

History of U.S. Military Contributions to the Study of Sexually Transmitted Diseases

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Sexually transmitted diseases have posed a threat to military service members throughout history. Among these diseases, syphilis, gonorrhea, and human immunodeficiency virus infections have accounted for the most significant morbidity and mortality rates in the U.S. military. In response, military researchers have made significant contributions to the treatment and prevention of these diseases. We review the impact of these diseases through the history of the U.S. Armed Forces and review selected sexually transmitted disease-oriented publications of U.S. military researchers.

Introduction

Of the sexually transmitted diseases (STDs), three distinguish themselves as primary causes of morbidity and death among U.S. service members, namely, gonorrhea, syphilis, and human immunodeficiency virus (HIV). The first two, gonorrhea and syphilis, were significant disease threats before the availability of penicillin in the middle 1940s.¹ Medical records from the Revolutionary War indicate that these STDs had a significant impact in terms of lost person-days among members of the Continental Army.² In World War I, the Army lost nearly 7 million person-days and discharged more than 10,000 men because of STDs. Only the great influenza pandemic of 1918–1919 accounted for more loss of duty during that war.¹ The STDs remained a significant threat in the early years of World War II, prompting the War Department to embark on a massive educational and prophylactic campaign.³ Numerous posters were produced, warning soldiers and sailors of the dangers of excessively amorous behavior (Fig. 1). Today, gonorrhea and syphilis rarely cause significant morbidity or lost duty time.⁴ HIV, however, represents a grave threat to infected service members. At best, career options and overseas assignments are limited. At worst, severe illness and death are ever-present threats from this treatable but incurable disease. We review the history of these three diseases among members of the U.S. Armed Forces, as well as the contributions of military researchers to the treatment and control of these afflictions.

Gonorrhea

Neisseria gonorrhoea is a common cause of urethritis and cervicitis among young adults worldwide. If left untreated, it is

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capable of causing significant morbidity, including pelvic inflammatory disease, sterility, and disseminated infection. More than 600,000 new infections occur annually in the United States, and drug resistance is increasingly a problem.⁵

U.S. Military Significance

Gonorrhea caused significant numbers of lost person-days, disabilities, and even deaths before penicillin became available in the middle 1940s.¹ Today, it has little impact on operational readiness other than to signify by its presence a higher level of risk-taking behavior by the sufferer.⁴ The first estimates of gonorrhea rates among U.S. service members are from the Civil War. In a 2-year period, the Union Army documented more than 100,000 cases of gonorrhea. The admission rate for gonorrhea during that war peaked at 215 cases per 1,000 person-years (PY).² Gonorrhea rates again surged in later wars, particularly those in east and southeast Asia. In the Korean War, gonorrhea accounted for three-fourths of all STD diagnoses. Gonorrhea attack rates in some divisions reached 500 cases per 1,000 PY.⁶ The years following the end of the Korean War saw stubbornly high gonorrhea rates among troops stationed in the Far East. In 1963, troops in Vietnam were experiencing more than 300 cases of gonorrhea per 1,000 PY, and troops in Thailand contracted more than 500 cases per 1,000 PY. The concurrent rate among stateside troops was 26 cases per 1,000 PY.¹ Today gonorrhea remains a problem among U.S. service members, primarily during periods of overseas duty. Fortunately, rates among stateside troops are similar to those of their age- and gender-matched civilian counterparts. A recent study of soldiers at Fort Bragg, North Carolina, reported rates of approximately 5 cases per 1,000 PY, at or below the corresponding age-matched rates for local civilians and the nation at large.⁷

U.S. Military Contributions

Just before and during the early years of World War II, before penicillin was generally available, gonorrhea control research focused on prophylaxis after exposures. In 1943, U.S. Army CPT James Loveless and COL William Denton published a report on the successful use of sulfathiazole for postexposure prophylaxis following sexual contact. Untreated units experienced attack rates as high as 325 cases per 1,000 PY in that study.⁸ Later in the war, when penicillin was available in larger quantities, U.S. Army investigators published the first large-scale trial of penicillin treatment for gonorrhea. Led by LTC Thomas Sternberg and COL Thomas Turner, the investigators studied 1,686 patients with sulfonamide-resistant gonorrhea. They achieved a 92.5% cure rate using total penicillin doses of 160,000 units or less.⁹ In an unpublished trial conducted during the Korean War, penicillin prophylaxis was given to troops before liberty periods,



