Immunization to Protect the U.S. Armed Forces: Heritage, Current Practice, Prospects

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Immunization protects the personal health of United States military personnel and maintains their mission readiness. The immunization program of the U.S. Department of Defense (DoD) is broad-ranging, protecting the forces from an array of pathogenic threats. Because the active and reserve components of the U.S. DoD consist of over 2.2 million people at any given time, the program immunizes a significant percentage of the U.S. adult population.

This article updates and expounds on previous reviews of the U.S. military immunization program, (1-7) discussing historical perspectives, the rationale for current immunization policies, and future prospects. Military immunization requirements often exceed those provided to civilian adults, because of the travel and other occupational hazards confronted by soldiers, marines, sailors, airmen, and coast guardsmen. Military immunization requirements are quite similar for each of the five Armed Forces (i.e., Army, Marine Corps, Navy, Air Force, Coast Guard). The requirements and recommendations are described in a joint immunization regulation, (8) summarized in table 1.

Immunizations have both direct benefit to the recipient and indirect benefit to the people in the community the vaccinee resides in or works with (i.e., “herd immunity”). “Herd immunity” or “community immunity” results when a decreased number of susceptible people and the decreased excretion of infectious particles impairs disease transmission. In military settings, the indirect benefit takes on an additional dimension, insofar as an immunized service member is less likely to succumb to a disease that threatens his or her team’s mission. By staying healthy, the immunized service member helps other team members accomplish their mission and return home safely. Due to both direct and indirect benefits, most U.S. military immunizations are required, rather than voluntary. Figures 1 and 2 illustrate records used to document immunizations of troops during World War II.

Senior preventive-medicine officers from the five Armed Services develop vaccine recommendations for military trainees and other military personnel, with decisions made by the Army, Navy, and Air Force Surgeons General and the Coast Guard Director of Health & Safety. Immunization policies consider epidemic potential, exposure risk (e.g., travel, occupation), and the potential for contingency work in unsanitary conditions. During policy development, advice may be sought from the Armed Forces Epidemiological Board (AFEB), an expert advisory board of civilian physicians and scientists. (9, 10) Before the Food & Drug Administration (FDA) took its present dominant role in vaccine regulation in the mid-1970s, the AFEB’s cutting-edge expertise was pivotal in deciding immunization dosing schedules and vaccine composition.

Modern immunization policy development takes into account public-health recommendations published by the Centers for Disease Control and Prevention (CDC), in consultation with its Advisory Committee on Immunization Practices (ACIP). Recommendations, guidelines, and disease-surveillance information are also considered from other agencies and expert bodies, such as the National Vaccine Advisory Committee, the American Academy of Pediatrics, the American College of Physicians, the American College of Obstetricians and Gynecologists, the World Health Organization, and others. With respect to malicious infections and bioweapons, risk-assessment information is gathered from the Defense Intelligence Agency, the Armed Forces Medical Intelligence Center, the Department of Homeland Security and similar organizations.

Immunization to Protect the U.S. Armed Forces

A synopsis of vaccines commonly administered at various historical points to U.S. military personnel appears in table 2. (1-18) The U.S. military contributions to vaccine development are summarized in table 3.

The following sections, grouped categorically, review major vaccine-preventable infectious threats to military personnel. These reviews begin with smallpox, a disease that spans several of these categories during the last 230 years.

SMALLPOX

The first immunization program implemented for the U.S. military was variolation (i.e., variola inoculation) of trainees entering the Continental Army in 1777. (3, 11, 13, 16, 19-23) Impetus for this program began in fall 1775, as British forces expelled smallpox cases and recently variolated people from Boston, and sent them across siege lines maintained by the fledgling Continental Army. In the winter of 1775-76, up to half of the Continental Army task force advancing on Québec was ill with smallpox. The Americans suffered 5,500 smallpox casualties among their force of 10,000 colonial troops. Major General John Thomas, their commander, died of smallpox during the campaign, as did many other soldiers. Decimated, the U.S. forces lost the Battle of Québec and were obliged to retreat in May 1776. Arguably, the British colony of Canada was not incorporated into the fledgling United States because of this smallpox outbreak.

In response to the military defeat outside Québec, John Morgan, the Director General of the Army Hospital, along with his successor William Shippen, Jr., and Benjamin Rush (influential physician and signer of the Declaration of Independence), recommended to George Washington that the Continental Army be variolated. (16, 23) Variolation was an archaic and dangerous method of preventing smallpox with a 1 to 2% mortality risk, but the best method then available. Variolation involved applying smallpox-infected material, such as ground-up scabs, to an incision of the skin to induce immunity. Viral particles embedded in fibrin scab were felt to be less virulent than direct exposure to lesions or droplets.

Variolation had its roots in Africa and Asia. First introduced in England in 1719, the mortality from intentional variolation could reach as high as 12%, particularly if people were pretreated with bleeding and fasting. Further, variolated people could spread smallpox to others for several weeks after the procedure. Washington was reluctant to initiate such a drastic, unpredictable measure. Variolation was attended by rumors of serious complications. Respected leaders like Benjamin Franklin opposed the practice; Franklin later changed his view after his son died of smallpox. (19, 23)

At Morristown, New Jersey, in January 1777, Washington finally ordered a mandatory inoculation program for his troops (principally new recruits), if they had not survived smallpox infection earlier in life, because the lethal risk from infection (~16%) was judged far greater than from variolation (1 in 300). (16)

> “Should the disorder infect the Army in a natural way and rage with its usual virulence, we should have more to dread from it than from the sword of the enemy.” (22)

America’s Continental Army was thus the first army in the world to adopt an organized program requiring smallpox inoculation, with measurable reductions in both morbidity rates and mortality (to less than 1%). Within the British Army, variolation was voluntary. To prevent smallpox the disease from spreading via secondary contact with variolated troops, Washington and his medical leaders performed the procedure in “inoculation hospitals” and isolated the troops in vaccination huts. (11, 19, 23) For examples, recruits passing through Virginia to join the Army were inoculated at Alexandria. General Washington’s variolation policy enabled a fighting force strong enough to achieve the surrender of British units at Saratoga. Had variolation been adopted earlier, an American victory at Québec could have hastened the end of the Revolution. (3, 11, 16)

Variolation was later replaced by vaccination with cowpox virus. Edward Jenner's 1798 report that intentionally injecting the less virulent cowpox (now vaccinia) virus would cross-protect against variola virus represented a major advance in vaccine safety. (4, 13, 19) Jenner's success met stubborn resistance among some, related to safety and ethical concerns. But the value of vaccination was readily apparent and soon made its way across the Atlantic Ocean. For the War of 1812, the U.S. War Department ordered that vaccination be substituted for variolation to prevent smallpox. (11, 16) In 1848, the U.S. Navy did the same.

Smallpox vaccination was gradually, but incompletely, adopted among the civilian populace. But smallpox remained an endemic and sometimes epidemic disease in the United States and around the globe. During the American Civil War, use of smallpox vaccine expanded on both sides of the conflict, including in training camps. Nonetheless, an estimated 19,000 cases of smallpox occurred among the troops, with ~ 7,000 deaths. (4, 12, 16, 24, 25)

In France in 1869, an estimated 200,000 people died of smallpox. (19) During the Franco-Prussian War of 1870-71, the Prussian Army of 800,000 men revaccinated their personnel every 7 years. The Prussians suffered 8,463 cases of smallpox, with a case-fatality ratio of 5.4%. In contrast, the French Army was unvaccinated. They suffered 125,000 cases of smallpox, with a fatality rate if infected of 18.7%.

In the Spanish-American War of 1898, volunteer troops were vaccinated against smallpox as they mustered into service. More smallpox cases occurred among these volunteers than among the Regular Army. Most of the 825 smallpox admissions (258 fatal) occurred in the Philippine Islands during that conflict. (4, 12, 16, 19, 25)

Military training camps continued to administer smallpox vaccine during World War I. (26) There were 853 smallpox admissions (780 within the United States) with 14 deaths. In 1919, an American citizen named Charles Higgins sent an angry and lengthy manuscript to President Woodrow Wilson, pleading that he stop smallpox vaccination for Armed Forces, listing both true and erroneous risks of smallpox vaccination. (27) But vaccination continued through the decades, successfully, leading eventually to a global vaccination program that eradicated naturally occurring smallpox infection from the planet. (19)

The United States military conducted major smallpox vaccination programs during World War II, for its own personnel and for local populations at risk of smallpox. (14, 15, 26) Among U.S. troops, there were 115 smallpox cases (105 overseas). Cases were attributed to three main causes: Failure to vaccinate properly, an inadequate cold chain to keep the vaccine potent, and failure to read and interpret vaccination reactions properly. Additional cases occurred shortly after the war, accompanying large population movements returning to the Japanese home islands or returning to the Korean peninsula. Among the last Americans to contract smallpox were five Soldiers, one of whom died, during the 1953 smallpox outbreak amid the Korean War.

By the early 1970's, with smallpox not circulating within the United States, routine smallpox vaccination of civilians (especially children) was no longer practiced, because complications like eczema vaccinatum and encephalitis were not considered justified risks in the face of no disease threat. (19) US service members were routinely vaccinated against smallpox until 1984. (1, 28)

In 1984, routine military smallpox vaccinations were limited to new troops entering basic training. Between 1984 and 1990, smallpox vaccinations at basic training sites were intermittent, due to a shortage of vaccinia immune globulin, to treat certain adverse events after vaccination, pressure from civilian authorities (who perceived the variola threat as a weapon to be negligible), and the appearance of the novel clinical entity of HTLV-III infection (now called human immunodeficiency virus, HIV). (9) In March 1990, the Department of Defense "temporarily discontinued" smallpox vaccination of basic trainees, even though trainees were essentially in medical quarantine. (29) Military vaccination was limited to special circumstances, such as for laboratory workers exposed to other orthopox viruses.

This "temporary" policy seemed to be a permanent state of affairs, until the anthrax attacks along the eastern seaboard in fall 2001 heightened concerns about bioterrorism generally. President Bush announced a national smallpox vaccination program on December 13, 2002. (28)

In this plan, smallpox vaccinations resumed for medical and epidemic response teams, and for troops deployed to high-threat areas. Troops were included to protect them in case of a bioweapon attack and enable them to continue their missions. Two hundred years after Edward Jenner popularized the use of an orthopox virus to cross protect against variola, vaccinia vaccine was called into service again. The current program is described below, in the bioweapon-countermeasure section.

