was to grind up gummas (syphilitic growth) in the testes of rabbits infected with the Nichols and Frew strains of the bacteria. This proved extremely difficult as rabbits had to be

flown in from the VDRL in Staten Island to Cutler in Guatemala City; many neither survived the trip nor developed enough of an infection. In addition, the researchers tried to make inoculum from scrapings of the chancres on the bodies of already infected asylum inmates, or men from the army that had a “street strain,” picked up by local prostitutes not involved in the study itself.<sup>40</sup> Once the sample was obtained (by either killing the rabbits to scraping the men’s penile chancres), the live inoculum had to be made quickly since the spirochetes could not last more than 45 to 90 minutes outside a body. This left very little time to remove the materials, centrifuge it with fresh homemade beef heart broth, and prepare to deliver it to the subjects. Some inoculum was created with heat-killed bacteria and others with the living spirochetes.

Then the inoculum had to be introduced in the bodies of the subjects. On the women inmates, because of what was called “local prejudices against male viewing of the body, even by physicians,” the inoculum was inserted after needles were used to abrade the women’s forearms, face or mouth. With the men, the inoculation was often much more direct after what soldiers for generations had called the “short arm” inspection. They chose men with “at least moderately long foreskins [to keep the mucus membranes moist]” and who could “sit or stand calmly in one spot for several hours.” In the experiments, a doctor held the subject’s penis, pulled back the foreskin, abraded the penis slightly just short of drawing blood by scraping the skin with a hypodermic needle, introduced a cotton pledget (or small dressing) and dripped drops of the syphilitic emulsion onto the pad and through it to the roughed skin on the man’s penis for at least an hour, sometimes two.

This was compared to other forms of introducing the syphilis to the body, including scraping the forearm before providing the inoculum, or ingestion of syphilitic tissue mixed with distilled water, the removal of spinal fluid that was then infused with the syphilitic mixture and reintroduced into the body, and venipunctures of the mixtures into the medial cubital vein of the forearm.<sup>41</sup> In other studies of prophylaxis at an army barracks, the men were allowed to have sex with uninfected prostitutes, then had the syphilitic inoculum put into the meatus of their penis, told to urinate an hour later and apply differing kinds of chemical prophylaxis.<sup>42</sup> In still other studies, the inoculum was placed on the cervix of prostitutes before they were allowed to have sex with the prisoners.

Cutler's scientific fervor was impressive, for his sense of the dangers of syphilis was acute. The experiments varied the ways the inoculations were done, whether the syphilitic mixture came from a single chancre, a combination of "donors," or from the rabbits or the bodies of infected prostitutes and inmates and soldiers. The researchers gave out differing kinds of chemical prophylaxis to some of their subjects, or set up other men as controls who had no prophylaxis. They made sure no one had the disease, or had taken anything for it, before they began the experimentation. Anyone infected was given penicillin and presumed to be cured, although there appears to have been no real follow up to determine this. The studies involved hundreds of men and women, many of whom had their photographs taken and left in the files.

### Deception

Deception was central here, as in Tuskegee. Cutler, writing to famed penicillin researcher and PHS physician R.C. Arnold in 1947, admitted they were not really telling very many people that the inoculum contained the syphilis

bacteria. "As you can imagine," Cutler reported to his colleague, " we are holding our breaths, and we are explaining to the patients and others concerned with but a few key exceptions, that the treatment is a new one utilizing serum followed by penicillin. This double talk keeps me hopping at time."<sup>43</sup> In a second letter he repeated his concerns that "a few words to the wrong person here, or even at home, might wreck it or parts of it..."<sup>44</sup>

Leading scientists knew that secrecy, and even law breaking was sometimes necessary to further research. Thomas Rivers, the famed virologist who led the Rockefeller Institute for Medical Research Hospital in New York, made this clear in his 1967 memoir when he recalled:

Well, all I can say is, it's against the law to do many things, but the law winks when a reputable man wants to do a scientific experiment. For example, the criminal code of the City of New York holds that is a felony to inject a person with infectious material. Well, I tested out live yellow fever vaccine right on my ward in the Rockefeller Hospital. It was no secret, and I assure you that the people in the New York City Department of Health knew it was being done....Unless the law winks occasionally, you have no progress in medicine.<sup>45</sup>

