DESK REFERENCE on VACCINES & IMMUNITY

(Emphasizing Military Vaccination Programs)

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Vaccines Licensed in the United States, 1999

	Vaccines Against Bacteria	**Vaccines Against Viruses**
Inactivated Vaccines (vaccines containing inactivated microbes)	Anthrax Cholera Diphtheria * *Haemophilus influenzae* type b Lyme disease Meningococcal Pertussis Plague Pneumococcal Tetanus * Typhoid (injectable)	Hepatitis A Hepatitis B Influenza Japanese encephalitis Poliovirus (injectable) Rabies
Live Vaccines (vaccines containing live microbes)	Tuberculosis (BCG) Typhoid (oral)	Adenovirus ** Measles Mumps Poliovirus (oral) Rubella Smallpox (vaccinia) ** Varicella (chickenpox) Yellow fever

* a specific kind of vaccine called a toxoid (an inactivated toxin).

** not currently in production.

Vaccines Typically Administered to Military Personnel, 1999

(U.S. Army, U.S. Navy, U.S. Marine Corps, U.S. Air Force, U.S. Coast Guard)

Timing	**Vaccine**	**Routine Schedule for Basic Immunity ****
Recruits:	(Adenovirus)	Single dose
	Diphtheria	Single, every 10 yrs
	Influenza	Annual
	Measles	Single dose
	Meningococcal disease	Single dose
	Mumps *	Single dose
	Poliovirus	Single dose
	Rubella	Single dose
	Tetanus	Single, every 10 yrs
	Varicella *	Two doses
	Yellow fever *	Single, every 10 yrs
During advanced individual training (AIT) and then throughout career (both active-duty and reserve component):	Anthrax (policy in AVIP phase III)	Six-dose series
Routine during career (both active-duty and reserve component):	Diphtheria	Single, every 10 yrs
	Influenza	Annual
	Tetanus	Single, every 10 yrs
Alert forces; when deploying or traveling to high-risk areas (both active-duty and	Anthrax (current policy)	Single, every 10 yrs
	Cholera ***	Two doses
	Hepatitis A	Two doses

reserve component):	Hepatitis B Japanese encephalitis Meningococcal disease (Plague) Rabies Typhoid Yellow fever	Three doses Three doses Single dose Three doses Three doses Dosage varies Single, every 10 yrs
Individualized according to occupational or personal needs:	*Haemophilus influenzae* type b Hepatitis B Lyme disease Meningococcal disease Pneumococcal disease Rabies Varicella	Single dose Three doses Three doses Single dose Single dose Three doses Two doses

* Vaccination policy varies among Military Services, based on individual needs.

** Booster doses may be required at annual or other intervals to sustain immunity.

*** Seldom used; vaccine offers only short-term protection, with painful injections.

Vaccines listed in parentheses may not be available due to manufacturing limitations.

Adapted from: United States Army Regulation 40-562; Navy Bureau of Medicine & Surgery Instruction 6230.15; Air Force Joint Instruction 48-110; Coast Guard Commandant Instruction M6230.4E. Immunizations & Chemoprophylaxis. Washington, DC, 1 November 1995. [http://afpubs.hq.af.mil/pubfiles/af/48/afji48-110/afji48-110.pdf]

See also: Takafuji ET, Russell PK. Military immunizations: past, present, and future prospects. *Infectious Disease Clinics of North America* 1990;4:143-158.

Introduction: What is a Vaccine?

What is a vaccine?

A vaccine is a kind of medication intended to prevent an infection.

How do vaccines work?

Vaccines do not work directly. They work indirectly, by stimulating the body's immune system to produce antibodies. The human body responds to different vaccines by making different kinds of antibodies. For example, measles vaccine causes the body to make anti-measles antibodies. Vaccines against tetanus or polio make anti-tetanus or anti-polio antibodies, respectively. These antibodies then circulate throughout the body, on surveillance patrol, on the watch for germ invaders. These antibodies neutralize measles virus or tetanus toxin or other microbes that they encounter in the future.

People compare vaccines to shadow-boxing or dress-rehearsals, to explain how vaccines prepare the body for a later encounter with a dangerous microbe. Vaccines give the body time to prepare defenses against harmful invading germs.

How important are vaccines?

Experts at the Centers for Disease Control & Prevention say that only one thing has saved more lives than vaccines: clean water. In 1900, smallpox, diphtheria, measles, and other infections were leading causes of death in the United States. Our grandparents feared them. Today, these diseases are distant memories, due to the success of vaccines.

What happens if we stop vaccinating?

If we stop vaccinating people, the number of people who are susceptible will gradually increase. When a large enough group is vulnerable to a contagious disease, outbreaks or epidemics can occur. This happened in England, Sweden, and Japan in the 1970s, when many people stopped vaccinating their children against pertussis (whooping cough). Once people started using pertussis vaccine again, the infections came back under control. Remember, infections uncommon in your area are never farther away than an airplane ride.

How long have vaccines been around?

The first reliable vaccine was developed by Edward Jenner in 1796, to prevent smallpox. Louis Pasteur developed an anthrax vaccine for animals in 1880 and a rabies vaccine for humans in 1885. The pace of vaccine research accelerated in the 1950s and 1960s with advances in laboratory methods for growing microbes in cell cultures. The pace is accelerating again now, with recent advances in biotechnology.

How are vaccines invented and researched?

Scientists develop a candidate vaccine based on what they know of microbiology and human immunology. The candidate vaccine is tested in animals, then tested in people in three stages or phases.

Phase I studies involve a dozen people to see if the vaccine provokes an antibody response, and to begin collecting information about vaccine safety. Phase II studies usually include one

or two hundred people, to gather more information about effectiveness and to determine the proper dosage. Phase III studies typically involve a few thousand people, with an unvaccinated (placebo) control group, to definitively measure how good the vaccine is in preventing infection.

If the Food & Drug Administration is satisfied that the vaccine has been shown to be safe and to be effective, then it grants a license to the vaccine's manufacturer, permitting the vaccine to be widely distributed.

What do safety and efficacy (effectiveness) mean?

FDA defines "safety" as the condition where the benefits of a drug outweigh adverse effects the drug may cause. A safe drug is considered to pose a reasonably low risk of harm, injury, or loss when used in an appropriate manner. Because vaccines are typically given to healthy people, without disease, vaccines are held to the highest standards of safety of all medications. That is, vaccines must cause fewer side effects than other medications.