PROPHYLAXIS OF DISEASES RELATED TO POOR HYGIENE OR SANITATION

During military deployments to developing countries or military exercises, the risk of contracting endemic infections is a serious concern. Some of these infections may not be evident until the deployment is well underway or even after return to the United States, for infections with prolonged incubation periods. During actual conflict, sanitation is often compromised and wound and blood-borne infections become a greater hazard to military forces.

The science of vaccinology advanced slowly, so smallpox vaccine was the only vaccine available for nearly the whole century. A few troops may have received post-exposure prophylaxis against rabies using Pasteur's vaccine. (30) Endemic diseases that today can be prevented by immunization took a heavy toll on military rosters, despite aggressive efforts at promoting personal hygiene and maintaining proper sanitation in the camps. Measles, hepatitis, typhoid, dysentery, malaria, and typhus were significant causes of non-battle-related illnesses.

But by the 1890s, an awareness of the potential benefits of immunization was increasing. Beginning as early as the Spanish-American War or 1898, the U.S. Army established scientific advisory boards to address issues such as typhoid, yellow fever, malaria, dengue fever, pneumonia, and influenza. (2, 16, 25) These boards were crucial in the development of specific preventive strategies and research efforts in vaccine development.

Preventive medicine gained new prominence as a contributor to the war effort during World War I, but the lack of antibiotics or specific vaccines forced a reliance on passive immunization via antitoxins. Diphtheria antitoxin was an important form of therapy. (4) Antitoxins to treat gas gangrene (i.e., Clostridium perfringens or welchii and related organisms), botulism, and dysentery (i.e., Shigella dysenteriae or flexneri) provided some therapeutic value. (4, 7, 15) Antibiotics largely replaced these products by the end of World War II.

Typhoid fever

In 1898, the battleship USS Maine blew up in Havana harbor, leading to the Spanish-American War. Volunteer soldiers, their officers, and physicians marched to the trainee camps, where they began to get sick and die. Army Surgeon General George M. Sternberg appointed Major Walter Reed to lead an investigative team. Building on John Snow's observations on cholera in London, the team showed the cause to be typhoid fever, due to contamination of the water supply. During the war, America experienced 280 battle fatalities. But at the five main training camps, before getting anywhere near a battlefield, there were 20,738 cases of typhoid fever, 1,590 of them fatal. In the Army overall, there were an estimated 2,620 typhoid fever deaths. (1, 2, 3, 16, 25, 31-35)

During the late 1800s and early 1900s, scientists developed vaccines against infections such as typhoid fever, cholera, plague, and rabies. Almroth Wright developed a typhoid vaccine in Britain, based on the hypothesis that dead bacilli could evoke a protective antibody response. (36, 37) The British Army used early forms of typhoid vaccine during the Anglo-Boer War in southern Africa in 1899. Among 14,626 immunized British soldiers, there were 1,417 cases of typhoid fever and 163 deaths (11/1,000 soldiers). In contrast, among 313,618 unimmunized soldiers, there were 48,754 cases and 6,991 deaths (32/1,000). (38) Of the cases, 19,454 were invalided back to the British Isles for discharge with a medical pension. Lieutenant Colonel William Leishman continued this research in the United Kingdom, standardizing production methods and performing studies to

show by 1908 that two typhoid immunizations gave excellent protection.

Major Frederick Russell of the Army Medical School adapted British and German production methods to produce the inactivated whole-cell typhoid vaccine supply for the entire United States. The Army Medical School was the first school of preventive medicine and public health in the United States and is the forerunner of today's Walter Reed Army Institute of Research (WRAIR) and Uniformed Services University of Health Sciences. Voluntary immunization of some American soldiers against typhoid fever began in 1909. (4, 12, 13, 16, 39-41) In 1911, Army Chief of Staff Major General Leonard Wood (who began his Army career as a military physician) ordered mandatory typhoid immunization for a 15,000-man division, using Russell's vaccine. Wood also required that immunizations be recorded in medical records. Only two cases of typhoid fever occurred. A few months later, immunization became mandatory for all soldiers. The Navy adopted typhoid immunization as well.

With a vaccine to shield troops from typhoid bacteria during World War I, a mere ~ 2,000 cases of typhoid fever, with 227 deaths, were reported among 4.1 million Americans in uniform. (4, 12, 13, 42) The tragically high rates of typhoid morbidity and mortality during the Spanish-American War faded to nearly nothing by World War I. Had the typhoid incidence rates of 1898 been applied to the troops mobilized for World War I, there would have been 500,000 cases and over 50,000 deaths. (15, 32, 43)

Various vaccine combinations of typhoid, paratyphoid A, and paratyphoid B antigens were used during the 20th century. (4, 12, 42, 43) The trivalent vaccine was commonly known as TAB vaccine, triple vaccine, or enteric vaccine. Inactivated by heat and phenol, the vaccine contained whole-cell preparations of *Salmonella typhi, Salmonella paratyphi* (A), and *Salmonella schottmuelleri* (B). In 1916, the U.S. Army Medical School discovered paratyphoid A and B bacilli and developed a vaccine against them. But the paratyphoid components were of questionable efficacy. In the following decades, TAB vaccine was withdrawn, reintroduced, and then withdrawn again. In 1940, the triple TAB formulation was relicensed. Around 1945, paratyphoid A & B components were removed again from U.S. formulations. Typhoid fever affected 0.42 cases per thousand soldiers in World War I, but only 0.05 cases per thousand in World War II, due to expanded immunization.

Various typhoid vaccines were developed at WRAIR, notably the acetone-killed and dried (AKD) and heat-phenol (H-P) treated formulations. (3, 7, 44) The AFEB preferred the AKD vaccine for its clinical efficacy. (9) Today, clean, chlorinated water supplies (a technique developed in 1910 by Army Major (later BG) Carl R. Darnall) (16) and other public-health practices prevent typhoid bacteria from entering military training camps (and cities) in the United States. The risk for typhoid fever is encountered overseas, so that typhoid immunization is standard before overseas deployments, but not part of trainee immunization itself. Development of the typhoid Vi polysaccharide injectable vaccine and live attenuated typhoid vaccine capsules rendered obsolete the whole-cell typhoid vaccines, renowned for high degrees of injection-site pain and swelling, fever, and systemic reactions. (7, 45)

Tetanus

Traumatic injuries complicated by tetanus spores within wounds were a major cause of morbidity and mortality until World War I. Passive immunization with tetanus antitoxin was relatively effective. But it had a harsh side-effect profile, notably a systemic hypersensitivity reaction known as serum sickness, due to its equine protein content. In 1933, tetanus toxoid was licensed in the United States, but was adopted slowly for the civilian populace. Tetanus toxoid offered the ability to prevent tetanus, rather than treating it after a wound occurred. On the other hand, many more people needed to receive a prophylactic intervention, compared to a therapeutic one. Using active rather than passive immunization for tetanus was another example of immunization as a means of planning ahead to prevent disease. (4, 7, 12, 13, 43, 46)

The Army Surgeon General requested use of tetanus toxoid for all active-duty American troops in May 1940. (3, 4, 14, 15, 47, 48) Routine tetanus immunization was approved by the War Department in June 1941. This decision featured the adoption of a promising new technology that had not been widely used. A record of tetanus toxoid doses administered was stamped on Soldiers' identification tags (e.g, “T 41-42”), as well as in paper records. (14) The example in Figure 3 reflects tetanus immunizations in 1942 and 1944. Booster toxoid doses were routinely given before entering an overseas theater and following a wound. Many duplicative immunizations resulted when records were not forwarded with the troops upon deployment to a new theater. The incidence of local reactions after immunization increased when booster doses were administered at short intervals. The U.S. Navy tended to use alum-precipitated toxoid, which induced more persistent antibody concentrations, compared to the fluid toxoid used by the U.S. Army at that time. (49)

Only 12 cases of tetanus were reported throughout World War II, from all theaters of operations, despite more than 12 million Americans in uniform who incurred more than 2.7 million hospital admissions for wounds or injuries. (3, 4, 47) All 12 cases were in unimmunized or incompletely immunized troops.

Across the Atlantic, the German Army (the Wehrmacht) did not give tetanus toxoid to its troops, continuing to rely on now-obsolete tetanus antitoxin. (4) The Wehrmacht suffered high rates of morbidity and mortality from tetanus. In contrast, the German Air Force (the Luftwaffe) immunized its men with tetanus toxoid and suffered much less morbidity and mortality.

Today, tetanus-diphtheria (Td) toxoids are administered to all trainees upon entry into military service. The recently licensed tetanus-diphtheria-acellular pertussis (Tdap) vaccines will likely warrant switching to Tdap, to prevent prolonged cough illness among service members, and provide indirect benefit to service members’ children. (50, 51) Td (or soon Tdap) booster immunizations are given every 10 years to military members, consistent with ACIP recommendations. People who may not have received a basic immunizing series earlier in life receive a complete series.

Hepatitis A

During the second year of the Civil War, an estimated 5% of Union troops were jaundiced. During World War II, 180,000 troops developed infectious hepatitis (i.e., hepatitis A), principally in North Africa, Italy, the South Pacific, and post-war Germany. Within the Pusan perimeter during the Korean War, 4,000 Americans were hospitalized with hepatitis. (4, 14, 17, 52, 53)

Edwin Cohn, John Oncley, and colleagues at Harvard University isolated the gamma-globulin fraction of serum in 1944, under contract to the U.S. Navy. Their methods 6 and 9, featuring a cold-ethanol fractionation process, yielded immune globulin for intramuscular administration (IGIM, “gamma globulin”). Joseph Stokes, Jr., and John Neefe reported the utility of IGIM in reducing the incidence of hepatitis A in 1945. Clinicians primarily used this drug to prevent or mitigate measles, mumps, hepatitis A, and hepatitis B. (1, 2, 3, 6, 7, 9, 10, 46, 52-57) IGIM prevented post-transfusion hepatitis in battle casualties, if given promptly. (58) IGIM was routinely given to troops assigned to Korea or Vietnam in the 1960s. (9, 57, 59-62)

In 1985, COL Leonard Binn and colleagues tested a formalin-inactivated hepatitis A vaccine at WRAIR. They began a collaborative research program with SmithKline Beecham (SKB). Merck Vaccine Division also built on the work of WRAIR scientists in developing its hepatitis A vaccine. In 1991, LTC Bruce Innis and a team of WRAIR scientists began an efficacy trial of the SKB vaccine in Thai school children. In 1991, Werzberger and colleagues began an efficacy trial of Merck’s vaccine in upstate New York. (7, 53, 63, 64)

Hepatitis A prophylaxis was transformed in February 1995, with the U.S. licensing of SKB’s inactivated hepatitis A vaccines, rendering obsolete serial painful injections of IGIM into the buttocks. The FDA licensed Merck’s vaccine in 1996. With hepatitis A infection the most common vaccine-preventable infection among international travelers, (7, 10, 65, 66) a universal

immunization policy for U.S. military personnel was a logical step.