Rather than law breaking, in Guatemala the secrecy added to the difficulties of an already challenging project. Experiments on prophylaxis needed to determine how much inoculum to give, the time it was allowed to enter the body and the kinds of "antiseptic agents" and "spirocheticidal" therapy to provide.<sup>46</sup> Keeping track of the hundreds of subjects proved complicated, especially in the asylum when patient's names were forgotten, or the staff called them, for example, "The mute of St. Marcos." Eliese Cutler, a Wellesley College alumna and. Cutler's wife, helped because she "got to know the patients and helped keep things straight," while also photographing them and the inoculations for the record. Some of the inmates were given the syphilis



emulsions numerous times and another, they lamented, “after scarification, and the first application of emulsion...fled the room and was not found until 2 hours later with the pledget still in place.”<sup>47</sup> Once it became clear that some of the inoculum took, researchers were “scrupulous” they asserted in making sure the penicillin was given to cure anyone who became infected, and the blood testing continued.<sup>48</sup>

The Guatemalan officials had their own demands. They asked Cutler to test and treat men in army barracks, to do surveys of disease in the lowlands, and to provide more penicillin for the country as part of the price for cooperation. He traded off drugs for malaria at the orphanage for the right to continue blood testing. His bosses in the PHS worried, however, that Cutler might be making too many promises of supplies and developing too ambitious a program. The PHS was already fighting a battle at home to continue its work in venereal disease in the face of the seemingly easy penicillin cure, so the project in Guatemala became difficult to justify.<sup>49</sup> After multiple letters Cutler promised to be careful and promised, “we shall use our supply sparingly so as to have it available at all times for use in demonstration programs and to build good will.”<sup>50</sup>

Cutler remained confident that he had a gold mine for the research. While he was getting pressure from home to justify the abrading and inoculations, he reminded his supervisors “normal sex leads to this kind of trauma and minute lacerations.” Writing to his director supervisor (the famed PHS researcher John F. Mahoney, who had first demonstrated penicillin’s power over syphilis in 1943), Cutler noted “with the opportunity offered here to study syphilis from the standpoint of pure science just as Chesney studies it in the rabbit it should be

possible to justify the projects in the event of the impossibility of resolution of the prophylactic program.”<sup>51</sup>

Back in the United States, leading scientists were also hopeful, at first. Inoculation studies earlier in the century had caused much controversy, and after the 1910s most of it proceeded on animals, not humans.<sup>52</sup> Mahoney told Cutler in October 1946 “your show is already attracting rather wide and favorable attention up here. We are frequently asked as to the progress of the work. Doctor T. B. Turner at Johns Hopkins wants us to check on the pathogenicity in man of the rabbit spirochete; Doctor Neurath of Duke would like to have us follow patients with his verification procedures; Doctor Parran [the Surgeon General] and probably Doctor Moore [the leading syphilologist at Hopkins] might drop in for a visit after the first of the year.”<sup>53</sup> Harry Eagle of the National Cancer Institute, who had created one of the serology tests for syphilis and did major work on penicillin, wanted in on the studies as well, since his theory that penicillin could be used as a prophylaxis had only been tested in animals, not humans. He was so angry he was not allowed in on the data that he went to the Surgeon General over it.<sup>54</sup>

The studies in Guatemala proved problematic, however, both for scientific and political reasons. Mahoney admitted that Cutler’s data were not showing enough infection could be transferred and that “the circumstance confirms the conclusion drawn from the Terre Haute study that a very important factor other than the presence of the organism must be operative in the transmission of the disease.”<sup>55</sup> By the fall of 1947, interest in prophylaxis was waning at home, and Mahoney told Cutler that there would be very little money if the study were just for serologies and penicillin therapy. Yet assumed racial and climatic differences

would require a broader sweep. "A comprehensive study of the reliability of serology as a diagnostic instrument among aboriginal peoples in tropical America would require a different approach being used at present," Mahoney argued. "We would be obliged to canvas the South and Central American nations, the Mexican Indians, the Indian tribes in the United States, and finally, the southern negro."<sup>56</sup>