FDA defines "efficacy" as the ability to prevent, treat, diagnose, or otherwise manage a disease or other medical condition. A similar term is effectiveness. An effective vaccine is one that can reduce the risk of infection. Vaccine efficacy of 90% implies that a vaccinated group would have a risk of infection 90% less than the risk of a similar unvaccinated group.

How is safety assessed after FDA licenses a vaccine for widespread use?

Manufacturers, government agencies, and academic groups conduct what is called "post-marketing surveillance" of all medications (including vaccines) after licensing. This surveillance identifies uncommon side effects. It may also be used to gather information about groups of people who may not have received the vaccine during initial research studies, such as elderly people, children, pregnant women, or other groups.

Initial clinical studies of medications do not usually include more than 5,000 people, nor extend longer than 5 to 8 years. Except for delaying availability of promising medications, post-marketing surveillance is the only way to study larger groups of people for longer periods of time.

How are vaccines manufactured?

Vaccines are produced on an industrial scale under rigorous conditions that are approved and audited by the Food & Drug Administration. Each lot (or batch) of vaccine must be individually approved by FDA before it can be released for use by the public. Vaccines receive this extra scrutiny, compared to other medications, because vaccines are complex biological mixtures that must be carefully manufactured to assure reproducible potency.

How are vaccines tested for potency, safety, sterility, and purity?

The Food & Drug Administration sets the standards for all vaccines used in the United States. Potency is assessed by survival of vaccinated laboratory animals after lethal challenge. Safety is confirmed by testing for weight gain and absence of fever in other animal tests using at least two species. Sterility is tested using two kinds of culture media. Purity is measured by chemical assays.

How are vaccines administered to people?

Most vaccines are injected into the body, although a few can be swallowed by mouth. If injections are required, it is because stomach acid would prevent the vaccine from provoking a protective antibody response, or because not enough of the vaccine would get into the blood stream. Typically, vaccines administered by mouth correspond to a microbe that enters the body through the oral route. An influenza vaccine administered as a nasal mist showed promise in recent clinical studies.

Do I have to get vaccinated in the buttocks?

No. No vaccine should be administered in the buttocks. Vaccines are injected into the deltoid area (below the shoulder) in adults, adolescents, and older children. Younger children get injected in the front of the thigh. People traveling to places with poor sanitation used to get antibodies administered in the buttocks, because of the large volume of fluid to be injected. But we now have hepatitis A vaccines for international travelers that make this unnecessary.

How fast do vaccines work?

After a vaccine is injected or swallowed, the body begins a complex set of steps to process the antigens in the vaccine. Antibodies begin to appear in the blood about 10 to 14 days after the vaccination. Typically, live vaccines protect for many years with just a single dose or two. With inactivated vaccines, a series of several doses is typically needed to develop persistent immunity.

What kinds of side effects do vaccines cause?

In general, inactivated vaccines cause side effects that are limited to the injection site, such as redness, tenderness, and swelling. These reactions typically develop in ¼ to ½ of vaccine recipients and persist for a few days before going away on their own.

In general, live vaccines cause side effects similar to a mild case of the corresponding natural infection. Thus, measles and varicella vaccines can cause a mild rash or fever in a minority of vaccine recipients.

All vaccines can cause allergic reactions, although severe allergic reactions are very rare (about one case per million doses). A few vaccines cause unusual reactions in rare cases (consult Vaccine Information Statements, VISs, for details). But these reactions are either temporary or so rare as to be overshadowed by the consequences of the disease being prevented. If FDA determined that the benefits of a vaccine did not outweigh its side-effect profile, FDA would revoke the manufacturer's license to distribute the vaccine.

Why do shots hurt?

The sensation when a needle pierces the skin is probably best described by the word *sting*, rather than *pain*. Nerves are in the surface of the skin. Once a needle passes through the outer layer of the skin, there is no more sensation. After the needle enters the body, one can let a syringe dangle unsupported without causing any pain.

After any fluid is pushed through the needle into the tissue or muscle, the body has to adjust to

the presence of that fluid. As a result, the injection site may become sore or tender after a few hours. Redness and hardness close to the needle-entry site are not uncommon. The soreness and redness go away after a few days.

Vaccines that contain aluminum to increase the antibody response may cause a lump (nodule) at the injection site. These lumps usually go away after a few weeks.

What if something serious does occur?

Go get medical care right away. Ask your health-care provider to report the event to VAERS, the Vaccine Adverse Events Reporting System (800-822-7967, www.fda.gov/cber/vaers/vaers.html). The FDA and CDC monitor these reports weekly for routine safety purposes.

Why do immunization recommendations change from time to time?

Scientists routinely develop new vaccines or new recipes for existing vaccines. As these improvements are found to be valuable, national policies change to reflect the current state of scientific knowledge.

Who should avoid vaccines?

Very few people should avoid vaccines. If someone develops a true serious allergic (immediate hypersensitivity) reaction to a vaccine, that person should probably not receive additional doses of that specific vaccine. It may be acceptable or desirable to give other vaccines, however. For example, someone whose throat swells after a dose of influenza vaccine, or whose throat swells after eating eggs, should not receive flu shots in following years.

What kind of vaccine records should be kept?

Everyone should have a personal record of vaccinations received during his or her lifetime. People should keep these records readily available and take them to health-care visits. Health-care providers keep records of vaccines they administer. State health departments are developing immunization registries to record this information centrally, a big help with a population as mobile as that of the United States.

What is the most used vaccine in America?

Influenza vaccine, with about 70 to 80 million doses distributed each year.

What infectious disease kills more Americans than any other (and has a vaccine that could prevent it if used more)?

Pneumococcal disease, caused by *Streptococcus pneumoniae*.

What was the first vaccine used in the United States?

In 1800, Benjamin Waterhouse introduced the new technique of vaccination against smallpox to the U.S., immunizing his 5-year-old son, Daniel. Anti-vaccinationists decried the practice as

sacrilegious. On the other hand, President Thomas Jefferson strongly advocated the novel form of medical intervention, helping the practice spread throughout Virginia.

When did federal regulation of vaccines begin in the United States?

In 1813, the U.S. Congress empowered President James Madison "to appoint an agent to preserve the genuine vaccine matter [i.e., smallpox vaccine], and to furnish the same to any citizen of the United States," as well as establishing a National Vaccine Agency. The U.S. Post Office was required to carry mail up to one-half ounce containing vaccine material for free.

In 1902, the U.S. Congress passed "An act to regulate the sale of viruses, serums, toxins, and analogous products," later called the Biologics Control Act. The first modern federal legislation to control the quality of pharmaceutical products, the Act created the Hygienic Laboratory of the U.S. Public Health Service to control all biological drugs imported, exported, or engaged in interstate commerce. This function later was transferred to the National Institute of Health Division of Biologics Standards, and then to the Food and Drug Administration (FDA) Center for Biologics Evaluation & Research (CBER).