Hepatitis B

In 1942, infectious hepatitis and serum hepatitis were first clearly differentiated. This came about when some lots of yellow-fever vaccine were unknowingly manufactured with tainted serum albumin, added as a stabilizer (discussed below). We now know these two forms of liver disease to be caused by hepatitis A and hepatitis B viruses, respectively. (9, 52, 53, 67-69)

No immunologic means of preventing hepatitis B were available until the FDA licensed the first hepatitis B vaccine in 1981. IGIM was found to provide temporary prophylaxis against both hepatitis A and hepatitis B infections in troops assigned to Korea. (53, 57, 61)

Today, hepatitis B immunization policy for U.S. military personnel focuses on several cohorts at occupational risk (e.g., medical and mortuary affairs). Personnel assigned to the Korea peninsula or other high-risk areas since 1986 have been immunized, as have accessions since 2001. (9, 53, 70) Because of the vaccine's relatively high cost, hepatitis B vaccine initially was administered intradermally, but this route of administration fell out of favor nationally with several vaccines (e.g., hepatitis B, rabies), due in part to inconsistent injection technique and antibody response. (7, 71, 72)

Cholera

The first injectable cholera vaccines date back to the 1890s. The bacterial strains used in the U.S. were selected at the Army Medical School during World War II. (3) From the 1940s to the 1980s, injectable whole-cell cholera vaccine was given to alert units. But the vaccine fell into disfavor as cholera immunization ceased being a condition for passage of international borders, as well as the vaccine's tendency to evoke substantial injection-site and systemic reactions, modest efficacy (50% disease reduction), and short duration of protection (~ 6 months).

The AFEB recommended cessation of routine cholera immunization in 1973. (9) Emphasis on sanitation is now considered more important in a healthy adult military population than reliance on a vaccine with limited efficacy. Still, if supply or transport disruptions stranded an American military force in a cholera-endemic area, widespread disease outbreaks could occur. At present, the oral cholera vaccines developed under US Army contract by the University of Maryland and licensed in Europe and Canada are unlicensed in the United States. (7, 33, 73, 74)

PROPHYLAXIS OF CONTAGION & EPIDEMICS

Until 1990, loss of life due to non-traumatic causes had decimated more armies than bullets in American military campaigns. (16, 75) The Russo-Japanese war of 1904-05 was a notable exception. Military personnel encounter disease threats in several settings: during training, deployments, mobilization for war, and actual combat. During basic training, military accessions come from disparate locations with varying degrees of innate or naturally acquired immunity, are placed in relatively confined living quarters and subjected to a high degree of physical stress. As with college freshmen in dormitories, respiratory pathogens, in particular, can spread easily in this setting.

As sanitation and personal hygiene improved, airborne-transmitted infections (e.g., mumps, measles, meningococcal meningitis, influenza, pneumonia), were recognized as the leading causes of morbidity and mortality among trainees. New chemotherapeutic drugs, such as sulfonamides, became available in the 1920s, but the need for vaccines directed at primary prevention was obvious. As new and improved vaccines were developed, each was considered for its potential military value.

Influenza

During 1918-19, a worldwide outbreak of viral influenza killed 25 to 50 million people, over 1% of the world population. (3, 4, 6, 12, 13, 16, 43, 76-79) This pandemic caused the greatest loss of life from any cause in such a short period of time throughout history. More than 500,000 deaths occurred in the U.S. The global death toll was comparably staggering. The world-wide pandemic killed more Americans than the military death tolls of all of America's wars in the 20th century combined. Scientists tried a vaccine against Pfeiffer's bacillus (now called *Haemophilus influenzae*) in the mistaken belief that the epidemic had a bacterial cause, but the effort naturally failed to quell the tragedy. (80-82)

The first indication of the developing American outbreak came in March 1918 at Camp Funston, Kansas, near present-day Fort Riley. By April, cases appeared in most American cities as well as among the American Expeditionary Force under General John Pershing, helping the Allies repel the German Kaiser's army from France. The hospital commander at Camp Funston reported:

> "There are 1,440 minutes in a day. When I tell you there were 1,440 admissions in a day, you will realize the strain put on our Nursing and Medical force." (78)

During those first few months, the infection was incapacitating, but not very lethal. By August, however, virulence increased and people increasingly died. In response to the incapacitation and deaths, theaters, dance halls, bars, schools, and other places of public assembly were closed, including churches. Football games were cancelled and telephone booths were padlocked. The pandemic weakened German military forces perhaps more than Allied troops. U.S. Army statistics showed that 791,907 soldiers were admitted to hospital in the U.S. or France for influenza, and 24,664 of them died. (83) Overall, one in 67 American soldiers died of influenza or pneumonia in 1918. (4, 12, 43, 78, 79)

Remembering how the outbreak quickly sapped the fighting strength of American troops, the U.S. Army Surgeon General commissioned research to develop influenza vaccines in the 1940s, the first iterations of the vaccines we still use today. (1-4, 9, 12, 13, 84, 85) Double-blinded field trials began in U.S. service members, demonstrating as much as 80% efficacy. In 1943, the first influenza vaccine against types A and B infection was used. Subsequent military and civilian vaccines contained at least one type A and one type B component. In fall 1945 and spring 1946, all 7 million troops were immunized against influenza. Efficacy of all such vaccines was dependent on correlation of the vaccine's antigens with circulating viral types, but scientists did not yet fully appreciate the unceasing antigenic variation of influenza virus. The vaccine was not considered effective in the fall-winter 1947 season, because we now know it was mismatched antigenically. By the early 1950s, annual immunization for all military personnel was routine, a policy continued ever since. (3, 7, 9, 86-88)

Assessments of influenza vaccine containing various mineral-oil adjuvants in the late 1940s and 1950s were promising, but not pursued. Despite concerns about the safety of the adjuvanted vaccine, no prolonged morbidity or mortality effects were evident two decades after immunization. (3, 9, 89, 90)

Memories of the 1918-19 influenza pandemic arose again when an outbreak of severe respiratory illness occurred in a basic training camp at Fort Dix, New Jersey. Among 230 infected soldiers, 13 were severely ill, with one fatality in February 1976. (91-96) Laboratory analysis showed the influenza virus isolate to be one that had not circulated among humans for more than 50 years, and that was not matched in the contemporary influenza vaccine formulation. Scientifically designated A/New Jersey/76 (Hsw1N1), the public called it "swine flu." This finding set in motion a process that led to the National Influenza Immunization Program, which DoD participated in. (95, 96) In November 1976, several cases of Guillain-Barré syndrome (GBS), a demyelinating neuromuscular disorder, were reported from Minnesota. Nationwide, 532 cases (32 fatal) were reported among vaccinees. Epidemiologic investigation suggested an increased risk among civilian influenza vaccine recipients that year, (97-100) but not among military vaccine

recipients. (101)

One of the starkest modern examples of the importance of preventing influenza in military communities comes from the USS Arkansas, a cruiser sailing from its homeport in February 1996. (102) After influenza virus that did not match strains used for immunization entered the ship's spaces, 42% of the ship's company became ill. The rate of incapacitating illness was sufficient to cause the ship to cancel its training exercise and make an unscheduled return to the nearest port.

Over the decades, the benefits of influenza immunization have become more apparent for increasing sectors of the nation's population. Today, the most widely used vaccine in America is influenza vaccine, one of several vaccines developed through military research.

Today, all active-duty members and most personnel in the National Guard or military reserves are immunized annually, usually by the end of December. Basic trainees receive influenza vaccine through its empiric June-30 expiration date each year. The annually revised composition of the influenza vaccine is based on the prevalence of strains of influenza A and B likely to circulate, using the same vaccine formulation adopted for civilian personnel. To assist the global health community in selecting the most appropriate antigens for the annual influenza vaccine formulation, DoD sponsors an extensive, global, laboratory-based influenza surveillance program. (103)

Meningococcal disease

Meningococcal meningitis is a life-threatening bacterial infection that can spread rapidly in dense populations. It primarily is a disease of early childhood and then wanes as colonization in the gut and upper airways with related bacteria results in natural Immunity. A secondary peak of disease incidence occurs in early and late adolescence, especially when susceptible people come together, as in military training camps, colleges, and religious pilgrimages. (3) It occurs with low frequency, but a high case-fatality ratio. Survivors may suffer brain damage, learning disability, hearing loss, or loss of limbs. The disease occurred with disturbing frequency in military trainees in the 1960s. Antibiotic prophylaxis was used initially, but the *Neisseria meningitidis* organisms became increasingly drug resistant.

In 1966, a meningococcal research unit was organized at WRAIR. (2-4, 6, 7, 12, 13, 104-107) The first human tests of a vaccine to protect against disease caused by group C meningococci began in July 1967. In 1968, scientists led by Goldschneider, Gotschlich, and Artenstein at WRAIR developed a serogroup C vaccine that prevented disease and also reduced the bacterial carrier rate. This was the first modern polysaccharide vaccine. Large clinical trials were conducted in thousands of military trainees. Their team defined the humoral responses to the meningococcal organism and the fact that the subunit polysaccharide vaccine could stimulate protective immunity. Later, they developed its serogroup A counterpart vaccine.

A few years later, colleagues at the Institut Mérieux in France manufactured similar vaccines using the WRAIR formulation. (7, 12) The work of both teams permitted a massive response to meningococcal serogroup A epidemics that swept Finland and Saõ Paulo, Brazil. In 1973, the entire population of Finland, over 4 million people, was immunized against group A at a series of mass immunization clinics to control an epidemic. The Brazilian epidemic of 1974 produced 150,000 cases of meningococcal disease and 11,000 deaths. In one of the most dramatic mass immunization efforts ever, 100 million doses of serogroup A vaccine were administered during the Brazilian epidemic. These and successor vaccines are now used to prevent disease outbreaks among military trainees and in other settings. (2-4, 12, 107)

Widespread use of meningococcal A/C vaccine among U.S. military trainees began in 1971. Along with reducing trainee class sizes, immunization reduced the risk of fatal meningococcal disease during basic training. (2-4, 12, 107) Meningococcal immunization has been part of the core immunization requirement for new trainees ever since. Sanofi Pasteur's tetravalent vaccine against serogroups A, C, Y, and W-135 (*Menomune)* received a U.S. license in January 1978. (7) The military success with meningococcal immunization among repeated iterations of

newly assembled cohorts was cited when recognition of elevated rates of meningococcal disease among college freshman and dormitory residents led to calls for immunization in those populations since the late 1990s. (108)

Meningococcal immunization marked another advance in January 2005 when the FDA licensed Sanofi Pasteur's protein-conjugated meningococcal vaccine, *Menactra*. Its protein-conjugated characteristics may offer prolonged duration of immunity, compared to polysaccharide immunization. (7) Unfortunately, attempts to develop a serogroup B meningococcal vaccine have not yet been fruitful.