### Should They Do This?

There was also what bioethicists would later call the "yuck factor" of all the work.<sup>57</sup> PHS physician R.C. Arnold, who supervised Cutler from afar, was more troubled than was Cutler about the ethics of the project. Eight months after the "Doctors' Trials" at Nuremberg had ended, he confided to Cutler, "I am a bit, in fact more than a bit, leery of the experiment with the insane people. They can not give consent, do not know what is going on, and if some goody organization got wind of the work, they would raise a lot of smoke. I think the soldiers would be best or the prisoners for they can give consent. Maybe I'm too conservative....Also, how many knew what was going on. I realize that a pt [patient] or a dozen could be infected, develop the disease and be cured before anything could be suspected...In the report, I see no reason to say where they work was done and the type of volunteer."<sup>58</sup>

Everyone involved with these studies seemed to know they were treading on complicated ethical grounds. There had been debates within the National Research Council in the early 1940s over the ethics of the Terre Haute prison study on gonorrhea. The PHS knew that such studies had to be methodologically sound and scientifically fruitful, historian Harry Marks has argued, to justify the risks to prisoners.<sup>59</sup> Yet the PHS knew there were very few other ways to get at

this information and to find a way to stop syphilis' spread through prophylaxis before the disease was established, not just cure afterward. While the gonorrhea studies had failed in Terre Haute, they still hoped the new trials on gonorrhea and syphilis in Guatemala would prove so successful that the risks would have been worth it. Malaria specialist G. Robert Coatney, who had done prison malaria studies, visited the project in February 1947. In reporting to Cutler after he returned to the States, he explained that he had brought Surgeon General Thomas Parran up to date and that with a "merry twinkle [that] came into his eye...[he] said 'You know, we couldn't do such an experiment in this country.'"<sup>60</sup>

Cutler, too, acknowledged that other syphilologists thought human experimentation on penicillin as a prevention for syphilis that required inoculation with the disease "could not be ethically carried out." Concerned that discussion of this ethical problem was taking place in the United States just as information on their grant in Guatemala was published in *Journal of the American Medical Association*, Cutler told Mahoney, "it is becoming just as clear to us as it appears to be to you that it would not be advisable to have too many people concerned with this work in order to keep down talk and premature writing.... We are just a little bit concerned about the possibility of having anything said about our program that would adversely affect its continuation."<sup>61</sup>

Mahoney continued to worry. There is a good deal of "gossip" in high places about what was going on in Guatemala, he warned Cutler. "I hope you will not hesitate to stop the experimental work in the event of there being an undue amount of interest in that phase of the study." Mahoney, as with Arnold, seemed less concerned with the prostitute transmission studies taking place in

the prison, but seemed more squeamish about the politics and morality of the inoculation studies taking place in the asylum.<sup>62</sup>

There was also the problem that such studies, requiring such effort to induce infection, could not be duplicated elsewhere. Mahoney told Cutler about a year and half in to the project, “in syphilis, unless we can transmit the infection readily and without recourse to scarification or direct implantation, the possibilities of studying the subject are not bright.” The procedures were, he noted “drastic...[and] beyond the range of natural transmission and will not serve as a basis for the study of a locally applied prophylactic agent.”<sup>63</sup> Cutler did his best to try the studies in multiple ways, to use differing strains of the bacteria, to move between animal and human donors, and to emphasize the repeatability.<sup>64</sup>

Even as Cutler continued a number of differing studies, his PHS supervisors were acutely aware this had to stop. Supplies were limited, and the growing use of penicillin diminished political support for this kind of research. By 1948 Cutler was told to finish up his work, leave the laboratory materials for the Guatemalan venereal disease control effort, and to come home to be assigned elsewhere. Eventually, Cutler and his colleagues would write up the serology findings, and a colleague would publish some details in a Spanish-language public health journal.<sup>65</sup> Cutler put the final report and the hundreds of photographs his wife had taken in his papers, the only record of his decades long research career left behind.<sup>66</sup> The extraordinary efforts he had made to produce disease and understand various kinds of prophylaxis were buried in the files.

Does this Matter?