Fig. 1. Venereal disease prevention poster, ca. 1940 (from the National Library of Medicine, History of Medicine Collection; this image is in the public domain).

in an attempt to reduce gonorrhea morbidity. Rates decreased from 376 cases per 1,000 PY to 0 cases per 1,000 PY in one unit and from 1,228 cases per 1,000 PY to 55 cases per 1,000 PY in another. Following on this success, penicillin prophylaxis was authorized for general use, although with many restrictions. The few units that adopted this approach saw decreases in their STD rates.⁶

Military researchers during the Vietnam era noted the concerning rise of gonococcal resistance to penicillin therapy, documenting the ever-increasing doses of penicillin required to achieve cure. While serving as a lieutenant in the U.S. Navy, King K. Holmes conducted several studies of soldiers with urethritis in the Far East Command. Two studies documented the emergence of penicillin resistance and offered alternative treatment options.^{10,11} Another study provided important evidence supporting the role of *Mycoplasma*-like organisms as the cause of a "postgonococcal urethritis syndrome"; the responsiveness of this condition to tetracycline was also noted.¹² One of the more intriguing studies examined the per-contact risk of men acquiring gonorrhea from an infected woman, noted to be approximately 1 in 5.¹³ In addition, Holmes' contributions to the epidemiology and management of gonococcal infection were revolutionary. His descriptions of asymptomatic gonococcal infection and disseminated gonococcal infection remain standards today.^{14,15}

Another line of research at that time investigated the useful-

ness of vaccines as a means of prevention. Under the direction of COL (retired) Edmund Tramont, a vaccine directed against the gonococcal pilus was shown to produce measurable genital mucosal antibody, as well as providing protection from infection with a homologous strain.^{16,17} Unfortunately, the vaccine was not found to be effective in a larger field trial conducted among troops stationed in Korea.¹⁸

Summary and Key U.S. Military Contributions

War and deployments have always placed soldiers at risk for contracting gonorrhea. U.S. military researchers have made important contributions to the understanding and treatment of *N. gonorrhea* infections. The key U.S. military contributions include (1) the first successful use of antibiotic prophylaxis to prevent gonorrhea, (2) the first large-scale trial of penicillin for gonorrhea treatment, (3) quantifying the per-contact risk of gonorrhea acquisition, (4) describing the clinical findings for disseminated gonorrhea infection, and (5) investigating novel vaccine candidates to prevent gonorrhea.

Syphilis

Syphilis, caused by the spirochete *Treponema pallidum*, is another STD that can cause significant morbidity and death among untreated patients. It is capable of causing lifelong infection that can lead to significant disfigurement, as well as cardiac and neurological complications.⁵ Syphilis was the fourth leading cause of death in the United States before World War II, behind only tuberculosis, pneumonia, and cancer.¹⁹

U.S. Military Significance

Syphilis had a large impact on the U. S. military from its very beginning. In 1776, the Swedish physician Van Swieten wrote *The Diseases Incident to Armies with the Method of Cure*, which might have been the first manual for Army physicians because it carried the subtitle "Published, for Use of Military, and Naval Surgeons in America." In this text, "lues venera," ever the great mimicker, is described:²⁰

Small ulcers appearing at the extremity of the penis . . . are called venereal shancres: if the nervous papillae of the genital parts form little elevations, like warts, they are called venereal veruccae; if the internal superficies of the urethra are affected, there arises a difficulty and pain in making water, named a strangury, and a running of a yellowish, greenish, or sometimes brownish matter, it is then called a gonorrhoea; if swellings in the groins, buboes.