Adenoviruses

After World War II, adenovirus infections (particularly serotypes 4 and 7) were noted to infect up to 80% of military trainees and were linked with epidemic acute respiratory disease (ARD) outbreaks in training camps. (3, 109-118) Up to 60% of trainee ARD resulting in hospitalization was linked to adenovirus infections. Infections in seasoned military personnel were less frequent. Before widespread immunization of trainees, 600 to 800 acute respiratory-disease hospitalizations per week occurred at military basic-training sites in the northern United States in the early 1960s, disabling 40 to 50% of these closed communities. Adenovirus infection, which resembles influenza in clinical manifestations, represented the leading cause of military hospitalizations in the United States at that time. Hospitalization rates of 6 to 8% per week typically occurred during basic-training cycles.

In 1956, WRAIR developed formalin-inactivated vaccines against adenovirus types 4 and 7. (2-4, 6, 7, 12, 88, 109-119) Such vaccines were marketed by Parke-Davis as "common cold" vaccines from 1957 to 1965, with viral types 3, 4, and 7 represented in the vaccine. Maurice Hilleman's team at WRAIR demonstrated in 1958 that adenovirus vaccines of types 4, and 7 reduced adenovirus disease incidence by 60 to 90% among U.S. soldiers under the stressful and crowded conditions of basic training, with cross protection against type 3. A report estimated that the vaccine saved the Army about $5 million a year in 1973 dollars. (99)

Beginning in 1959, inactivated adenovirus and influenza virus antigens were combined in a Parke-Davis product known as *Resprogen*. (7) Several million doses were sold between 1959 and 1965. In retrospect, the need to make annual adjustments to influenza vaccine antigens made this combined product irrational. But the need to change influenza viral antigens annually was not fully recognized until the early to mid-1960s.

In 1963, viral seed lots for this vaccine were found to contain the oncogenic SV40 virus as well as SV40 genome in the adenovirus capsids. (31, 120-122) Safety concerns and lack of efficacy caused the product to be withdrawn from distribution. Several studies have shown no elevated risk of cancer in these vaccine recipients. The live types 4 and 7 adenoviruses used in the modern products have been shown not to be oncogenic. (123)

In 1964, clinical trials of live, attenuated type 4 vaccine began at WRAIR. (2-4, 6, 7, 12, 113, 114, 116-118, 124) Trials of type 7 begin in 1969 and type 21 in 1971. Type 7 adenovirus vaccine was added to the regimen given American military trainees in 1970. These vaccines were developed as oral tablets in the 1970s and licensed in July 1980. The tablets were given shortly after arrival at a basic training center, protecting within a few weeks after administration. (87) Adenovirus vaccines produced dramatic reductions in disease incidence. Immunization induces specific protective serum and secretory-intestinal antibodies, protecting against infection for at least 60 days and presumably longer.

By 1984, both vaccines were routinely administered as tablets to trainees at all basic-training camps year-round. Unfortunately, the manufacturer (Wyeth Laboratories) and DoD did not make capital improvements to the manufacturing facilities for these vaccines, and production ceased in 1996. (10) The last lots of these vaccines expired in 1998. Since then, disease outbreaks among trainee populations have recurred, including several deaths. (123, 125-128) A replacement manufacturing line for adenovirus type 4 and type 7 vaccines will be submitted for

regulatory review. (10, 129, 130)

Measles, Mumps, Rubella, Varicella

During the Revolutionary and Civil Wars, measles was one of the principle causes of death among troops. Measles and secondary pneumonias in 1917 led to 48,000 hospitalizations and 1 million lost work days, and represented 30% of all Army deaths. (43, 131, 132) During 1917 and 1918, mumps was a leading cause of days lost from active service by members of the American Expeditionary Force in Europe. (16, 43, 133) During World War II, measles, mumps, rubella, and varicella accounted for over 300,000 admissions to hospital or restrictions to quarters. (134-135) In 1961, Paul Parkman and colleagues at WRAIR were co-discoverers of the rubella virus, isolating the virus among trainees at Fort Dix. (3, 135) Even into the 1970s, measles and rubella caused a substantial number of hospitalizations and lost training time at basic training centers. (87)

Vaccines to prevent measles, mumps, and rubella were licensed in the U.S. between 1963 and 1969. The AFEB helped fund development of an attenuated measles vaccine. (136) For military trainees, rubella vaccine was adopted first, in 1972, with measles vaccine added in 1980, to immunize those who avoided infection as children. (9, 137, 138) Mumps outbreaks were less common than the other two diseases, so mumps immunization was not uniformly adopted until 1991. (10, 139) A varicella policy of screening and as-needed immunization was also adopted in 1991. (10) The FDA licensed varicella vaccine in 1995. Now that a large proportion of basic trainees enter military service immune to these infections, due to childhood immunization, the Services are testing for antibody and exempting those already immune. (10, 140-146)

Diphtheria

Diphtheria toxoid was first licensed in the United States in 1926 and was later combined with tetanus toxoid to simplify the task of injecting the two products. But diphtheria toxoid was known to cause substantial injection-site swelling if injected into someone already immune to diphtheria. So diphtheria immunization policy was complicated by whether or not to perform the Schick skin test to determine if an individual was immune (induration after injecting diphtheria toxin is considered a positive test, implying susceptibility). (7, 14, 147, 148)

Military clinicians noted the injection-site swelling that followed diphtheria toxoid administration in adults and developed a reduced-dose formulation. The work of Geoffrey Edsall and colleagues at the Great Lakes Naval Training Center in the 1950s demonstrated that this approach was comparably immunogenic, but with fewer injection-site symptoms. (3, 7, 149, 150) The practice of administering DT (full strengths of both diphtheria and tetanus toxoids) to children up to the seventh birthday and Td (full-strength tetanus and reduced-strength diphtheria toxoid) to older children and adults continues to this day. (7)

PROPHYLAXIS OF DISEASES WITH ECOLOGIC NICHES

Deployment vaccines include those vaccines administered to personnel sent to regions where the risk of contracting a specific endemic vaccine-preventable disease is increased. Deployment vaccines include typhoid, hepatitis B, meningococcal, yellow fever, Japanese encephalitis, and rabies. The first few were discussed above. Beyond its use in military basic training, meningococcal immunization may be required for specific assignments (e.g., personnel traveling to sub-Saharan Africa during the dry season (December to June)). (66)

Yellow fever

Yellow fever was a significant problem for U.S. troops throughout the southern United States in the 19th century. This infection was especially troublesome during the Spanish-American

War of 1898, particularly in Cuba. (2-4, 6, 12, 13, 16, 31, 151, 152) To investigate, Army Surgeon General Sternberg appointed another board of investigation. Walter Reed and his colleagues proved Carlos Finlay's hypothesis of transmission of the disease by mosquito. (153-157) The follow-up research ultimately led to the isolation of the virus. Separately, Max Thieler attenuated yellow-fever virus by serial cell culture passage in 1927. The resulting vaccine strain 17D is still used today for travelers to yellow fever-endemic areas of the world, including deployed military personnel.

During World War II, yellow fever was considered both a natural threat, with speculation about its use as a biologic weapon if adversaries could release infected mosquitoes. (158) As a result, a yellow-fever immunization program was instituted for selected personnel in the U.S. Armed Forces.

By April 1942, 7 million doses of the vaccine had been given. The program was complicated by reports of hepatitis in recipients. (2-4, 12, 54, 56, 68, 69) In March 1942, 100 cases of jaundice and hepatitis were noted at training camps in California, soon after yellow-fever immunization. Health authorities quickly realized that the diluent for yellow-fever vaccine contained human serum albumin that had not been heat treated. The albumin was contaminated with a previously unrecognized virus that caused hepatitis (i.e., hepatitis B virus). Immunizations ceased and the Rockefeller Foundation stopped producing the serum-containing product midway through 1942, until it could develop a serum-free formulation. By December 1942, over 50,000 cases of hepatitis B and 84 deaths followed some 2.5 million yellow-fever immunizations from certain lots. This accident helped reveal the differences between hepatitis A (then called "infectious hepatitis") and the newly recognized hepatitis B virus ("serum hepatitis"). This incident highlights the risks of using vaccines in large populations without preliminary safety testing, now required before licensure of any vaccine.

In 1985, follow-up studies interviewed and sero-screened 597 Army veterans from 1942. The authors concluded that hepatitis B virus caused the outbreak, that about 330,000 persons may have been infected, that the hepatitis B virus carrier state was a rare consequence, and that the outbreak induced hepatitis B-specific antibodies that appear to persist for life. (159) The small excess liver cancer mortality seen in a related cohort study and the results of a case-control study are consistent, nevertheless, with the now well-established etiological role of hepatitis B virus in liver cancer. (160)

In addition to the hepatitis-B issue, the yellow-fever vaccine of the 1940s was grown in eggs of chickens infected with avian leucosis virus. Evaluation identified no related harm in vaccine recipients. (161)

From the 1950s onward, yellow-fever immunization for adults proceeded with few problems, until recently. Yellow-fever vaccine is a live attenuated product given to personnel with assignments to yellow fever-endemic areas. As a general rule, all personnel assigned to Latin America or sub-Saharan Africa or with missions that may take them to these regions are immunized. But recent concerns about rare cases of yellow-fever vaccine-associated neurotropic disease raise questions about whether military forces should use the vaccine narrowly (i.e., focused on those traveling soon), or broadly (i.e., to those who may travel eventually, to minimize the number of immunizations given just before departure). Military policy makers, in concert with medical consultants, work to balance the two competing objectives. (10, 162) The goal is to optimize benefit and minimize risk for service members.

Japanese encephalitis

A Japanese encephalitis (JE) vaccine was produced in 1943 through efforts of Albert Sabin and colleagues in the Far Eastern theater, based on a Russian vaccine. JE vaccine was administered to a limited number of personnel in Japan (primarily Okinawa) in 1945 during an outbreak in the civilian population. (4, 12, 16, 163, 164) This vaccine was derived from virus-infected mouse brain.