Moore had been right that the penicillin cure for syphilis left many unanswered questions about the disease. Although Cutler's work helped refine serological testing, and suggested a better chemical prophylaxis, it made little impact on syphilis research. Cutler would go on to do another inoculation study five years later in 1953 with the PHS's Harold Magnuson at New York's Sing Sing Prison with sixty-two "human volunteers," using as he had in Guatemala both heat-killed and virulent organisms made from ground up rabbit testes. These inoculations, however, were done intra-cutaneously and subcutaneously. No one was abrading the penises of these American men, even in a prison. Anyone positive was treated, too, with penicillin. These prison studies were done to answer some questions about re-infection and whether having treated syphilis and then being provided with the "booster" of new disease created immunity to further infection. The extensively quoted and published report on this Sing Sing work covered much of the history of inoculation syphilis, but it made no mention of the studies in Guatemala.<sup>67</sup>

Why then does any of this work in Guatemala matter, besides the arcane history of Cutler's links to Terre Haute, Guatemala, Sing Sing and then Tuskegee, and our prurient and horrified sense of what they did without any individual permission? Do we need to have yet another awful story of the "bad old days" of medical research before the creation of institutional review boards that are presumed to protect human subjects? Does this suggest ways those who are concerned with policy toward subjects should rethink what happened in Tuskegee?

The Guatemala study matters for two reasons. First, it demonstrates the links between periphery and metropole in public health. There was traffic in

ideas, in practices, in justifications, and in the bodies of researchers that moved across borders.<sup>68</sup> Ways of treating subjects in one place, deceptions allowed in another, moved around and through the creation of a culture of research. It is not just public health practices, but also public health research, that crossed over from country to country.

Only by understanding this context can we understand the decisions made by the Public Health Service. While they had their qualms about what was being done in Guatemala, they allowed that work to continue for two years. Having made that decision, they might well have regarded the project in Alabama—which did not infect anyone—as relatively benign.

The story of the work in Guatemala also confirms that fact about non-infecting in the “Tuskegee” Study, since it shows the difficulty of infecting individuals with syphilis in a scientific project. The lengths that Cutler and his colleagues had to go to give the disease to the inmates of the asylum, prison and army barracks in Guatemala, and then later in less atrocious ways at Sing Sing, provides us with a way to say this is not what happened in Tuskegee. Surely, the survivors of the Study in Alabama would remember that this happened to them if there had been such injecting and abrading? In all the records (either in the federal archives or those at Tuskegee University) of aspirins, iron tonics, and pill jars shipped to Tuskegee there is no mention of money spent for rabbits, for laboratories to create the inoculums, or efforts to do this.

At the same time, the Guatemala story may make it even easier to imagine that the government doctors did infect men in Alabama. PHS researchers of the period were technically capable of infecting people with syphilis, even if doing so was more burdensome than the researchers wished. And they were morally

capable of infecting people with syphilis, for their faith in their cause allowed them to infect people with this dreadful disease without their consent or even knowledge—at least when those people lacked power and white skin. These facts so complicate the Tuskegee story that I deliberately omitted the Guatemala studies from my book *Examining Tuskegee*, lest they make it too hard to explain that the men in Alabama were *not* infected.

Policy makers often pick and choose differing historical accountings to justify the decisions they make. Historians have the luxury to wallow in context and knowable facts, while others make meaning, law and regulations from our work. The Study in Tuskegee is often told in a simple manner and frequently mis-remembered. The inoculation studies in Guatemala put the effort in Tuskegee in context but can also increase fear of medical research. For if the hue and cry has been to “remember Tuskegee” to justify control over medical research, we can only imagine what the sounds might be if these experiments in Guatemala are also in the portrait. As much as we can be squeamish and angry over what was being done in these studies, it forces us to consider how we tell these stories and the policy we make now.<sup>69</sup>

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<sup>1</sup> There is a debate, especially at Tuskegee University, over whether the Study should be called the Tuskegee Study or the United States Public Health Service Study of Untreated Syphilis in the Male Negro at Tuskegee to mesh the researchers who did the study with the its more formal title. Since it is primarily know as the Tuskegee Study, I use the term “Tuskegee” in quotes here or just refer to it as the Study.



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<sup>2</sup> Susan M. Reverby, *Examining Tuskegee: The Infamous Syphilis Study and its Legacy* (Chapel Hill: University of North Carolina Press, 2009), pp. 187-203.