What biological medication was closely associated with celebrations of the Fourth of July, Independence Day?

Before the population was routinely vaccinated against tetanus, fireworks explosions would cause burns and wounds that would too often result in tetanus ("lockjaw"). To treat or prevent lockjaw in such casualties, physicians and pharmacies would increase their inventory of tetanus antitoxin (anti-tetanus antibodies).

What U.S. president received a dire warning on the dangers of smallpox vaccination to U.S. soldiers and sailors?

Charles M. Higgins (an American citizen) sent a lengthy thesis enumerating alleged hazards of smallpox vaccine to Woodrow Wilson in 1919. Despite his appeal, this vaccine was eventually used to eradicate smallpox from planet Earth. [Higgins CM. *Horrors of Vaccination Exposed and Illustrated*. New York: DeVinne Press, 1920.]

Timeline: Humanity's Experience with Vaccines

(with notable military contributions)

1796 Jenner demonstrates cowpox vaccination to prevent smallpox.

1880 Pasteur develops live, but weakened anthrax vaccine to 24 sheep, 6 cows, and a goat. When Pasteur exposed the vaccinated animals to live anthrax germs 26 days later, they all survived, while a comparable heard of unvaccinated animals died.

1885 Pasteur administers live, but weakened rabies vaccine to Joseph Meister.

1889 Babes & Lepp give first specific animal serum (containing canine antibodies as the active ingredient) to prevent rabies in humans.

1890 Behring & Kitasato prepare first diphtheria antitoxin. First administered by Ehrlich to a young girl in Berlin in 1891.

1899 Almroth Wright proposed mass immunization of British troops during the Boer War against typhoid fever. Because of "opposition by influential people," he was able to vaccinate only 14,000 volunteers. Opposition was so high that vaccine shipments were dumped overboard from transport ships in Southampton. Catastrophe resulted: the British Army suffered more than 58,000 cases of typhoid fever, including 9,000 related deaths.

1911 Typhoid-fever vaccination became compulsory for U.S. soldiers, sailors, and marines, after first typhoid vaccine studies in the United States conducted by Major Frederick Russell at the U.S. Army Medical School, the first school of preventive medicine and public health in the U.S. During the Spanish-American War of 1898, America experienced 243 battle fatalities, but 20,738 cases of typhoid fever. In contrast, during all of World War I, a mere 1,529 cases of typhoid fever were reported, including 227 deaths, among 4.13 million Americans in uniform.

1917 Tetanus antitoxin made from horse serum used widely to prevent tetanus from combat wounds.

1918 During 1918-19, a worldwide outbreak of influenza killed at least 25 million people, the greatest loss of life from any cause in such a short period of time throughout history. More Americans died in that epidemic (>500,000) than from all combat deaths in the 20th century combined. Unfortunately, no influenza vaccine was available to quell the disaster. In the 1940s, the science of virology had progressed, allowing the Surgeon General of the U.S. Army to commission research that resulted in today's influenza vaccine. Today, the most widely used vaccine in America is influenza vaccine, the fruit of military research.

1920 Dog-sled team race against a blizzard to deliver diphtheria antitoxin from Anchorage to the small village of Iditarod, Alaska, where an epidemic threatened the town's children.

1923 Ramon modifies diphtheria toxin with formaldehyde, producing immunogenic toxoid.

1926 Glenny and colleagues report that alum precipitation enhances diphtheria toxoid activity.

1933 Tetanus toxoid licensed in the United States, but was not widely used by the civilian populace until after World War II.

1938 Immunization with tetanus toxoid begins in the British Army.

1941 Army Surgeon General gets authority from the War Department to administer tetanus toxoid to American troops. A record of each dose of tetanus toxoid administered was stamped on soldiers' identification tags. Only 12 tetanus cases were reported throughout the war, in all theaters of operations, despite the millions of Americans in uniform and more than 2.7 million hospital admissions for wounds or injuries. All 12 cases were in unimmunized or incompletely immunized troops.

The German Army (the *Wehrmacht*) did not give tetanus toxoid to its troops, relying instead on

tetanus antitoxin. It suffered high rates of morbidity and mortality from tetanus. In contrast, the German Air Force (the *Luftwaffe*) immunized its men with toxoid and suffered much less morbidity and mortality.

1940s Typhus and yellow-fever vaccines protect American troops, while endemic among war-torn civilian populations.

1943 Army Surgeon General sponsors clinical studies to assess value of influenza vaccine. Influenza vaccines are now the most used vaccines in America.

1944 "Gamma globulin" (antibody) portion separated from human serum by Cohn, Oncley, and colleagues at Harvard University, under U.S. Navy contract. Antibodies like this were used to prevent and lessen the symptoms of measles or hepatitis A.

1944 Effectiveness of pneumococcal vaccine shown in studies among U.S. Army Air Corps trainees in Sioux Falls, South Dakota.

1954 National Foundation for Infantile Paralysis conducts study with Salk's inactivated poliovirus vaccine in 650,000 children, including 200,000 children in the placebo control group.

1954 Dose of diphtheria toxoid for adults reduced to avoid injection site reactions, based on work of Edsall, Altman, and Gaspar at the Great Lakes Naval Training Center.

1952 Bruton at Walter Reed Army Hospital recognized the first human patient deficient in production of "gamma globulin," successfully treating the patient with antibody replacement therapy. In 1954, antibodies were decontrolled by the federal Office of Defense Mobilization for the first time since World War II.

1961 First of Sabin’s oral poliovirus vaccines licensed in the U.S.

1961 Parkman, Buescher, and Artenstein at Walter Reed Army Institute of Research isolate rubella virus, making rubella vaccine possible.

1963 Attenuated measles vaccine licensed in the U.S.

1960s Plague vaccine protects American troops in Vietnam, while endemic among war-torn civilian populations.

1974 FDA licenses *Neisseria meningitidis* (meningococcal) group A vaccine and group C vaccine developed at Walter Reed Army Institute of Research (WRAIR). Between 1973 and 1975, these vaccines were administered to the entire populations of Finland and Brazil (tens of millions of people) to stop epidemics.

1970s-80s Disease and birth defects from rubella was more quickly reduced in the United States than the United Kingdom, despite both countries having access to the same highly effective vaccine. The United States adopted a policy of universal immunization of all children, whereas the United Kingdom had a selective policy of vaccinating primarily teenage girls. In the 1990s, the UK adopted the US approach of vaccinating all children and disease rates promptly fell.