By the 1980s, military, diplomatic, and travelers' need for a JE vaccine led to studies led by military scientists that permitted U.S. licensure of JE vaccine. (7, 165-168) The FDA licensed JE vaccine in 1992. Because of an uncommon risk of delayed-onset urticaria and angioedema, the vaccine's labeling recommends deferring travel for 7 to 10 days after immunization. Current military policy provides this vaccine to military members on assignments to areas with a high endemnicity of disease, primarily on Okinawa with extended field exposure and rural areas of Thailand. The manufacturer intends to cease production in mouse brains and transition to a cell-culture production process.

Rabies

Today, pre-exposure rabies vaccine is provided to selected troops who have missions to areas endemic for rabies and who may have an elevated risk of being bitten by a rabid animal. The rationale for immunization derives from a lack of ready access to definitive medical care if bitten. In addition, veterinarians, veterinary technicians, and those with animal-control responsibilities receive standard occupational pre-exposure immunization. Prophylaxis policies follow ACIP guidelines. (7, 30, 168, 169)

PROPHYLAXIS AGAINST BIOWEAPONS

Smallpox

The historic use of smallpox vaccine was addressed above. In December 2002, a national program of smallpox vaccination resumed, to counter the consequences of a malicious release of variola virus. (28) A smallpox outbreak would significantly affect military readiness. An outbreak would degrade combat-mission capability among vulnerable troops; stress military medical operations to maximum capacity; restrict military operations; limit transit of international boundaries; and divert military manpower for health care or crowd control.

In a remarkable example of mass individualized immunization, more than 400,000 service members deploying to southwest Asia were screened for smallpox immunization. (28) After a trial run at Walter Reed Army Medical Center, military clinics used standardized education materials, concise screening forms, bandages, and staff training to educate recipients about the idiosyncrasies of smallpox vaccination, identify contraindications (e.g., atopic dermatitis), safely administer the vaccine, and care for the vaccination site appropriately.

The accompanying prospective surveillance system identified an elevated risk of myopericarditis in the second week after primary smallpox vaccination, especially among young adult Caucasian men. (170-172) The military smallpox vaccination program continues, to preserve critical military capabilities in case of an attack, with over 1,020,000 people screened and over 940,000 people vaccinated between December 2002 and January 2006.

Anthrax

The intelligence community and civilian experts consistently rank anthrax spores as the number one threat from bioweapons. This ranking is due to the stability of spores, which can persist for decades despite environmental extremes. Anthrax spores can be easily dispersed, as seen in the multiple releases via mailed letters or packages on the U.S. eastern seaboard in fall 2001. (173, 174)

Early anthrax vaccines were developed at Fort Detrick, Maryland, by George Wright and colleagues. (175-180) Anthrax vaccine adsorbed was tested in a human field trial in the 1950s, demonstrating 92.5% reduction in disease incidence (cutaneous and inhalation cases combined), (181) and licensed in 1970. (182, 183) Subsequent inhalation challenges in nonhuman primates and rabbits showed greater than 95% protection against lethal challenge. A comprehensive review

by the National Academy of Sciences (NAS) affirmed the efficacy of anthrax vaccine adsorbed. (179)

An estimated 150,000 American troops received one or two anthrax immunizations during the Persian Gulf War in 1991, but individual records were either not kept (in an attempt not to identify those unvaccinated, hence vulnerable to enemy bioweapons) or were marked with terms such as “Vaccine A.” (179, 184-188) In 1998, a much larger immunization program began that has now administered over 5.6 million anthrax immunizations to over 1.4 million troops. Anthrax immunizations are primarily intended for people serving in areas judged to be at higher risk (e.g., southwest Asia, Korea), as well as military personnel with homeland biodefense roles.

Anthrax vaccine was the target of prolonged skepticism, evoking the NAS review and an extraordinary array of post-marketing safety studies. These studies involved cohort studies of acute symptoms, (189-197) hospitalizations, (179, 198) disability evaluations, (199) and reproductive outcomes, (200-202) as well as secondary review of the spontaneous reports to the Vaccine Adverse Event Reporting System (VAERS). (203, 204) Anthrax-vaccinated and unvaccinated personnel had comparable rates of illness and health. Several of the cohort studies span observation for multiple years after immunization. (179, 198, 199, 201, 205, 206)

After the National Academy of Sciences heard from vaccinees and comprehensively reviewed the accumulated scientific data, it concluded that anthrax vaccine has an adverse-reaction profile similar to other adult vaccines. (179) The AFEB concurred. (10) However, an elevated rate of injection-site pain and swelling, occasionally with peripheral neuropathy, is associated with administering a vaccine adjuvanted with aluminum hydroxide by subcutaneous injection. Studies underway are evaluating rare adverse events (e.g., prolonged myalgia/arthralgia) and the relative effectiveness of intramuscular injection on immunogenicity and safety. The anthrax immunization program also pointed out needed improvements in the way DoD exchanges information with military personnel and their families and provides clinical immunization services in general.

Plague

A formalin-inactivated plague vaccine saw limited use during World War II. (3, 15, 180) American soldiers deploying to Vietnam during the 1960s received a similar inactivated plague vaccine. Conversely, the South Vietnamese government gave the live EV or EV76 strain of plague vaccine to its soldiers. (2, 3, 18, 180, 207-211) American use of plague vaccine declined substantially after the 1960s, given a relatively high degree of injection-site reactions and limited exposure to the bacteria. Today, no plague vaccine licensed by the Food & Drug Administration is manufactured. (7, 10, 130, 212)

A plague vaccine is potentially of interest in countering bioweapon threats, (213) but that whole-cell plague vaccine did not adequately protect mice against inhalation challenge with Yersinia pestis bacteria. (214) Modern technology may provide an improved plague vaccine containing F1 and V proteins as the principal antigens. (210, 211, 215)

PROPHYLAXIS OF OTHER INFECTIOUS HAZARDS

Pneumococcal Disease

Early tests of pneumococcal polysaccharide vaccines occurred at Camp Upton, New York, and Camp Wheeler, Georgia, in 1918-19. During the 1930s, polyvalent pneumococcal polysaccharide vaccine was tested in five trials in 120,000 men at Civilian Conservation Corps camps. (4, 7, 12, 13, 16, 216-219) In 1937, Frank Horsfall prepared a therapeutic rabbit pneumococcal antisera. It was less reactogenic than a similar product prepared with equine serum. Equine or rabbit pneumococcal antiserum was available from several sources as late as 1965. (4, 7)

Successful clinical trials of pneumococcal vaccine were conducted in military trainees in 1944-45 at Sioux Falls Army Air Force Technical School experiencing a high incidence rate of pneumococcal infections. (2-4, 12, 218, 219) Based on this work, E. R. Squibb & Son marketed two hexavalent pneumococcal polysaccharide vaccines, in either adult or pediatric formulations. These vaccines were not widely prescribed because of greater confidence in another newly introduced drug, penicillin. The vaccines were voluntarily withdrawn by the manufacturer in 1954, due to lack of acceptance and low sales. Subsequent studies showed that penicillin did not alter the death rates of pnuemococcal disease during the first four days of infection, renewing interest in prevention by immunization.

Today, pneumococcal polysaccharide vaccine 23-valent is given to asplenic military personnel. Based on episodic outbreaks, the vaccine has also been given to selected Marine Corps and special operations trainees; its value in training settings is being evaluated. (10, 220)

Poliovirus

The development of poliovirus vaccines can be traced to the AFEB in the 1940s. Jonas Salk was charged with developing a typing system for polioviruses and Albert Sabin was charged with developing an attenuated vaccine.

In 1955, the U.S. government licensed Jonas Salk's inactivated poliovirus vaccine. In 1961, the first of several formulations of Albert Sabin's oral attenuated vaccine was licensed, and 1 year later, the oral polio vaccine largely replaced the Salk vaccine in the U.S. (7, 18)

Initially, military poliovirus immunization was a "catch-up" program for adults who hadn't been immunized as children. Basic training centers switched from injectable vaccine to oral vaccine once the trivalent oral product became available in the early 1960s. (9) DoD policies have been revised over time as the global incidence of poliomyelitis has declined. Today, the Services administer one dose of inactivated poliovirus vaccine to their trainees, consistent with the ACIP recommendation for a single adult dose (after the basic immunizing series) for international travelers. (10, 221)

Historical Notes

Regrettably, the content above is not an exhaustive description of the details of the American experience. But several vaccines given to earlier generations of American troops, but no longer used, are worthy of brief mention. The military immunization experience includes long-term follow-up of laboratory personnel who received multiple common and exotic vaccines. (205, 222-227)

A formalin-inactivated typhus vaccine was primarily provided to troops serving in Europe during World War II and then in the Korean and Vietnam wars. Plotz and colleagues at WRAIR helped purify the specific antigen. The vaccine prevented louse-borne (epidemic) typhus, not murine or scrub typhus. The microbes were cultured in chicken-embryo yolk sacs and inactivated with formaldehyde, the Cox method, and first licensed for general use in 1941. (2-4, 7, 9, 228-231) However, subsequent attempts to purify this vaccine resulted in inadequate potency, so immunization eventually gave way to insecticides and antibiotics. Production voluntarily ceased in 1980 and the last batch expired in 1981.

During the late 1980s, an inactivated tick-borne encephalitis vaccine produced in Austria was administered as an investigational vaccine to certain inspectors enforcing the Intermediate-Range Nuclear Forces Treaty. (10, 130) These inspectors regularly visited rural and forested areas of the Soviet Union that are highly endemic for tick-borne encephalitis. A similar product was used in 1996 during U.S. military deployment to Bosnia. (7, 10, 130, 168, 232, 233)

In the 1950s, IGIM was used to treat patients deficient in the antibody-rich gamma-globulin fraction of serum, first described by COL Ogden C. Bruton, an Army pediatrician at Walter Reed Army Hospital. (234-236) His discovery opened new approaches in passive immunization and the

diagnosis and treatment of humoral (antibody) immune deficiencies. Human hyperimmune globulins largely replaced corresponding equine antisera and antitoxins in the 1960s. (7, 9, 46)

VACCINE-SAFETY SURVEILLANCE PROGRAMS

With the success of immunization in reducing the incidence of diseases discussed above, the military health system faces the same challenges that the civilian public-health sector does – increasing concerns about vaccine safety and adverse events experienced after immunization. Even one adverse event among thousands of vaccine recipients, if serious or with prolonged health impact, can cause concerns about the safety of an immunization program. Vocal objection to military immunization programs occurred with variolation in the 1770s, (6, 16) smallpox and typhoid vaccines in the 1910s, (27, 37) various vaccines in World War II, (14) and anthrax vaccine in the 1990s. (179)

Few conditions are uniquely caused by immunization. One of the few examples is paralytic poliomyelitis that rarely follows use of the live attenuated poliovirus vaccine. Instead, immunizations can be risk factors that increase the relative risk of an adverse event occurring (e.g., Guillain-Barré syndrome that was more likely with some annual formulations, but not others, of influenza vaccine). On the other hand, health conditions that occur in unvaccinated people are fully expected to occur in vaccinated people, at the same background rates of incidence. Discerning when an adverse event that occurs after immunization is an adverse reaction that should be causally attributed to immunization can be a clinical challenge. In addition, the important task of explaining benefit-risk ratios for individual patients requires time, experience, and training.