<sup>3</sup> There was also a debate well into the 1950s over whether penicillin should be given to those in the late latent stage of the disease. The standard of care was to decide this on an individual basis. This was not done in the Study.

The issue of whether any of the wives/sexual partners of the men were treated is still controversial. The now available medical records (in the Southeast Regional National Archives in Morrow, Georgia) have the wives' treatment status blacked out to protect their privacy making it impossible to evaluate claims that there had been some treatment for wives found to be in the contagious stage. When the Study ended, the PHS agreed to treat 22 wives, 17 children and 2 grandchildren who tested positive for syphilis. For more on how this was determined, see Susan M. Reverby, "The 'Tuskegee' Syphilis Study as a 'Site of Memory,'" in Ralph Katz and Rueben Warren, eds. *The Search for the 'Legacy' of the U. S. Public Health Syphilis Study at Tuskegee* (Lanham, MD: Rowman and Littlefield, forthcoming).

<sup>4</sup> James H. Jones, *Bad Blood* (New York: Free Press, rev. ed., 1993); Susan M. Reverby, ed. *Tuskegee's Truths: Rethinking the Tuskegee Syphilis Study* (Chapel Hill: University of North Carolina Press, 2000); Reverby, *Examining Tuskegee*.

<sup>5</sup> For more details and a timeline of the Study, see <http://www.examiningtuskegee.com>. The Study was not a secret. More than a dozen research articles were published in varying medical journals about it.

<sup>6</sup> Alessandro Portelli, *The Death of Luigi Trastulli and other Stories* (Albany: SUNY Press, 1990), p. 2.

<sup>7</sup> Sociologist Tamotsu Shibutani, quoted in Patricia Turner and Gary Alan Fine, *Whispers on the Color Line: Rumor and Race in America* (Berkeley: University of California Press, 2004), pp. 58-59.

<sup>8</sup> Susan M. Reverby, "More than Fact and Fiction: Cultural Memory and the Tuskegee Syphilis Study," *Hastings Center Report* 31 (September-October 2001): 22-28.

<sup>9</sup> For various versions of this argument see, Thomas G. Benedek and Jonathan Erlen, "The Scientific Environment of the Tuskegee Study of Syphilis, 1920-1960," *Perspectives in Biology and Medicine* 45 (Autumn 1999): 1-30; Richard Shweder, "Tuskegee Re-Examined," Spiked online. January 8, 2004; Robert W. White, "Unraveling the Tuskegee Study of Untreated Syphilis," *Archives of Internal Medicine* 160 (March 13, 2000):585-98.

<sup>10</sup> Joan Sherwood, "Syphilization: Human Experimentation in the Search for a Syphilis Vaccine in the Nineteenth Century," *Journal of the History of Medicine* 54 (July 1999): 364-386 and Susan E. Lederer, *Subjected to Science* (Baltimore: Johns Hopkins University Press, 1995).

<sup>11</sup> Marcos Cueto, *The Value of Health: A History of the Pan American Health Organization* (Washington, D.C.: Pan American Health Organization, 2007) argues the immediate post war era was a major point in "inter-American" public health exchanges; see also Pan American Sanitary Bureau, *The Pan American Sanitary Bureau: A History of its Organization, Function and Activities* (Mexico City: PASB, 1946). On the expansion of social welfare during the liberalization of politics in Guatemala between World War II and before the CIA backed coup in

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1954, see Susanne Jonas, *The Battle for Guatemala* (Boulder: Westview Pres, 1991, pp. 21-40.

<sup>12</sup> Jan Ackerman, "Obituary: John Charles Cutler/Pioneer in Preventing Sexual Diseases," *Pittsburgh Post-Gazette*, February 12, 2003, <http://www.post-gazette.com/obituaries/20030212cutler0212p3.asp>, accessed February 24, 2003. For more on Cutler's career, see Reverby, *Examining Tuskegee*, pp. 144-151.

<sup>13</sup> Pubmed lists his name on 58 articles published between 1946 and 1995.

<sup>14</sup> "The Deadly Deception," NOVA. Videotape, PBS. Directed by Denise DiIanni. Boston: WGBH Educational Foundation Films for the Humanities and Sciences, 1993.

