CDC Summary of Findings from the U.S. Public Health Service Sexually Transmitted Disease (STD) Inoculation Study of 1946-1948, Based on Review of Archived Papers of John Cutler, MD, at the University of Pittsburgh

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Summary

From 1946-48, the U.S. Public Health Service (USPHS) Venereal Disease Research Laboratory (VDRL) and the Pan American Sanitary Bureau collaborated with several government agencies in Guatemala on U.S. National Institutes of Health-funded studies involving deliberate exposure of human subjects with bacteria that cause sexually transmitted diseases (STD). Guatemalan partners included the Guatemalan Ministry of Health, the National Army of the Revolution, the National Mental Health Hospital, and the Ministry of Justice. Studies were conducted under the on-site direction of John C. Cutler, MD in Guatemala City, under the supervision of R.C. Arnold MD and John F. Mahoney, MD of the USPHS VDRL in Staten Island, New York; the primary local collaborator was Dr. Juan Funes, chief of the VD control division of the Guatemalan Sanidad Publica.

The work by Dr. Cutler and VDRL colleagues was recently brought to light by Professor. Susan Reverby of Wellesley College as a result of archival work conducted as part of the research of her 2009 book on PHS syphilis studies, *Examining Tuskegee*. Her article on the STD Inoculation studies is scheduled to be published in the Journal of Policy Studies in January 2011 and will be available on her departmental homepage in October 2010 (www.wellesley.edu/WomensSt/fac_reverby.html).

Upon learning of Professor Reverby's work, staff from the Centers for Disease Control and Prevention (CDC) conducted a review of materials in the papers of John Cutler, archived at the University of Pittsburgh, including several summary reports, experimental logs, correspondence between Dr. Cutler and professional colleagues, and subject-specific records. The findings from this review are consistent with the observations to be published in the paper by Dr. Reverby and are summarized as follows.

According to materials in the archives, the primary purpose of the studies was to develop human models of transmission of *Treponema pallidum,* the bacteria that causes syphilis, by sexual transmission and cutaneous and mucous membrane inoculation in order to assess effectiveness of potential chemoprophylactic regimens. Additional studies were conducted to assess potential for re-infection of persons with untreated latent syphilis or of those with recent treatment of syphilis with penicillin; to compare performance of various serologic tests for syphilis; and to develop human models of transmission and chemoprophylaxis of the agents of gonorrhea (*Neisseria gonorrhoeae)* and chancroid *(Hemophilus ducreyi)*.

Subjects for the transmission studies included female commercial sex workers (CSWs), prisoners in the national penitentiary, patients in the national mental hospital, and soldiers. These subjects were also involved in comparative serologic studies. Transmission studies initially included sexual exposure of prisoners to female CSWs experimentally infected with either syphilis or gonorrhea. Later, subjects underwent direct inoculation, primarily of skin and mucous membranes, by viable *T. pallidum. N. gonorrhoeae, and H. ducreyi.* The design and conduct of the studies was unethical in many respects, including deliberate exposure of subjects to known serious health threats, lack of knowledge of and consent for experimental procedures by study subjects, and the use of highly vulnerable populations.

According to a “Syphilis Summary Report” and experimental logs in the archives, syphilis studies included CSWs, prisoners, and patients in the mental hospital. In the series of syphilis studies, a total of 696 subjects of individual experiments (some representing the same patients involved in several experiments) were exposed to infection (by sexual contact or inoculation). Of these, 427 (61%) were judged to be infected, of whom 369 (86%) received what was considered to be “adequate treatment” with injections of penicillin (defined by the investigators as $\geq$ 3.4 million units).

Gonorrhea studies included CSWs, prisoners, soldiers, and mental hospital patients. In the series of gonorrhea studies, a total of 772 subjects of individual experiments (some apparently representing the same patients involved in several experiments) were exposed to infection (by sexual contact or inoculation). Of these, a summary report and

experimental logs indicate that 234 (30%) were infected, 233 (99.5%) of whom were stated to have received treatment with injections of penicillin (300,000 units).

Chancroid studies included soldiers and mental hospital patients. A total of 142 subjects were exposed to infection by inoculation. Of these, a summary report and experimental logs indicate that 138 (97%) were infected, 129 (93%) of whom were stated to have received treatment with sulfathiazole (1 gram PO per day for 5 days).

To supplement findings in the “Syphilis Summary Report” and experimental logs, a detailed review of subject-specific records for the syphilis inoculation studies was carried out for persons involved in the majority of the syphilis experiments, allowing unduplication of subjects involved in multiple experiments and including some subjects who may not have been included in the “Syphilis Summary Report”. This review included subject-specific records from 532 persons, 497 (93%) of whom were inoculated with infectious syphilis. Of the 497, prescription of adequate therapy with penicillin ($\geq$ 3.4 million units) could be documented for 332 (67%). Based on laboratory assessment, 433 (87%) could be considered to have evidence of syphilis; of these, adequate penicillin therapy was prescribed for 331 (76%), although completion of therapy was documented for only 85 (26%). Over the course of observation, 71 subjects were noted to have died, including one who developed fatal status epilepticus during penicillin therapy, although the records do not allow determination of the relationship of the deaths to study procedures. There was no systematic description of other adverse events arising during the study or follow-up observation period.

The study appears to have ended in 1948, although some follow-up laboratory testing and patient observation continued until the early 1950s. There is no indication that results of the STD inoculation experiments were ever published in the scientific literature or another forum.