1980 World Health Organization declares the planet free of smallpox, after an unprecedented vaccination campaign.

1980 FDA licenses live, attenuated vaccines against adenovirus types 4 and 7. Only vaccines designed to be administered as oral tablets.

1980s When hepatitis B vaccine was first licensed in 1981, the vaccine was recommended for health-care workers and various social groups (e.g., injection drug users, men who have sex with men). Limiting use of the vaccine to these small groups was insufficient to reduce the American hepatitis B epidemic and national policy changed in 1991 to a policy of universal coverage, vaccination of all American children, to protect them later in life. After this change, the number of new hepatitis B infections among the general population declined.

1989 First oral bacterial vaccine (capsules against typhoid fever) licensed by FDA.

1990s With the collapse of the Soviet Union, health services in Russia and nearby republics faltered. Cases of diphtheria skyrocketed, changing in a few years from a rare disease to one with more than 19,000 cases reported in 1993. Contributing factors include inadequate immunization of children and adults, delayed recognition and public-health response, and deteriorating social conditions.

1994 U.S. Army study of hepatitis A vaccine in Thailand provides pivotal information to allow 1995 licensure of hepatitis A vaccine in the United States.

1997 Secretary of Defense Cohen orders anthrax vaccination of active and reserve Service Members. Program begins in 1998.

Biological Weapons: Background

1300s: Tatars catapult plague-infected cadavers into city of Kaffa (now Feodossia, Ukraine).

1763: British commanders give blankets contaminated with smallpox scabs to Native Americans.

1776: American forces were too weak from smallpox in 1776 to capture Québec from the British. The Americans suffered 5,500 smallpox casualties among their force of 10,000 colonial troops over a few months, including the death of Major General John Thomas. It can reasonably be argued that the British colony of Canada was not incorporated into the fledgling United States because of smallpox.

1777: George Washington, commander-in-chief of the Continental Army, orders the entire army variolated. Variolation was an archaic and dangerous method of preventing smallpox, by intentionally introducing smallpox virus (variola) into the skin. Washington ordered variolated troops to be isolated until their skin reactions subsided, to avoid infecting uninoculated troops and nearby civilians. Variolation resulted in about two deaths for every 100 people variolated. But variolation was tolerated at the time, because people knew that natural smallpox infection killed

20% of those who contracted it. Variolation was the best available method until Jenner developed smallpox vaccination in 1796.

1812: War Department orders that vaccination be substituted for variolation to prevent smallpox.

early 1800s: Small groups of citizens in Britain and America objected to smallpox vaccination, variously criticizing it as unnatural, sacrilegious, or ineffective. Critics often exaggerated side effects, distributing cartoons showing children turning into animals. In Britain, a political party was formed on an anti-vaccinationist platform. Some of their street demonstrations turned into riots. In 1919, a U.S. citizen named Charles M. Higgins pleaded with Woodrow Wilson to stop mandatory smallpox vaccination of American soldiers and sailors. This smallpox vaccine was ultimately used to eradicate the smallpox disease from planet Earth.

1932-45: Japanese experiments test biological weapons on humans and attack 11 Chinese cities, Unit 731, Pingfan, Manchuria. See Harris' *Factories of Death*.

1942-70: US develops offensive biological weapon capability.

1970: President Nixon issues executive order terminating US offensive biological weapons program.

1979: Accidental release of anthrax spores from Soviet bioweapons plant in Sverdlovsk (now Yekaterinberg) kills at least 66 people and herds of livestock.

1984: Religious sect in Oregon intentionally contaminates salad bars and coffee creamers with *Salmonella typhimurium*; 751 people develop gastroenteritis (*JAMA* 1997;278(Aug 6):389-95).

1990: Members of Aum Shinrikyo sect releases anthrax spores and botulinum toxin in Tokyo, Yokohama, and Yokosuka, targeting Japanese government and U.S. Navy (*New York Times*, 1998;147(May 26):A1,A10).

1995: Iraq admits to United Nations that it loaded anthrax spores into missile warheads and other munitions during the Persian Gulf War of 1990-91.

1999: Soviet defector Ken Alibek publishes *BioHazard*, describing biological weapons programs of the Soviet Union in the second half of the 20th century.

Anthrax: The Disease

Anthrax Among Livestock: Anthrax primarily occurs among grazing animals. Some soil types are more conducive to persistent anthrax spores than others. Veterinary anthrax vaccines for cattle, horses, sheep, pigs, and other livestock have been licensed the U.S. Department of Agriculture for animal use for decades. The veterinary vaccine is a live vaccine, unlike the inactivated vaccine used for

humans.

Anthrax Among Humans: Only 6 reported cases in humans from 1980 through 1992 in the US. Estimates of the world incidence of anthrax in 1962 ranged from 20,000 to 100,000 cases per year, primarily due to agricultural exposure.

Anthrax As a Biological Weapon: Anthrax spores are considered one of the most dangerous biological weapons, because spores are stable for long periods of time despite exposure to sunlight, high temperatures, or disinfectants. Anthrax spores "package themselves," in contrast to viruses and other kinds of bioweapons. If an unvaccinated person develops symptoms after inhaling anthrax spores, the probability of death is 99%. Antibiotics and intensive medical intervention can reduce the likelihood of death to 80% (20% chance of survival).

Transmission: Contact with diseased tissue, contaminated soil, hair, wool, hides, or products of them. Spread of anthrax spores is considered a biological-warfare threat.

Incubation: 2 to 7 days

Communicability: No evidence of transmission from person to person

Timeline:

Anthrax may have been the "Fifth Plague" described in the Book of Exodus.

1849: Pollender discovers *Anthracis bacillus* (sic).

1881: Pasteur administers live, but weakened anthrax vaccine to 24 sheep, 1 goat, and 6 cows. All the animals survived challenge 26 days later with disease-causing bacteria, while control animals died.

1919: Soldiers (and civilians) contracted cutaneous anthrax from shaving brush bristles made from contaminated horse hair. COL F. F. Russell identified the solution: soak bristles in formaldehyde.

1950s-60s: Scientists at Center for Disease Control study anthrax vaccine in a well-controlled field trial among industrial workers at risk for anthrax. Vaccine efficacy of 92.5% reported by Brachman and CDC colleagues in *American Journal of Public Health* in 1962. CDC continued an observational study of the vaccine until 1970.

1970: Michigan Department of Public Health vaccine licensed on November 4, 1970.