The military health system that implements immunization programs also has a responsibility to implement safety surveillance programs. (237) In recent times, these surveillance programs may be best exemplified by assessments of anthrax vaccine safety and smallpox vaccine safety, where the U.S. DoD has been the primary user of these vaccines. (28, 170-172, 179, 189-206) A Navy allergist was among the first to recognize the role of gelatin in vaccine-associated anaphylaxis. (237)

PRACTICAL ISSUES IN PROGRAM IMPLEMENTATION

Most vaccines require continuous refrigeration. A few require storage in a freezer. Maintaining the “cold chain” to assure injection of potent vaccines appears simple, but requires considerable effort. (7, 14-17) In World War II, smallpox vaccine was transported by air using kerosene-powered refrigerators or packed in dry ice. Improper vaccine storage was one of the principle factors in breakthrough infections. In January 1946, a special shipment of smallpox vaccine was ordered from the U.S. mainland, after doubts arose about the potency of vaccine on the Korean peninsula. (26, 238) Today, monitoring devices can record the temperature of vaccine shipments, allowing improperly handled product to be discarded rather than injected.

Documentation of immunizations is important to record a healthcare encounter and to avoid redundant immunization at future healthcare visits. During World War II, tetanus immunizations were marked on troops’ identification tags (“dog tags,” Figure 3) and on paper records (Figures 1 and 2). Increasingly since in the 1990s, DoD uses electronic immunization tracking systems (i.e., registries) to permanently record immunizations, even if paper records are lost. (10, 239)

In civilian adult immunization programs, individuals can choose to accept or decline authoritative recommendations to be immunized. In military settings, mission-oriented teams place an extraordinary reliance on the health of each team member. The interdependence of members of a military unit has vital consequences in military settings, where the loss of one service member from an infectious disease could degrade unit performance and cause the loss of other service members due to enemy action. This interdependence leads to command policies requiring military immunizations. The unity of command inherent to military organizations allows public-health decisions to be applied consistently across dispersed military communities.

Immunization to Protect the U.S. Armed Forces

The administration of immunizations to new military personnel is based on several assumptions. First, entrance physical examinations establish that trainees comprise a healthy population without underlying conditions known to predispose people to serious adverse effects from immunization (e.g., immune deficiencies). Second, most trainees are assumed to have been exposed to childhood vaccine antigens through natural infection or childhood immunization programs. Vaccines with highest priority are those to prevent infections most transmissible in closed settings (e.g., meningococcal disease, influenza, measles, varicella). (8)

During training, accessions must acquire immunity to multiple infections within a short period of time. Thus, simultaneous immunizations have been provided to tens of millions of trainees over the last 65 years. (9, 10, 223, 239) The AFEB considered the issue and found that available data "do not demonstrate serious or long-term adverse health effects causally related to multiple, concurrent immunizations, and there is no reason to deviate from current consensus guidelines for adult immunization." (240) Similarly, an Institute of Medicine committee and others found the evidence favors rejecting a conclusion that simultaneous immunization causes heterologous infection, type-1 diabetes, or other patterns of adverse events. (241, 242) Additional work is needed to identify risk factors that might predispose to rare problems.

Because American adolescents today have a high degree of pre-existing immunity, the DoD increasingly uses sero-screening to individualize immunizations according to personal vulnerabilities. (10, 140-146, 243-246) Training sites are planning to separate immunizations into clusters based on acute versus long-range need. The first cluster would protect against pathogens posing an imminent risk in closed communities (e.g., influenza; meningococcal; measles, mumps, rubella; varicella). The second cluster would protect against pathogens posing a threat later in military service (e.g., hepatitis A, hepatitis B, poliovirus, tetanus-diphtheria). Additional vaccines can be given later during training. The Marine Corps, for example, administers yellow fever vaccine to trainees late in the training cycle. Typhoid or rabies immunization can be started during advanced or specialty training, based on first assignment or occupational specialty, respectively. (8)

Jet-injection devices were first developed in the private sector in the 1940s. Military scientists adapted the early devices to create needle-free multi-use-nozzle jet injectors capable of 600 or more subcutaneous injections per hour from 1949 onward, primarily for basic training camps. The Army's Aaron Ismach and Abram Benenson developed a nozzle for intradermal vaccination, used in civilian mass smallpox immunization campaigns in the 1960s. (3, 9, 19, 247-251) Unfortunately, the devices' use of the same unsterile nozzle and fluid pathway to inject consecutive patients allowed transmission of blood-borne pathogens (e.g., hepatitis B, human immunodeficiency virus) in civilian settings, and the devices have fallen into disfavor. (252, 253) In contrast, a new generation of disposable-cartridge jet injectors is being developed to avoid these safety concerns by using a disposable, sterile fluid pathway for each patient. These devices have not yet been widely adopted for military use because of relatively slow handling characteristics and high unit costs. But research is underway for automated prefilling and finger-free loading and ejecting of cartridges, to make future high-speed jet injectors suitable for mass-immunization programs.

RESEARCH PORTFOLIO

Military personnel confront infectious hazards for which there are not yet licensed vaccines. Over the past few decades, the U.S. military medical research community, working with civilian partners, developed several investigational vaccines, toxoids, and immune globulins, to counter specific military threats associated with high morbidity. These threats included natural, endemic diseases, and microbes that could be deployed as bioweapons. (130, 178) Such vaccines have been studied to prevent Argentine hemorrhagic fever (AHF, Junín virus), (152, 254, 255) botulism, (256) Chikungunya, (152, 257, 258) dengue fever, (254, 259) eastern equine encephalitis (EEE), (260) Ebola fever, (152, 254, 261, 262) Escherichia coli, (33, 263) hepatitis E, (264) HIV disease,

(265-268) Lassa fever, (152, 254, 261), malaria, (269-272) Mycoplasma pneumoniae, (273) Neisseria meningitidis serogroup B, (274, 275) Q fever, (180, 276, 277) Rift Valley fever, (152, 254, 278-282) shigellosis, (33, 283) tularemia, (180, 227, 284-287) Venezuelan equine encephalitis (VEE), (2, 168, 227, 288-290), and western equine encephaltitis (WEE). (291) A gonococcal vaccine produced neutralizing antibodies, but was not sufficiently protective in a field trial. (268, 292)

New versions of some of the older vaccines are in early clinical trials, including recombinant botulinum bivalent AB vaccine and live attenuated VEE V3526 vaccine. (293) Next-generation anthrax vaccines in clinical trials include recombinant protective antigen vaccine and a vaccine adjuvanted with CpG oliogdoxynucleotides. (294-296) The role of anthrax capsule/exosporium and toxin proteins and spores are being evaluated in animal models. A F1-V plague vaccine should enter clinical trials soon. (215) Vaccines advancing toward clinical trials include staphylococcal enterotoxin B/A vaccine, (297) Hantavirus vaccine, (152, 298, 299) and next-generation EEE (168, 289, 300) and WEE vaccines. (168, 289, 300) Novel approaches being pursued include RNA replicons as vaccines against Marburg and other filoviruses, (301, 302) and DNA vaccines against Hantavirus. (303) The candidate malaria vaccine RTS,S reduced the rate of parasitemia by 37% and severe malaria by 58% over a 6-month period in Mozambiquean children. (270, 271)

Like the movement toward more combination vaccines for children, multiagent vaccines for military personnel are also a priority. A panfilovirus vaccine protecting against Marburg and Ebola variants might be possible within a decade. Novel delivery systems being pursued include aerosols, micro-needle or adjuvanted patches, and oral dosage forms.

Similarly, human immune globulin preparations (e.g., hyperimmune globulins, antitoxins) have been investigated to treat or protect against Klebsiella and Pseudomonas infections in burned or severely wounded troops, (304) and to provide passive protection against Lassa fever, (152, 254), Ebola fever, (254, 305) Bolivian hemorrhagic fever (caused by Machupo virus), (152, 306) and botulism (307). Military researchers established the clinical value of IgG antibodies to prevent respiratory syncytial virus. (7, 133, 308) Polyclonal and monoclonal antibodies are being evaluated for treatment of anthrax infection.

VEE vaccines were given to 2 million horses in Texas to control an equine outbreak there that had contributed to 84 human deaths. (2, 168) The formalin-inactivated Rift Valley vaccine was given to 963 Swedish soldiers under the United Nations' peace-keeping flag in the Sinai Peninsula during the outbreak until 1979. (281, 280, 309, 310) More than 175,000 doses of the AHF vaccine have been administered in Argentina, dramatically reducing disease incidence. (152) Even successful vaccine research may not be carried through to commercial development and licensure, such as improved vaccines against Rocky Mountain spotted fever developed at WRAIR. (231, 311, 312) About 8,000 troops received investigational botulinum toxoid ABCDE during the Persian Gulf War. (184-188)

Military personnel need vaccines that are: (1) safe (associated with few adverse reactions), (2) effective (able to produce long-lasting immunity), (3) easy to administer, (4) durable (prolonged shelf life, tolerant of shipping conditions), and (5) affordable (offering good value for the price paid). The ideal vaccine formulation would produce immunity against several diseases through a single dose. Genetically engineered products may lend themselves to this ideal. Adjuvant research will help. (313) Yet even with 20 years experience in biotechnology, the development and licensing process is no shorter or simpler than it was in the 1980s.

Even so, DoD invests in the research and development of additional countermeasures to natural infectious diseases and bioweapons that might harm military personnel. In addition, DoD will take advantage of the fruits of private-sector research and development. The private-sector pipeline may soon deliver vaccines to prevent papilloma virus-related cervical cancer, rotavirus gastroenteritis, and herpes zoster.

SUMMARY

In 1900, smallpox vaccine was widely used, rabies vaccine was available as post-exposure prophylaxis after animal bites, and typhoid vaccine was just coming to public attention. A century later, 21 serious infections can be prevented with FDA-licensed vaccines. (6-8) As vaccines increase in number and national focus on vaccine safety continues, the complexity of managing clinical immunization challenges will undoubtedly increase. Information technologies are increasingly used to disseminate immunization information (e.g., www.vaccines.mil) and conduct long-distance, on-demand training (e.g., www.projectimmunereadiness.amedd.army.mil).