When the virus, having gained the blood circulates with the humors, where-ever it stops, it produces evils of different kinds. . . . (p 101)²

Finding statistics specific to syphilis rates among service members before World War I is difficult, because rates of venereal diseases (largely syphilis and gonorrhea) were often lumped together in earlier reports. During World War I, the high rates of syphilis among draftees caused large numbers of men to be deferred.³ Among World War II draftees, the rates of syphilis varied by region, with a peak prevalence of 11.3 cases per 100 selectees from the southern Atlantic states and a low of 1.1 cases per 100 selectees from New England. Overall, the preva-

lence among selectees in 1942 was 4.5 cases per 100 men.¹⁹ During World War II, the estimated time lost because of morbidity, convalescence, and treatment of syphilis was 300 person-hours in 65 weeks.¹⁹ Stated more eloquently by Stokes and Ingraham, the loss in person-hours “depends on the man,” for “a screwy pilot (with syphilis of the brain, or taking ‘tablets’ for gonorrhea) can crash 400,000 person-hours of bomber in one motion.”¹⁹ The significance of syphilis as a threat to the military was much lower after World War II. As Gilbert and Greenberg wrote in their article on preventive medicine in Vietnam, “Syphilis cases have been reported, but they are relatively uncommon (p 781).”²¹

U.S. Military Contributions

The decline in syphilis rates can be attributed in part to the availability of penicillin. Although it was discovered in 1929, penicillin was not proven efficacious for syphilis treatment until 1943.²² Penicillin was not initially a cure-all. There were often shortages of the drug, and early treatment failures were noted. These failures occurred most frequently in the setting of neurosyphilis, for which higher doses of penicillin are necessary for cure. One of the first to suggest the use of higher-dose intravenous penicillin therapy for neurosyphilis was then U.S. Army LTC Edmund Tramont, in his description of two cases of persistent *Treponema pallidum* in the cerebrospinal fluid after standard penicillin therapy.²³ In that article, Dr. Tramont questioned the efficacy of then-current (1976) guidelines, which called for 1.2 million units of benzathine penicillin G given intramuscularly three times weekly for all late-stage syphilis, even neurosyphilis.²³ Over the years, the contributions to the management of syphilis by Dr. J.P. Sanford (Ret.) and U.S. Army COL Tramont (Ret.) have been invaluable. Dr. Sanford’s input on advisory committees regarding therapy for syphilis, and in particular neurosyphilis, was a driving force behind the institution of the current practice of using high-dose aqueous penicillin for this disease.

The use of penicillin, along with many other factors, eventually led to greater control of syphilis in the United States, such that the disease is no longer screened for among new recruits.²⁴ Evidence of the declining importance of syphilis as a major cause of STDs in the U.S. military was demonstrated in a study of the social aspects of STDs aboard a U.S. Navy destroyer. Conducted during a 7-month tour in the 1970s, that study, with a high rate (48%) of STD acquisition among the crew, reported only 2 syphilis cases of 210 total STD diagnoses.²⁵ A study by U.S. Navy CAPT Richard J. Thomas and colleagues in 2002 revealed the 1999 case rate of 3 cases per 100,000 PY to be an all-time low for U.S. sailors and Marines.²⁶ Although the rate has not reached the target of <0.4 cases per 100,000 noted in the Centers for Disease Control and Prevention 2005 National Plan to Eliminate Syphilis in the United States, it is similar to the U.S. civilian rate of 2.5 cases per 100,000 population reported by the Centers for Disease Control and Prevention in October 1999.²⁷

Summary and Key U.S. Military Contributions

Syphilis has not posed a significant threat to the U.S. military since World War II. U.S. military research in this area has consequently been limited in recent years. The key U.S. military

contributions include (1) identifying the need for more aggressive treatment of neurosyphilis, (2) constructing effective treatment guidelines, and (3) maintaining active surveillance efforts for soldiers at high risk.