1991: About 250,000 doses of anthrax vaccine administered to some 150,000 American troops, about 25% of those deployed for the Persian Gulf War.

1998: Michigan Biological Products Institute (previously known as Michigan Department of Public Health) sold by State of Michigan to BioPort Corporation.

Anthrax Vaccine At-A-Glance

Official Name: Anthrax Vaccine Adsorbed (AVA)

Manufacturer: BioPort Corporation, Lansing, Michigan, 517-335-9934, www.bioportcorp.com

Description: Inactivated, acellular bacterial vaccine.

Efficacy: In early studies, vaccinated mill workers had 92.5% fewer infections than unvaccinated workers after six doses of vaccine. In these studies, no cases of inhaled anthrax occurred among the vaccinated group and five cases of inhaled anthrax occurred among other workers. The difference between zero and five involved too few people to be considered statistically meaningful, although the trend is obvious.

More recently, 44 of 45 Rhesus monkeys given one or two doses of anthrax vaccine survived aerosol challenge with anthrax. The one fatality occurred with an exposure 2 years after vaccination.

Mechanism of Action: Anthrax vaccine induces protective antibodies that neutralize toxins of *Bacillus anthracis*. These toxins are common to all strains of anthrax bacteria.

Uses (Indications): To prevent anthrax disease, caused by spore-forming bacteria called *Bacillus anthracis*. Need for vaccination is based on likelihood of exposure.

During the 1970s and 1980s, anthrax vaccine was used primarily by at risk veterinarians and other people handling potentially infected animals (e.g., livestock), as well as people working with imported hides, hairs, or bones. Roughly 68,000 doses of vaccine were distributed between 1974 and 1989.

Dosing Schedule: Three doses of 0.5 milliliters (ml) at 2-week intervals, followed by three additional doses 6, 12, and 18 months after the first dose. Given by subcutaneous injection, into the fat layer beneath the skin.

Booster Dose: Give 0.5 ml at 1-year intervals, if continued immunity is needed.

Limitations: Anthrax vaccination after exposure will not produce an antibody response quickly enough to protect the person exposed. Appropriate antibiotics to treat this infection (e.g., ciprofloxacin, doxycycline, penicillin) are warranted, until enough doses of the vaccine are given for long-term protection.

Bars to Use (Contraindications): *Absolute:* People who have had a serious adverse event after a prior dose. *Relative:* Vaccination may need to be delayed until after an acute illness, pregnancy, or other short-term condition concludes.

Pregnancy: Like most vaccines, no specific studies have been conducted of this

vaccine in pregnant women. There are no examples of inactivated vaccines that impair fertility, complicate pregnancy, or cause birth defects. In fact, national experts recommend tetanus, influenza, hepatitis B, and meningococcal vaccine during pregnancy for susceptible women. In general, public-health experts consider inactivated bacterial vaccines, like anthrax vaccine, to be valuable in pregnant women at substantial risk of infection. Nonetheless, to error on the side of caution, DOD policy is to defer doses of anthrax vaccine until pregnancy is completed.

Side Effects: Like all vaccines, anthrax vaccine may cause soreness, redness, itching, swelling, and lumps at the injection site. About 30% of men and 60% of women report mild local reactions, but these reactions usually last only a few days. Lumps can persist a few weeks, but eventually go away. For both genders, between 1% and 5% report moderate reactions of 1 to 5 inches in diameter. Larger reactions occur after about one in a hundred vaccinees or less.

Beyond the injection site, from 5% to 35% will notice muscle aches, joint aches, chills, fever, headaches, nausea, loss of appetite, malaise, or related symptoms. Again, these symptoms usually go away after a few days. Over-the-counter pain relievers or antihistamines before or after vaccination may help reduce bothersome symptoms.

Serious events, such as those requiring hospitalization, are rare. They happen about once per 50,000 doses. Severe allergic reactions can occur after any vaccination, less than once per 100,000 doses.

Production Method: A strain of *Bacillus anthracis* that does not produce toxin (nontoxigenic) is grown in a synthetic liquid culture medium under conditions with little oxygen (microaerobic). The culture material is filtered to remove bacterial cells. This filtrate contains "protective antigen" (PA), a protein common to all anthrax strains, that provokes protective antibodies when injected into humans. The filtrate is adsorbed onto aluminum hydroxide, yielding an opaque suspension. The final product contains 0.85% sodium chloride to make the product isotonic with body fluids, not more than 0.02% formaldehyde, and 0.0025% benzethonium chloride as an antimicrobial preservative for the multidose vial.

Potency Test: The potency of the vaccine is assayed via protection of vaccinated guinea pigs against challenge with 1,000 spores of the virulent Vollum strain of anthrax (21 CFR 620.20 through 620.24).

Packaging: 5.2 milliliter (ml) multidose vial, yielding ten 0.5 ml doses.

Storage/Stability: Store at 2^{o} to 8^{o}C (35^{o} to 46^{o}F). Do not freeze.

Shelf Life: Expires within 12 months.

Date FDA Licensed: November 4, 1970.

Anthrax Vaccine: Similar to Many Other Vaccines

Anthrax Vaccine …	**… just like …**	**… unlike …**
is an inactivated bacterial vaccine…	…cholera, diphtheria, *Haemophilus influenzae* type b, Lyme disease, meningococcal, pertussis, plague, pneumococcal, tetanus, and certain typhoid vaccines.	…tuberculosis (BCG) and certain typhoid vaccines.
is a cell-free (acellular or subunit) vaccine…	…diphtheria, *Haemophilus influenzae* type b, Lyme disease, meningococcal, pneumococcal, and tetanus vaccines.	…cholera, plague, and certain typhoid vaccines.
contains FDA-approved aluminum hydroxide, an adjuvant to increase antibody responses…	…vaccines against diphtheria, *Haemophilus influenzae* type b, hepatitis A, hepatitis B, Lyme disease, pertussis, and tetanus.	…vaccines against cholera, influenza, Japanese encephalitis, meningococci, plague, poliovirus, rabies, and typhoid fever.
contains FDA-approved 0.85% sodium chloride (NaCl), added to make the vaccine similar to body fluids…	…vaccines against diphtheria, *Haemophilus influenzae* type b, influenza, pertussis, plague, and tetanus.	
contains trace amounts of FDA-approved formaldehyde as a preservative…	…vaccines against diphtheria, hepatitis A, influenza, Japanese encephalitis, and tetanus.	
contains trace amounts of FDA-approved benzethonium chloride added as an antimicrobial preservative…	…multidose vials of medications containing butorphanol, ketamine, orphenadrine, and thrombin.	
is listed in FDA Pregnancy Category C, no human studies conducted…	…all vaccines licensed in the United States.	(without exception)