Today, military units in the United States conduct immunization programs at training camps, before overseas deployments, and annually during influenza immunization campaigns. The goal is to protect individual health and to keep units strong so they can accomplish their military missions. The FDA-licensed vaccines selected protect against infections during training itself, as well as during subsequent years. The vaccines of most acute need during military training protect against pathogens that represent an imminent risk of contagious disease in settings of close contact. Other vaccines are given to prevent infections more likely to occur later, during international travel or during extended periods of military service when poor sanitation or bioweapons could threaten their lives.

Military immunization programs maintain the health of soldiers, marines, sailors, airmen, and coast guardsmen, the most important resources within the Department of Defense, the resources most critical to military success. These people deserve the best available protective measures.

Some immunization needs are universal for all in military service (e.g., tetanus) while others derive from specific environmental or occupational risks (e.g., Japanese encephalitis, rabies). But military immunization programs need to be individualized based on personal contraindications or prior immunity. The proper conduct of military immunization programs respects the need for detailed education of military personnel about the immunizations they get, maximizes quality in immunization delivery, and supports quality clinical care to prevent and treat adverse events after immunization.

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Abbreviations

ACIP - Advisory Committee on Immunization Practices
AFEB - Armed Forces Epidemiological Board
AHF - Argentine hemorrhagic fever
AKD – acetone killed and dried (typhoid vaccine)
ARD - acute respiratory disease
CDC - Centers for Disease Control & Prevention
DoD – U.S. Department of Defense
DT – Diphtheria-tetanus toxoids (pediatric strength)
EEE – eastern equine encephalitis
FDA - Food & Drug Administration
GBS - Guillain-Barré syndrome
HIV - human immunodeficiency virus
IGIM - immune globulin intramuscular
JE – Japanese encephalitis
NAS - National Academy of Sciences
SKB - SmithKline Beecham
Td - tetanus-diphtheria toxoids (adult strength)
Tdap - tetanus-diphtheria-acellular pertussis vaccine
VAERS - Vaccine Adverse Event Reporting System
VEE – Venezuelan equine encephalitis
WEE – western equine encephalitis
WRAIR – Walter Reed Army Institute of Research

TABLE 1. Vaccines typically administered to U.S. military personnel, 2006

Population Segment	Vaccine	Routine Schedule for Troops †
Trainees:	Diphtheria	Single dose
	Hepatitis A	Two doses
	Hepatitis B	Three doses
	Influenza	Annual, seasonal
	Measles	Single dose
	Meningococcal disease	Single dose
	Mumps	Single dose
	Pertussis, acellular	Single dose (pending)
	Poliovirus	Single dose
	Rubella	Single dose
	Tetanus	Single dose
	Varicella *	Two doses
	Yellow fever *	Single dose
Routine during career (both active-duty and reserve component):	Diphtheria	Every 10 years
	Hepatitis A	Two doses
	Influenza	Annual, seasonal
	Pertussis, acellular	With Td (pending)
	Tetanus	Every 10 years
Individualized based on deployment or travel to high-risk areas (both active and reserve components), various alert forces:	Anthrax	Multidose series
	Hepatitis B	Three doses
	Japanese encephalitis	Three doses, boosters
	Meningococcal disease	Single dose, boosters
	Smallpox	Single, every 10 years
	Typhoid	Dosage varies
	Yellow fever	Single, every 10 years
Individualized based on occupational or personal needs:	*Haemophilus influenzae* type b	Single dose
	Hepatitis B	Three doses
	Meningococcal disease	Single dose
	Pneumococcal disease	Single dose
	Rabies	Three doses, boosters
	Varicella	Two doses

* Immunization policy varies among Military Services, based on individual needs.
† Assumes basic immunizing series received earlier in life. Booster doses may be required at appropriate intervals to sustain immunity.

Derived primarily from references 7 and 8.

TABLE 2. Immunizations used widely during major U.S. conflicts *

Conflict, Era	Vaccines (specific type)	Antibodies
American Revolutionary War, 1775-1783	Smallpox (by variolation, inoculation with variola virus)	
War of 1812, 1812-1815	Smallpox (vaccination with live cowpox and later vaccinia virus)	
Mexican-American War, 1846-1848	Smallpox (live)	
Civil War, 1861-1865	Smallpox (live)	
Spanish-American War, 1898	Smallpox (live)	
World War I, 1917-1918	Smallpox (live), typhoid (whole cell)	Therapeutic tetanus antitoxin, diphtheria antitoxin
World War II, 1941-1945	Routine: Influenza (whole inactivated), smallpox (live), tetanus (toxoid), typhoid (whole cell), paratyphoid A&B (whole cell). Selected: Cholera (whole cell), diphtheria (toxoid), plague (whole cell), scarlet fever (whole cell), typhus (whole cell), yellow fever (live)	Therapeutic diphtheria antitoxin, gas gangrene antitoxin, tetanus antitoxin. Immune globulin (measles prophylaxis)
Korean War, 1950-1953	Cholera (whole cell), influenza (whole inactivated), plague (whole cell), smallpox (live), tetanus-diphtheria (toxoids), typhoid (whole cell), paratyphoid A&B (whole cell), typhus (whole cell), yellow fever (live)	Therapeutic diphtheria antitoxin. Immune globulin (hepatitis A, hepatitis B, and measles prophylaxis)
Vietnam War, 1964-1973	Cholera (whole cell), influenza (whole inactivated), measles (live), meningococcal A/C (polysaccharide), plague (whole cell), poliovirus (live), smallpox (live), tetanus-diphtheria (toxoids), typhoid (whole cell, AKD or H-P), typhus (whole cell), yellow fever (live)	Immune globulin (hepatitis A and hepatitis B prophylaxis)
Persian Gulf War, 1990-1991 (i.e., Operation Desert Shield/Desert Storm)	Adenovirus type 4 and type 7 (live), anthrax (acellular, limited use), botulinum toxoid (very limited use), hepatitis B (subunit), influenza (split inactivated), measles-rubella or measles-mumps-rubella (live), meningococcal A/C/Y/W-135 (polysaccharide), poliovirus (live), rabies (inactivated, special operations), tetanus-diphtheria (toxoids), typhoid (whole cell, AKD or H-P), yellow fever (live)	Immune globulin (hepatitis A prophylaxis)
Global War on Terror, 2001 to present (i.e., Operation Enduring Freedom (Afghanistan)	Anthrax (acellular), hepatitis A (inactivated), hepatitis B (subunit), influenza (split inactivated virus injection or live attenuated virus intranasal), measles-mumps-rubella	

and Operation Iraqi Freedom)	(live), meningococcal A/C/Y/W-135 (polysaccharide), poliovirus (inactivated), rabies (inactivated, for special operations), smallpox (live), tetanus-diphtheria (toxoids, soon with pertussis vaccine), typhoid (Vi subunit or live-attenuated), varicella (live), yellow fever (live)	

* This list is not an exhaustive list of all licensed vaccines and antibodies for these eras, nor an assertion that each service member in a conflict received each product. Rather, this is a list of widely used products for service members during these time intervals.
Derived primarily from references 1-18.

TABLE 3. Major contributions of U.S. military medicine to human immunization

Date	Disease	U.S. Military Contribution to Immunization	Key People
1775 - 1783	Smallpox	Variolation of Continental Army	General George Washington, Benjamin Rush
1898	Typhoid Fever	Typhoid Board improves camp sanitation, shows cause of outbreak and carrier state	MAJ Walter Reed, MAJ Victor C. Vaughan, MAJ Edwin O. Shakespeare
1900	Yellow Fever	Virus carried by *Aedes aegypti* mosquitoes shown to transmit yellow fever	MAJ Walter Reed, James Carroll, MAJ Aristide Agramonte, MAJ Jesse Lazear, MAJ (later BG) William Gorgas
1909	Typhoid Fever	First American typhoid vaccine produced at US Army Medical School	CPT (later BG) Frederick F. Russell
1942	Tetanus	First large-scale use of tetanus toxoid	
1940s	Influenza A&B	Inactivated vaccines developed	Thomas J. Francis, Jr.; Jonas E. Salk
1940s	Typhus	Sonic vibration of infected yolk sacs used for vaccine manufacture	CPT Joseph E. Smadel, COL (later BG) Stanhope Bayne-Jones, Theodore E. Woodward
1940s, 1950s	Japanese encephalitis	Asian JE vaccines adapted for American use; given to 250,000 military personnel. Discoveries in epidemiology, ecology	CPT Joseph E. Smadel, MAJ Albert B. Sabin, COL Edward L. Buescher, William F. Scherer
1944-1950	Hepatitis B	Investigation of jaundice outbreak among yellow-fever vaccinees	
1945	Hepatitis A, Measles, Mumps	Immune globulin fractionated from plasma. Passive immunization with immune globulin intramuscular prevents or attenuates disease	Edwin J. Cohn, John L. Oncley, Joseph Stokes, Jr., CPT John R. Neefe Jr., John F. Enders
1945	Pneumococcal disease	Multivalent polysaccharide vaccine tested at Army Air Corps Technical School, Sioux Falls, South Dakota	Colin M. MacLeod, Michael Heidelberger
1950s	Diphtheria	Advantages of low-dose diphtheria toxoid for adults demonstrated	Geoffrey Edsall
1950s	Immune Deficiency	Immune globulin intramuscular used to treat child with agammaglobulinemia	COL Ogden C. Bruton
1957	Influenza	Antigenic shift and drift of influenza described	Thomas Francis, Jr.