HIV/Acquired Immunodeficiency Syndrome

Infection with HIV, the virus that causes acquired immunodeficiency syndrome (AIDS), is the most significant infectious disease threat in the world today. In January 2000, a National Intelligence Estimate by the Central Intelligence Agency identified HIV as a significant threat to global security (<http://www.cia.gov/cia/reports/nie/report/nie99-17d.html>). In February 2004, George Tenet, then director of the Central Intelligence Agency, referred to HIV as a “. . . global humanitarian crisis that also endangers social and political stability” in an address to the Senate Select Committee on Intelligence.²⁸

U.S. Military Significance

In 1984, an U.S. Army recruit fell ill shortly after vaccination against smallpox. He was diagnosed with cryptococcal meningitis and admitted to the Walter Reed Army Medical Center for further evaluation and treatment. HIV was isolated and a Western blot assay for HIV was positive, and the patient was diagnosed as having AIDS. Four weeks after his vaccination, he developed an ulcer at the vaccination site, quickly followed by multiple pustular lesions covering his lower extremities. Vaccinia virus was recovered from biopsy specimens of the lesions. The patient recovered from the generalized vaccinia after treatment with vaccinia immunoglobulin. Unfortunately, he died 18 months later from complications of AIDS.²⁹ This was the first recognized military HIV case but unfortunately far from the last.

In response to this case, the Department of Defense initiated force-wide HIV testing in October 1985. A policy was formulated whereby all recruits were tested upon entry into military service, with those testing positive being excluded from service. This was thought to be consistent with the standard practice of excluding many common chronic conditions, such as asthma and diabetes. Personnel testing positive when already on active duty were retained, their health permitting. The primary restrictions in place were prohibitions from overseas assignments and deployments. The rise of the HIV epidemic threatened the U.S. military’s policy of nonpunitive methods of STD control. Various proposals circulated in Congress, mandating separation and other administrative actions for HIV-infected service members. These measures were never enacted, and the original policies remain in place today, in close to their original form. Department of Defense Directive 6485.1 reaffirmed those principles in 1991 and remains in effect.

Rates of HIV infection steadily declined in the U.S. Army, Navy, and Air Force in the first several years of testing but now appear to be stable. The Army rates declined from 0.43 seroconversions per 1,000 PY in 1985 to 0.08 per 1,000 PY in 1999.³⁰ The seroconversion rate in the Navy was 0.69 per 1,000 PY in 1985, whereas the rate among Marines was 0.28 per 1,000 PY. These rates declined thereafter.³¹ Seroconversion rates among Air Force personnel fell from 0.19 per 1,000 PY in 1987 to 0.17 per 1,000 PY by 1990.³² The rate currently stands at approximately 0.08 per 1,000 PY. A total of 1,373 cases had been

diagnosed among U.S. Air Force personnel as of January 2004; fewer than 155 members remain on active duty, and 561 are deceased (B. Agan, unpublished data).

U.S. Military Contributions

Early in the epidemic, much productive research was performed at the various military treatment facilities caring for HIV-infected Army, Navy, Air Force, and Marine Corps personnel. The Henry M. Jackson Foundation for the Advancement of Military Medicine was established by Congress in 1983 and soon became an integral part of the military's HIV research efforts. The Henry M. Jackson Foundation for the Advancement of Military Medicine World Wide Web site (<http://hivresearch.org>) currently lists 276 HIV-related publications covering 1998–2002 alone, with an additional 143 publications from Wilford Hall Medical Center dating from 1986 to 2001. These publications cover many research areas, including basic science, epidemiology, clinical manifestations, natural history, therapeutics, and vaccines.

Some significant contributions include the publication in 1986 of the Walter Reed staging system, one of the first methods of predicting the course of disease among HIV-infected individuals.³³ Early studies conducted by Air Force investigators under the direction of Col Neil Boswell examined the natural history of new seroconverters, monitoring the declines in CD4⁺ cell counts and progression in Walter Reed stage with time.^{34,35}

Other research focused on identifying modes of HIV transmission and risk factors for HIV acquisition among U.S. troops. In 1986, military researchers published evidence supporting the then-controversial notion that HIV could be transmitted through heterosexual contact.³⁶ Contact with commercial sex workers (CSWs) was identified as a common risk factor among certain groups. In a study published in 1993, 42% of 1,744 sailors on one ship reported having sex with CSWs during liberty periods; this occurred on a 6-month sea tour around the Atlantic Ocean and Mediterranean Sea during peacetime.³⁷ Another study of deployed Marines revealed that 10% of 1,028 Marines deployed to the Pacific Ocean reported CSW contact during a 3-month period.³⁸ Armed Forces personnel stationed in the Continental United States tended to have lower rates of CSW contact, with only 5% of STD clinic attendees reporting sex with CSWs. Despite the lower frequency of CSW contact in that study, 63% of subjects had one or more high-risk partners (defined as partners at increased risk for HIV infection) in the preceding year.⁴ The global movement of U.S. Navy personnel broadens the variety of HIV strains to which service members are exposed. A study of Navy seroconverters reported cases of HIV subtype E, D, and A, acquired in Thailand, Kenya, and Uganda respectively.³⁹ A later publication covering all Department of Defense personnel found heterosexual contact with CSWs to be the primary risk factor for acquisition of non-B HIV subtypes.⁴⁰ These studies emphasize the importance of "bridge populations" in the spread of infectious diseases.