Anthrax Vaccine: Criticism & Facts

Criticism:	**Fact:**
Anthrax vaccine protects against anthrax of the skin, but might not protect against inhaled anthrax…	The original studies of anthrax vaccine showed 93% fewer infections among vaccinated people (jointly against cutaneous and inhaled forms of anthrax). No cases of inhaled anthrax occurred among vaccinees, but five cases of inhaled anthrax occurred among unvaccinated people. This difference involved too few people to be statistically conclusive, but the trend is obvious. More recently, 44 of 45 Rhesus monkeys given one or two doses of anthrax vaccine survived aerosol challenge with anthrax. The one fatality occurred with an exposure 2 years later. It is unethical to intentionally expose human beings to aerosolized anthrax to test the vaccine.
Anthrax vaccine protects against only some strains of the disease…	Anthrax vaccine causes the body to make antibodies against the key disease-causing protein that is common to all strains of anthrax.
Adversaries might have anthrax weapons genetically engineered to elude our vaccine…	There is no evidence to support this concern. Even if it is true, our vaccine will still protect against standard anthrax. Our body armor won't stop all bullets, but we wear it anyway, to stop the ones it can.
Anthrax vaccine should have been recalled due to manufacturing problems…	FDA inspectors found deficiencies during routine visits to the manufacturing plant in 1996. Many deficiencies involved documentation of production controls. The findings caused FDA to issue a stern warning to the manufacturer. But the findings were not sufficient for FDA to order a recall, which is within FDA authority. The FDA findings were part of the reason the Secretary of Defense ordered supplemental testing of purity, potency, safety, and sterility of all batches of anthrax vaccine before use. Before these findings, the manufacturer elected to stop production with current facilities and invest over $20 million in a state-of-the-art production suite. No vaccine may be released from the new production facility until FDA confirms quality safeguards in the new facility.
Anthrax vaccine might have been rushed into use with inadequate testing…	Anthrax vaccine had all the testing that all other vaccines get before it was first used. FDA had evidence for its safety and effectiveness before the vaccine was first licensed in 1970. There were no waivers or short-cuts in the licensing of anthrax vaccine.
Anthrax vaccine might cause miscarriages…	Out of every 100 women who find out they are pregnant, 6 to 10 will have a spontaneous miscarriage. So the key question is: among vaccinated people, is the risk of miscarriage greater than 6% to 10%? We have seen no change in the miscarriage rate among

	vaccinated troops or their spouses.

Criticism:	**Fact:**
Anthrax vaccine might cause birth defects…	Out of every 100 children born in the U.S., 3 to 5 will have some form of birth defect. So the key question is: among vaccinated people, is the risk of birth defect greater than 3% to 5%? We have seen no change in the rate of birth defects among vaccinated troops or their spouses. In fact, rubella vaccine is given to avoid rubella infection, which can cause terrible birth defects and miscarriages. Rubella vaccine prevents birth defects and miscarriages.
Anthrax vaccine might cause sterility…	Often mentioned in short newspaper clippings, this criticism is mere rumor. No vaccine causes sterility. In fact, mumps vaccine is given to avoid the mumps virus, which can cause inflamed testicles and sterility. Mumps vaccine prevents sterility.
Anthrax vaccine might cause cancer…	In all of history, no vaccine was or is shown to cause any kind of cancer. Cancer occurs frequently in people who have not been vaccinated. So what you really want to know is: Is the risk of cancer higher among vaccinated people? No vaccine has ever been shown to increase the risk of cancer.
Anthrax vaccine might be one of the causes of Gulf War illnesses…	The prestigious Institute of Medicine, the Presidential Advisory Committee, the National Institutes of Health, and the Defense Science Board have independently concluded that there is no evidence that anthrax vaccine causes any illness among Gulf War veterans. They drew this conclusion, in part, because unexplained symptoms were reported both among Gulf War veterans who got the vaccine and in veterans who didn't get the vaccine.
The anthrax vaccine package insert says no testing has been performed on carcinogenic action, fertility, or pregnancy…	No vaccine has these tests conducted before the vaccine is widely used. These data can only be gathered over time as the vaccine is used in large numbers of people in routine use. These tests are not routinely performed because vaccines have not previously caused these problems.
The military doesn't care about the health of	The strength of America's Armed Forces is in the strength of our individual Service Members. We vaccinate the Force to

Military Personnel…	keep it strong. We are conducting more studies to rule out concerns about this vaccine, but abandoning this vaccine would leave the Force vulnerable to our adversaries' bio-weapons.

VAERS Reports: What They Are & What They Aren't

One of the methods used to assess unexpected adverse events after vaccination is the FDA/CDC Vaccine Adverse Event Reporting System (VAERS), originated in 1990. Other methods are used to assess common side effects. Although VAERS is limited in some regards, it is an important component of the multi-faceted surveillance system for the safety of anthrax vaccine. This chart considers what VAERS reports mean and what they don't:

VAERS Reports…	**VAERS Reports…**
…tell a story about events that happen shortly after vaccination. Some of those events are caused by the vaccine and some of those events are coincidences.	…do not necessarily mean that the vaccine caused the bad event in the report.
…lack a control group, a group to show what happens among unvaccinated people of comparable age, gender, and other characteristics.	…cannot prove that the bad event would not have happened in the absence of the vaccine.
…give scientists clues about unexpected adverse events.	…need to be followed-up with more rigorous controlled studies.
…should be submitted for all important events, without attempting to prove cause-and-effect at the individual level.	…for inconsequential events dilute the effort of VAERS analysts.
For example: Assume that "Joe" is vaccinated against influenza (gets a "flu shot"). Three days after the flu shot, "Joe" gets a runny nose, fever of 101°F, feels generally miserable, and misses two days of work.	*Possible Explanations*: a. "Joe" was infected with influenza virus before he got vaccinated, so there was no chance for the vaccine to protect. (*Vaccines don't have any protective effect in the first 10 to 14 days.*) b. "Joe" was infected with some other rhinovirus or adenovirus or other respiratory virus, but not influenza virus. (*Nobody took a viral sample to find out what kind of virus "Joe" had.*)

	c. "Joe" might have had an adverse reaction to the vaccine. Explanations (a) and (b) are quite likely, based on what we know of human physiology and microbiology. Explanation (c) is unlikely, because inactivated vaccines do not cause symptoms like "Joe" had. (*We know this from placebo-controlled studies of influenza vaccine.*) By itself, a VAERS report about "Joe" cannot tell us which explanation is correct.