1950s to 1970s	Adenovirus	Adenoviruses isolated at Fort Leonard Wood (1952). Burden of adenovirus infection on hospitalizations measured. Inactivated vaccines developed (1956). Live vaccines developed in 1960s-70s	Maurice R. Hilleman, COL Edward L. Buescher, COL Franklin H. Top, Jr. COL (later MG) Phillip K. Russell
1961	Rubella	Rubella virus isolated from trainee hospitalized at Fort Dix, New Jersey	CPT Paul D. Parkman, Malcom S. Artenstein, COL Edward L. Buescher
1960s-1970s	Meningococcal disease	Immune responses to bacteria described. First meningococcal polysaccharide A (1970) and C (1978) vaccines developed	Malcolm S. Artenstein, CPT Irving Goldschneider, CPT Emil C. Gotschlich, MAJ Ronald Gold
1960s, 1970s	Hepatitis B	Advances in viral subtyping. Protective effect of antibodies demonstrated	COL William H. Bancroft; COL Marcel E. Conrad
1980s	Japanese encephalitis	Efficacy of two JE vaccines compared in Thailand	COL Charles H. Hoke, Jr.
1980s	Gonorrhea	Gonococcal pilus vaccine produces measurable genital mucosal antibody, but not effective in field trial	COL Edmund C. Tramont COL John W. Boslego
1980s	Respiratory syncytial virus	Polyvalent high-titer anti-RSV immune globulin effective prophylaxis in infants	MAJ Gerald W. Fischer, Val G. Hemming, Greg A. Prince
1980s to present	Human immuno-deficiency virus	gp160 vaccine immunogenic, but did not effect disease progression	COL Edmund C. Tramont, LTC Robert R. Redfield
1985-1995	Hepatitis A	Prototype hepatitis A vaccine developed. Army conducts pivotal efficacy trial in Thailand	Leonard N. Binn, COL Charles H. Hoke, Jr., LTC Bruce L. Innis, MAJ Stanley M. Lemon
1980s-1990s	Tick-borne Encephalitis	American experience with European-licensed vaccines	
1990s	Plague	Recognition of F1 and V antigens on virulence and immunity	COL Arthur M. Friedlander
1990s	Cholera	Oral WC/rBS cholera vaccine tested with Peruvian Army and Navy	COL Jose L. Sanchez, COL David N. Taylor
1990s to present	Anthrax	Animal challenge studies of vaccine efficacy. Cohort studies of anthrax vaccine safety	COL Arthur M. Friedlander, COL John F. Brundage, Others

Derived primarily from references 1-18 and other references cited in the text.

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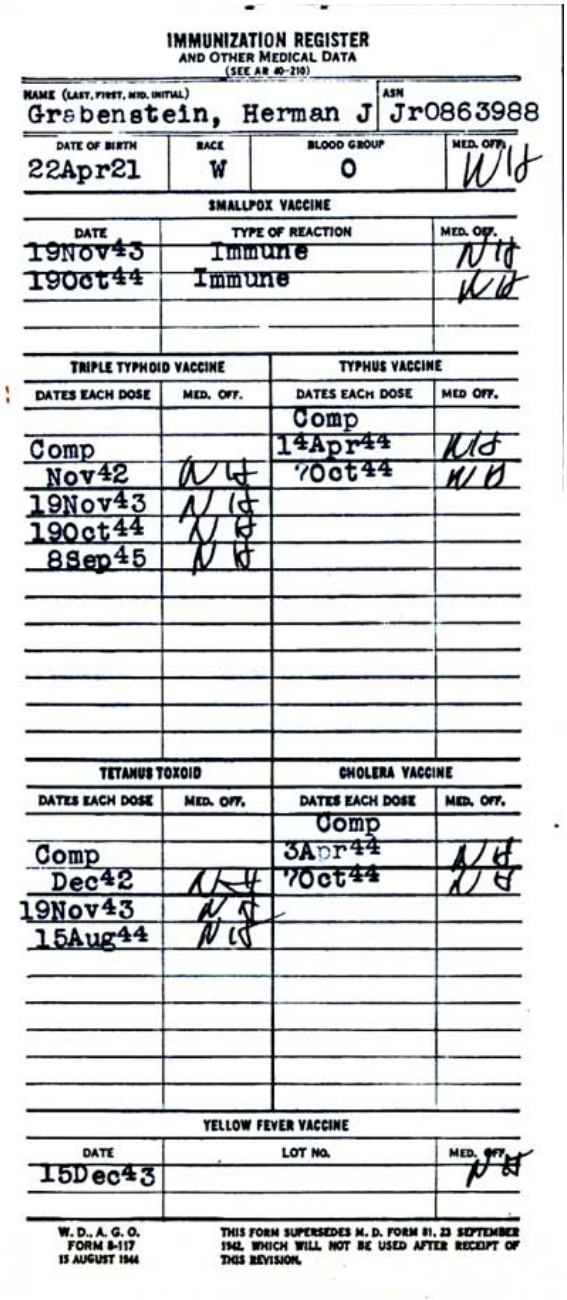
FIGURE 1. Immunization records of 1st Lieutenant Herman J. Grabenstein, Jr., U.S. Army Air Corps, 1940s *



IMMUNIZATION REGISTER
AND OTHER MEDICAL DATA
(SEE AR 40-210)

NAME (LAST, FIRST, MID. INITIAL)	ASN
Grabenstein, Herman J	Jr0863988

DATE OF BIRTH	RACE	BLOOD GROUP	MED. OFF.
22Apr21	W	O	

SMALLPOX VACCINE

DATE	TYPE OF REACTION	MED. OFF.
19Nov43	Immune	
19Oct44	Immune	

TRIPLE TYPHOID VACCINE		TYPHUS VACCINE	
DATES EACH DOSE	MED. OFF.	DATES EACH DOSE	MED OFF.
		Comp	
Comp		14Apr44	
Nov42		70ct44	
19Nov43			
19Oct44			
8Sep45			

TETANUS TOXOID		CHOLERA VACCINE	
DATES EACH DOSE	MED. OFF.	DATES EACH DOSE	MED. OFF.
		Comp	
Comp		3Apr44	
Dec42		70ct44	
19Nov43			
15Aug44			

YELLOW FEVER VACCINE

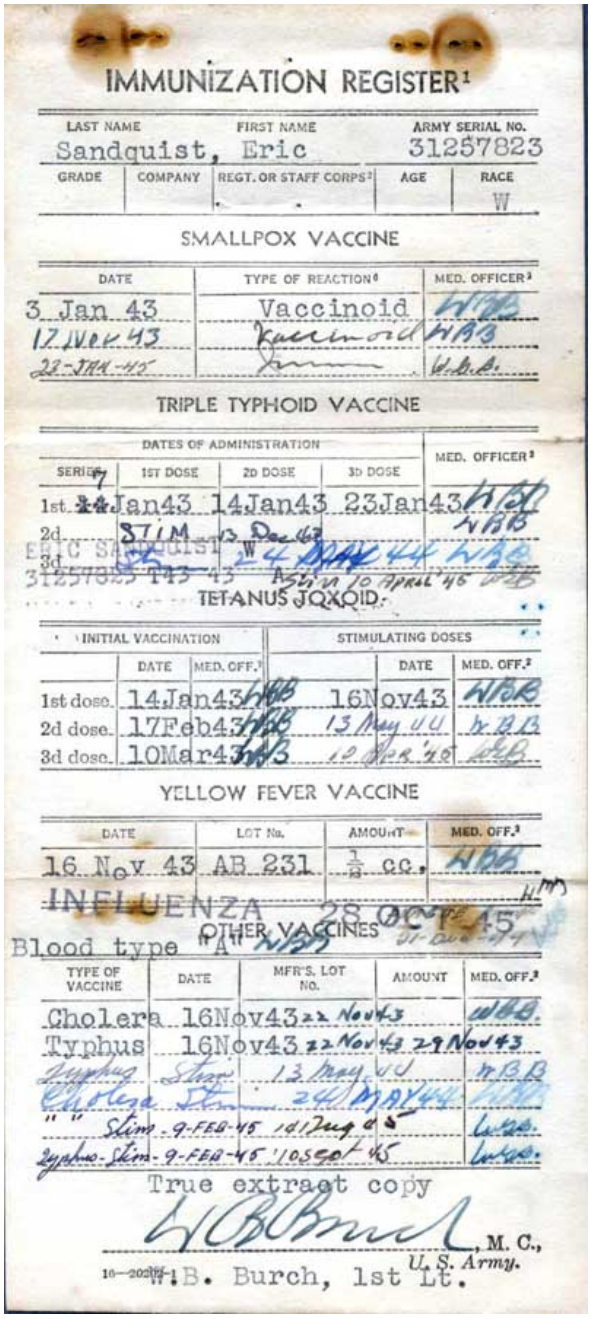
DATE	LOT NO.	MED. OFF.
15Dec43		

W. D., A. G. O. FORM 8-117 15 AUGUST 1944

THIS FORM SUPERSEDES M. D. FORM 81, 23 SEPTEMBER 1942, WHICH WILL NOT BE USED AFTER RECEIPT OF THIS REVISION.

* The authors seek additional examples of individual military immunization records from other eras.

FIGURE 2. Immunization records of Staff Sergeant Eric W. Sandquist, U.S. Army Air Corps, 1940s



IMMUNIZATION REGISTER[1]

LAST NAME	FIRST NAME	ARMY SERIAL NO.
Sandquist,	Eric	31257823

GRADE	COMPANY	REGT. OR STAFF CORPS[2]	AGE	RACE
				W

SMALLPOX VACCINE

DATE	TYPE OF REACTION[4]	MED. OFFICER[3]
3 Jan 43	Vaccinoid	WBB
17 Nov 43	Vaccinoid	WBB
28-JAN-45		W.B.B.

TRIPLE TYPHOID VACCINE

SERIES	DATES OF ADMINISTRATION 1ST DOSE	2D DOSE	3D DOSE	MED. OFFICER[3]
1st.	14Jan43	14Jan43	23Jan43	WBB
2d.	S71M	13 Dec 43		WBB
3d.		24 MAY 44		WBB

ERIC SANDQUIST W
31257823 T43 43
ASSIGN TO APRIL '45

TETANUS TOXOID

	INITIAL VACCINATION DATE	MED. OFF.[3]	STIMULATING DOSES DATE	MED. OFF.[3]
1st dose.	14Jan43	WBB	16Nov43	WBB
2d dose.	17Feb43	WBB	13 May 44	WBB
3d dose.	10Mar43	WBB	10 Nov '44	WBB

YELLOW FEVER VACCINE

DATE	LOT No.	AMOUNT	MED. OFF.[3]
16 Nov 43	AB 231	1/5 cc.	WBB

INFLUENZA 28 OCT 45

OTHER VACCINES

Blood type "A" WBB

TYPE OF VACCINE	DATE	MFR'S. LOT No.	AMOUNT	MED. OFF.[3]
Cholera	16Nov43	22 Nov43		WBB
Typhus	16Nov43	22 Nov43	29 Nov43	
Typhus	Stim	13 May 44		WBB
Cholera	Stim	24 MAY 44		WBB
" "	Stim - 9-FEB-45	10 Aug 45		WBB
Typhus	Stim - 9-FEB-45	10 Sept 45		WBB

True extract copy

W. B. Burch, 1st Lt. M. C., U. S. Army.

10—20376-1

FIGURE 3. Military identification tag of Thornton T. Perry, who received tetanus toxoid in 1942 and 1944 (“T42 44”)