<sup>15</sup> Nancy Tomes, "Introduction: Imperial Medicine and Public Health," in *Colonial Crucible: Empire in the Making of the Modern American State*, eds. Alfred W. McCoy and Francisco A. Scarano (Madison: University of Wisconsin Press, 2009), pp. 273-276.

<sup>16</sup> Harry F. Dowling, *Fighting Infection: Conquests of the 20<sup>th</sup> Century* (Cambridge: Harvard University Press, 1977), pp. 125-157; John Parascandola, *Sex, Sin and Science* (New York: Praeger Press, 2008).

<sup>17</sup> Quoted in Reverby, *Examining Tuskegee*, p. 139. The left over questions about the biology of syphilis have resurfaced with those who think there is a connection between untreated syphilis and HIV/AIDS. See Harris L. Coulter *AIDS and Syphilis—The Hidden Link* (Berkeley: North Atlantic Books, 1993) and Coleman Jones, "Challenging Dissident Dogma: The Role of Infectious Co-Factors in AIDS,"

<http://breakfornews.com/aidsmyth./news/000529syphilisdebate.htm>, accessed March 19, 2010.

<sup>18</sup> John C. Cutler, "Current Concepts of Prophylaxis," *Bulletin of the New York Academy of Medicine* 52 (October 1976):866-896. For the counter view to the position on prophylaxis taken by Cutler and the PHS, see Joseph Earle Moore, *The Modern Treatment of Syphilis* (Springfield: Charles C. Thomas, 2<sup>nd</sup> edition, 1943), pp. 564-567. On tensions between the PHS doctors and Moore see John F. Mahoney to John C. Cutler, April 19, 1948, Box 1, Folder 13, John C. Cutler Papers, University Archives, University of Pittsburgh, Pittsburgh, PA, hereafter referred to as the Cutler Papers.

<sup>19</sup> Inoculum was both cultured and taken from the penis of one infected man and put into the penis of another. See John F. Mahoney et. al., "Experimental Gonococcal Urethritis in Human Volunteers," *American Journal of Syphilis, Gonorrhoea and Venereal Diseases* 30 (January 1946): 1-39. For more on the policy debate over the Terre Haute research, see Harry M. Marks, *The Progress of Experiment* (New York: Cambridge University Press, 1997), pp. 100-105. On a revived interest in prison research see Institute of Medicine, *Ethical Considerations for Research Involving Prisoners* (Washington, D.C.: Institute of Medicine, 2006); Barron H. Lerner, "Subjects or Objects? Prisoners and Human Experimentation," *New England Journal of Medicine* 356 (May 3, 2007): 1806-07.

<sup>20</sup> Jeanne L. Brand, "The U.S. Public Health Service and International Health," *Bulletin of the History of Medicine* 63 (Winter 1989), p. 582-583.

<sup>21</sup> Hugh S. Cumming, who had been the Surgeon General when the "Tuskegee" Study began, served as the director of the Pan American Sanitary Bureau from 1936 (when he left the PHS) to 1947, see Ralph Chester Williams, *The United*

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*States Public Health Service 1798 to 1950* (Washington, D.C. : Commissioned Officers Association of the U.S. P.H.S., 1951), p. 446.

<sup>22</sup> Marcos Cueto, "Introduction," in *Missionaries of Science: The Rockefeller Foundation and Latin America* (Bloomington: Indiana University Press, 1994), p. xiii.

<sup>23</sup> See Jonas, *The Battle for Guatemala* (Boulder: Westview Press, 1991); Stephen Kinzer and Stephen Schlesinger, *Bitter Fruit: The Story of the American Coup in Guatemala* (Cambridge: Harvard University Press, 1999); David McBride, *Missions for Science* (New Brunswick: Rutgers University Press, 2002).

<sup>24</sup> George Cheever Shattuck, "Syphilis and Yaws in Guatemala," in *A Medical Survey of the Republic of Guatemala*, ed. George Cheever Shattuck (Washington: Carnegie Institution of Washington, 1938), p. 142. Shattuck also summarizes medical beliefs about racial differences in the virility and existence of syphilis, see "Appendix B, "The Clinical Case of Syphilis in Various Races," pp. 153-156; see also George Cheever Shattuck, "Lesions of Syphilis in American Indians," *American Journal of Tropical Medicine* 18 (1938): 577-586.