Sources of Reliable Vaccine Information

Source Telephone Internet

Centers for Disease Control

& Prevention (CDC) 404-639-3311 www.cdc.gov/nip/

Disease Information Hotline 404-332-4555 www.cdc.gov/diseases/immun.html

Fax-back information service 888-CDC-FAX

Recorded information 800-CDC-SHOT

Vaccine specialist, in English 800-232-2522

en Español 800-232-0233

Vaccine Adverse Events Reporting www.fda.gov/cber/

System (VAERS) 800-822-7967 vaers/vaers.html

Immunization Action Coalition 651-647-9009 www.immunize.org

(offers "IAC-Express" email newsletter free)

Immunization Gateway:

Your Vaccine Fact-Finder www.immunofacts.com

(free direct links to authoritative documents)

Infectious Diseases Society of America www.idsociety.org/vaccine/

(offers "Vaccine Initiative Information index.html

Network" news summary free

three times a week)

Institute for Vaccine Safety,

Johns Hopkins University 410-955-2955 www.vaccinesafety.edu

National Coalition for www.medscape.com/

Adult Immunization 301-656-0003 affiliates/NCAI/

National Foundation for Infectious Diseases 301-656-0003 www.nfid.org/

Public Affairs Offices, Medical Departments of: www.anthrax.osd.mil

U.S. Army 703-681-6822

U.S. Navy 202-762-3222

U.S. Marine Corps 202-614-6101

U.S. Air Force 202-767-4813

U.S. Coast Guard 202-267-0920

Glossary

Acellular: Free of cells, referring to a vaccine that contains certain bacterial components, but not entire cells. Acellular vaccines typically cause fewer side effects than whole-cell vaccines.

Active immunity: Persistent immunity from natural infection or from vaccination. Contrast with passive immunity, temporary immunity derived from administering someone else's antibodies.

Adsorbed: Attachment to the surface of an object. Several vaccines are adsorbed onto the surface of aluminum compounds, to increase the body's antibody response to the vaccine.

Adjuvant: A substance that aids another substance in its action (e.g., aluminum hydroxide in vaccines).

Adverse event: An undesirable event associated with an exposure to a medication, an

environmental chemical, or some other stimulus, for which a cause-and-effect relationship with that exposure has not yet objectively been determined.

Adverse reaction: An undesirable event for which objective evidence is available to establish a cause-and-effect link between an exposure (such as to a medication or an environmental chemical) and an adverse outcome. Synonymous with side effect.

Allergen: A substance that causes an allergy.

Allergy: An inappropriate and harmful response of the immune system to normally harmless substances.

Anaphylaxis: A severe allergic (hypersensitivity) reaction. May include hives or swelling of the mouth, difficulty breathing, drop in blood pressure, shock, or other symptoms. Synonymous with anaphylactic reaction.

Antibody: Protein produced by plasma cells, in response to an antigen. Antibodies bind with antigens on bacteria and viruses to protect against infection. Synonymous technical terms are immune globulin or immunoglobulin.

Antigen: A substance that can combine with an antibody. The "active ingredient" in a vaccine.

Antiserum: Serum that contains antibodies.

Antitoxin: Any antibody that binds and inactivates a toxin.

Attenuated: Weakened. A type of live vaccine containing microbes too weak to cause disease, but potent enough to provoke a protective antibody response.

Bacterium (singular), bacteria (plural): Single-cell microorganisms.

Basic series: A series of several vaccine doses initially needed to establish immunity.

B-cells: Also called B-lymphocytes. Small white blood cells crucial to immune defenses. Some B-cells develop into plasma cells that manufacture antibodies.

Biologicals: Category of complex medications derived from biological sources (e.g., animals, microbes). Synonymous with biologics.

Biological warfare, biological terrorism: Use of biological agents (e.g., viruses, bacteria, toxins, molds) to kill or injure military personnel or civilians.

Biotechnology: The use of living organisms or their products to make or modify a substance. Biotechnology includes recombinant DNA techniques (genetic reengineering).

Culture: The growth medium used to sustain and reproduce bacteria and viruses.

Efficacy: Ability to prevent, treat, diagnose, or otherwise manage a disease or other medical condition.

Endemic: Common in an area. An endemic disease is one that is always present, but at not at epidemic levels.

Epidemic: A disease that spreads widely through a region or country in a short period of time.

Epidemiology: The study of the distribution of health in a population of people.

Excipients: Inactive ingredients in a medication necessary for production, such as preservatives, adjuvants, and residues of production processes.

Filtrate: A liquid that has passed through a filter, leaving cells and large molecules behind.

Formaldehyde: A powerful antiseptic and disinfectant, often used to kill bacteria or viruses in vaccine manufacturing. Formalin is a solution of formaldehyde in water.

"Gamma globulin:" An obsolete term for immunoglobulin.

Germ: See microbe.

Guillain-Barré syndrome (GBS): An uncommon illness involving paralysis. GBS is caused by viral infections, medications, and other stimuli. GBS is usually self-limited and reversible. Though most people with GBS recover without residual weakness, approximately 5% of cases are fatal. Also known as Landry-Guillain-Barré syndrome, Landry-Guillain-Barré-Strohl syndrome, and polyradiculoneuropathy.

Herd immunity: The relative degree of susceptibility of a group or community to a disease. The resistance of a community to infection and spread of an infectious agent, derived from the resistance to infection of a high proportion of individual members of the community.

Humoral immunity: Immune protection provided by soluble substances (like antibodies) that circulate in the body’s fluids or "humors," primarily serum and lymph.

Hypersensitivity: An exaggerated or inappropriate response that causes tissue damage. A group of responses more commonly (and imprecisely) called allergy.

Immediate hypersensitivity: The proper name for what is commonly called an allergic reaction. It consists of an immediate reaction (within 15 minutes or less) involving swelling and redness, and/or anaphylaxis. Examples include allergies to pollen, foods, and insect stings. A severe case of immediate hypersensitivity is called anaphylaxis.

Immune: Resistant to infection or disease.

Immune globulin: A sterile solution containing antibodies, generally used for maintenance of certain immunodeficiencies or for passive immunization against specific diseases. See antibody.

Immunization: The process of administering a vaccine and becoming immune, protected from an infection. CDC considers immunization and vaccination to be synonymous. Purists argue that vaccination is the process of administering the vaccine, reserving immunization for the process of becoming immune (that distinction arises because no vaccine is 100% protective).

Immunity: Resistance to infection or disease, usually associated with antibodies or certain cells in the blood stream that counteract microbes or toxins.