Aware that military members will continue to be placed in situations where STD acquisition risk is increased,^{37–39,41–43} military researchers have sought methods of reducing risk-taking behavior among U.S. troops. This has never been an easy prospect, with the difficulty being summed up nicely in 1972 by LTC Jerome Greenberg, then the U.S. Army Director of Health and Environment. He lamented that, "With regard to preventing ve-

neral disease in soldiers, we cannot even tell them how to cut their hair anymore, let alone change their sex habits" (p 1087).¹ A recent series of publications by U.S. Navy researchers demonstrated the effectiveness of a multicomponent educational and motivational approach with sailors and Marines. The percentage reporting high-risk sexual behaviors decreased significantly; unfortunately, no impact on the rate of STD acquisition was noted.^{42,44–46}

Vaccine trials conducted by U.S. Army researchers under the leadership of COL Edmund Tramont explored the use of a recombinant gp160 vaccine as a therapeutic vaccine among HIV-infected patients. The vaccine was able to induce cellular and humoral immune responses, although it had no effect on disease progression among the vaccinated individuals.^{47,48} Military-supported research in this field continues, with Phase III trials of combination vaccine products underway in Thailand.^{49,50} Finally, U.S. Air Force investigators, in collaboration with Veterans Affairs Health Care System researchers, have carried out high profile research into the genetic determinants of HIV infection and disease progression. These studies examined the roles of various chemokine receptors and their ligands (monocyte chemoattractant protein 1 and major intrinsic protein 1 α) in altering the resistance to HIV infection, as well as the progression of neurological and other complications.^{51,52}

Summary and Key U.S. Military Contributions

Military investigators have been extremely productive in HIV research in recent years. The active duty force continues to be exposed to high-risk situations, and new infections occur every year. Military researchers in collaboration with civilian agencies have made many important contributions. The key U.S. military contributions include (1) the Walter Reed staging system, (2) descriptions of the natural history of HIV disease, (3) early identification of heterosexual disease transmission, (4) identification of host genetic factors that affect disease progression, and (5) investigation of HIV vaccination strategies.

Conclusions

Throughout history, STDs have affected the health of U.S. service members. The primary threats have changed with time, as have the weapons we use to face them. Researchers in military medicine have contributed significantly to the body of knowledge in this field, in many cases pioneering novel treatment and prevention efforts and exploring the fundamental mechanisms of disease. The nature of military deployments, both combat related and noncombat related, will continue to place soldiers in situations where the risk of STD acquisition is high. The history of STDs in the military has largely focused on infections acquired by men while deployed. The expanding role of women in military service adds a new variable to this equation, the impact of which will be known only with time. Medical officers in the U.S. military must remain active in facing the STD problems of the present and must remain on alert to identify and combat future challenges. Researchers in the U.S. military medical services have been active in their efforts to mitigate the impact of sexually transmitted infections. Their findings have benefited military members as well as society at large. The key U.S. military contributions to the study of STDs include (1)

etiology of nongonococcal urethritis, (2) monitoring emerging drug resistance in gonococci, (3) quantifying transmissibility of gonorrhea, (4) penicillin treatment for gonorrhea, (5) treatment of neurosyphilis, (6) natural history of HIV infection, (7) genetic determinants of HIV infection and disease progression, (8) epidemiological evidence supporting heterosexual transmission of HIV, (9) behavioral interventions to reduce STD risk factors, and (10) ongoing HIV vaccine research.

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