On the use of race to matter and not matter, see Reverby, *Examining Tuskegee*. See also Chester North Frazier and Li Hung-Chiung, *Racial Variations in Immunity to Syphilis: A Study of the Disease in the Chinese, White and Negro Races* (Chicago: University of Chicago Press, 1948).

<sup>25</sup> "Untitled Report," February 24, 1954, Folder 1, Box 1, Cutler Papers.

<sup>26</sup> *Ibid.* p. 2 and Sherwood, "Syphilization."

<sup>27</sup> On the search for a better prophylactic, see R. C. Arnold and John C. Cutler, "Experimental Studies to Develop Local Prophylactic Agents Against Syphilis," *British Journal of Venereal Diseases* 32 (1956): 34-36. For directions on how to use a World War II pro-kit if infection was suspected, see <http://med-dept.com/vd.php>, accessed March 23, 2010.

<sup>28</sup> "Untitled Report," p. 6.

<sup>29</sup> "Untitled Report," p. 7.

<sup>30</sup> John C. Cutler to R.C. Arnold, June 5, 1947, Box 1, Folder 13, Cutler Papers. All correspondence in this folder unless otherwise noted.

<sup>31</sup> Elliott L. Harvlow to John M. Mahoney, June 30, 1947.

<sup>32</sup> Sacha Levitan et. al., "Clinical and Serologic Studies with Reference to Syphilis in Guatemala, Central America," *American Journal of Syphilis, Gonorrhea, and Venereal Diseases* 36 (July 1952): 379.

<sup>33</sup> Cutler believed that widespread liver disease in Guatemala due to malnutrition might also affect the tests.

<sup>34</sup> "Untitled Report," p. 16.

<sup>35</sup> *Ibid.*, p. 5 and Levitan, et.al., "Clinical and Serologic Studies," p. 379.

<sup>36</sup> Levitan, et.al., "Clinical and Serologic Studies," p. 387. They argued that "significantly higher percentages of positive and doubtful reactions were obtained from Kahn and Mazzini tests than with the Kolmer test and the VDRL slide test." Today, syphilis serological diagnosis requires a reactive nontreponemal test confirmed with a treponemal test.

<sup>37</sup> "Untitled Report," p. 24

<sup>38</sup> *Ibid.* p. 25.

<sup>39</sup> *Ibid.*, p. 32.

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- <sup>40</sup> "Part II Final Syphilis Report" discussion of the various strains of the disease used, p. 1-5, Box 1, Folder 2, Cutler Papers.
- <sup>41</sup> "Untitled Report," p. 48. See also instructions from R.C. Arnold to Cutler, July 21, 1947. On the history of various kinds of inoculation techniques, see Harold J. Magnuson et. al, "Inoculation Syphilis in Human Volunteers," *Medicine* 35 (February 1956): 33-82. On the difference with gonorrhea inoculation, see Mahoney et. al. , "Experimental Gonococcic Urethritis in Human Volunteers." Cutler was a co-author on both of these articles. Prison studies seem to use the term "human volunteers" in their titles.
- <sup>42</sup> Cutler to Mahoney, December 27, 1947
- <sup>43</sup> Cutler to Arnold, June 5, 1947.
- <sup>44</sup> Cutler to Arnold, June 27, 1947.
- <sup>45</sup> Saul Benison, *Tom Rivers: Reflections on a Life in Medicine and Science, An Oral History Memoir prepared by Saul Benison* (Cambridge: The M.I.T. Press, 1967), p.187.
- <sup>46</sup> John C. Cutler, "An Experimental Resurvey of the Basic Factors Concerned in Prophylaxis in Syphilis," Unpublished typescript, Box 1, Folder 9, Cutler Papers.
- <sup>47</sup> "Part III Final Syphilis Report," p.25, Box 1, Folder 3, Cutler Papers.
- <sup>48</sup> "Untitled Report," pp. 34-39.
- <sup>49</sup> Allan M. Brandt, *No Magic Bullet* (New York: Oxford, 1987, 1993). By 1950, the VDRL stopped all research on chemical prophylaxis, see John C. Cutler, "Current Concepts of Prophylaxis," *Bulletin of the New York Academy of Medicine* 52 (October 1976): 886-896.
- <sup>50</sup> Mahoney to Cutler, November 18, 1946; Cutler to Mahoney, November 30, 1946; Mahoney to Cutler, December 18, 1946.
- <sup>51</sup> Cutler to Mahoney, September 18, 1947.
- <sup>52</sup> Susan E. Lederer , *Subjected to Science* (Baltimore: Johns Hopkins University Press, 1995, pp 82-87 on Hideyo Noguchi's controversial syphilis experiments at the Rockefeller Institute in New York in 1911.
- <sup>53</sup> John F. Mahoney to John C. Cutler, October 15, 1946.
- <sup>54</sup> Mahoney to Cutler, May 5, 1947. Eagle was then working at the National Cancer Institute and this may have been part of a turf battle with the PHS. There is no evidence that Eagle ever participated in the Guatemala work.
- <sup>55</sup> Mahoney to Cutler, August 11, 1987. Mahoney concluded: "It is becoming obvious also that experimental infection cannot be produced with sufficient frequency to assure an adequate background for the study of prophylaxis."
- <sup>56</sup> Mahoney to Cutler, September 8, 1947.
- <sup>57</sup> Jussi Niemela, "What Puts the 'Yuck' in the 'Yuck Factor,'" *Bioethics*, online 25 February 2010, <http://www3.interscience.wiley.com/journal/123303185/abstract?CRETRY=1&SRETRY=0>, accessed March 25, 2010.
- <sup>58</sup> R.C. Arnold to Cutler, April 19, 1948, Box 1, Folder 17, Cutler Papers.
- <sup>59</sup> The National Research Council, established in 1916, oversees scientific research policy for the U.S. government and had a subcommittee of the Committee on Medical Research during World War II specifically focused on venereal disease research, see Marks, *The Progress of Experiment*, pp. 100-105.
- <sup>60</sup> G. Robert Coatney to Cutler, February 17, 1947, Box 1, Folder 17, Cutler Papers.

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<sup>61</sup> Cutler to Mahoney, May 17, 1947, Box 1, Folder 11.

<sup>62</sup> Mahoney to Cutler, June 30, 1947. The Doctors' Trial at Nuremberg was taking place between December 9, 1946 and August 20, 1947, although neither Mahoney nor Cutler mentioned it in their correspondence.

<sup>63</sup> Mahoney to Cutler, September 8, 1947, Box 1, Folder 13.

<sup>64</sup> Arnold to Cutler, July 30, 1947, Box 1, Folder 11.

<sup>65</sup> Sacha Levitan et. al, "Clinical and Serologic Studies with Reference to Syphilis in Guatemala Central America I," *American Journal of Syphilis, Gonorrhoea, and Venereal Diseases* 36 (July 1952): 379-87; John C. Cutler et. al., "Studies on the Comparative Behavior of Various Serologic Tests for Syphilis II," *ibid.* 36 (November 1952): 533-44; Joseph Portnoy et. al, "Clinical and Serologic Studies with Reference to Syphilis in Guatemala, Central American III," *ibid.* 36 (November 1952): 566-70.

<sup>66</sup> Juan Funes et. al, "Serologic and Clinical Studies in Syphilis in Guatemala, Central America, II," *Boletin de la Oficina Sanitaria Panamericana* 34 (January 1953): 14-18;

<sup>67</sup> Magnuson et.al, "Inoculation Syphilis." One of the other physicians on this project was Sidney Olansky, who had directed the work in Tuskegee in the 1950s. For more on Olansky and Cutler, see Reverby, *Examining Tuskegee*.

<sup>68</sup> See Warwick Anderson, "Pacific Crossings: Imperial Logics in United States' Public Health Programs," in *Colonial Crucible*, pp. 277-287.

<sup>69</sup> The issue of human subject protection is even more relevant now as the percentage of foreign trials for drugs in the United States has become even more common. See Gardiner Harris, "Concern over Foreign Trials for Drugs Sold in U.S." *New York Times*, June 21, 2010, p. A14; Adriana Petryna, *When Experiments Travel: Clinical Trials and the Global Search for Human Subjects* (Princeton: Princeton University Press, 2009).