Immunogenicity: Capacity to cause the body to produce antibodies.

Immunoglobulins: A family of large proteins, also known as antibodies. See antibody.

Immunosuppression: Impairment of immune responses.

Inactivated vaccine: A vaccine composed of killed bacteria or isolated bacterial or viral components that will induce active immunity.

Infection: Habitation of microbes within a part of the body. Infection is usually synonymous with disease, but not always. For example: a person with a positive skin test has been infected with tuberculosis, but may not develop disease unless the tuberculosis bacteria spread away from their initial point of entry.

Inflammation: Redness, warmth, swelling, and pain in response to infection or other causes, resulting from increased blood flow and an influx of immune cells and fluids.

Inoculation: Injection of a microorganism, serum, or toxoid into the body, not necessarily for the purpose of immunization. Regarding vaccines, immunization or vaccination are more precise terms.

Intramuscular: Into the muscle. A route of administration for many vaccines.

Isotonic: Having the same tonicity, that is, having the same osmotic pressure as body fluids.

Jet injection: The technique of injecting a drug through the skin without puncturing it. Jet injectors use a nozzle that ejects a fine spray of liquid with sufficient speed and pressure to penetrate the skin. [Mechanical paint sprayers use a similar mechanism.] This method is capable of immunizing large numbers of people quickly and economically, but is capable of transmitting disease, if performed improperly.

Labeled: Included in the product insert for a given medication. To be "labeled," a fact must be scientifically proven to the satisfaction of the FDA.

"Liberty Measles:" Patriotic name in the United States for rubella during World War I (otherwise called "German measles").

Live vaccine: A vaccine containing live, weakened bacteria or viruses that induces active immunity. These vaccines can be dangerous in an immunocompromised patient who cannot mount an effective defense against even weakened microorganisms.

Medication: A substance used to diagnose, prevent, treat, cure or mitigate a disease or health condition.

Memory cells: Sensitized T- and B-lymphocytes (cells) generated during an immune response to a specific antigen. Memory cells are long-lived and allow an accelerated immune response when the host is challenged again by the same antigen.

Microbe: A microorganism or germ, primitive living organisms. The three major types of microbes are bacteria, viruses, and funguses.

Microorganism: See microbe.

Pandemic: A wide-ranging epidemic, spanning nations.

Passive immunity: Temporary immunity resulting by administering antibodies obtained from other people or animals. Contrast with active immunity, persistent immunity derived from natural infection or from vaccination.

Placebo: An inert substance, used in experimental research to mimic drugs or vaccines being tested. Use of a placebo increases the likelihood that differences between an intervention group and a placebo group are due to the intervention itself, and not due to the research personnel or conditions.

Potency: Strength.

Prophylaxis: Prevention.

Protein: Organic compounds made up of amino acids.

Recombinant: Involving the recombination of the genes of two organisms. Typically, gene fragments of one organism are inserted into the genetic material of another organism, such as to produce a certain protein that would not otherwise be produced.

Relative risk: The ratio of the risk of an outcome among an exposed group to the risk among an unexposed group.

Safety: Condition where the benefits of a medication outweigh adverse effects it may cause. A drug poses a reasonably low risk of harm, injury, or loss when used in an appropriate manner.

Serum: The fluid component of blood, containing any antibodies that were present in the whole blood. The clear liquid that separates from blood when it is allowed to clot. Blood which has had cells removed.

Subcutaneous: Involving the fat layer beneath the skin. A route of administration for many vaccines.

Subunit vaccine: A vaccine that uses merely one or a few components of an infectious agent, rather than the whole microbe, to stimulate an immune response.

Systemic: Generally, having an effect throughout the body. Systemic reactions to vaccination occur at sites distant from the injection site. Systemic reactions can range from mild (headache) to severe (anaphylaxis).

Toxin: A poison produced by a living organism.

Toxoid: A modified toxin. Toxoids are rendered nontoxic, but retain the ability to stimulate production of antitoxins (i.e., specific antibodies against the unaltered toxin).

Vaccination: Literally, inoculation with cowpox virus (originally called vaccine virus) to prevent smallpox. Broadly, to deliver any vaccine to develop active immunity. See Immunization.

Vaccine: That category of medications used to induce active immunity.

Variolation: An archaic method of protecting people against smallpox, by inoculating materials from smallpox eruptions into the skin.

Virus (singular), viruses (plural): A simple microbe, consisting only of nucleic acid surrounded by a protein coat. Multiplication of viruses is referred to as replication, with reproduction reserved for bacteria and more complicated cells. A virus is incapable of copying itself on its own; it requires living cells to replicate.

List of Abbreviations

AAP: American Academy of Pediatrics

ACIP: Advisory Committee on Immunization Practices, civilian experts who advise the CDC

ACP: American College of Physicians

AFEB: Armed Forces Epidemiological Board, civilian experts who advise the DoD

AMSA: Army Medical Surveillance Activity, a division of USACHPPM

APHIS: Animal & Plant Health Inspection Service, a division of USDA

AVEC: Anthrax Vaccine Evaluation Committee, civilian medical experts who evaluate reports of adverse events after anthrax vaccination; coordinated through VICP and HRSA

AVIP: Anthrax Vaccine Immunization Program

BCG: Bacillus Calmette-Guérin, a kind of tuberculosis vaccine

CBER: Center for Biologics Evaluation & Research, a division of FDA responsible for vaccines and antibodies

CDC: Centers for Disease Control & Prevention, Atlanta, GA; division of U.S. Public Health Service (PHS)

CDER: Center for Drug Evaluation & Research, a division of FDA

DHHS: U.S. Department of Health & Human Services

DMSS: Defense Medical Surveillance System, a set of medical databases

DoD: U.S. Department of Defense

DPT: See DTP

DT: Diphtheria & tetanus toxoids, pediatric strength

DTaP: Diphtheria & tetanus toxoids with acellular pertussis vaccine

DTP: Diphtheria & tetanus toxoids with pertussis vaccine, pertains to both DTwP and DTaP generically

DTwP: Diphtheria & tetanus toxoids with whole-cell pertussis vaccine

FDA: Food & Drug Administration, Rockville, MD; division of U.S. Public Health Service (PHS)

GBS: Guillain-Barré syndrome, also Group B streptococci

HAV: Hepatitis A virus, also hepatitis A vaccine

HBV: Hepatitis B virus, also hepatitis B vaccine

HCFA: Health Care Financing Administration, a division of DHHS

HHS: U.S. Department of Health & Human Services

HRSA: Health Resources & Services Administration, a division of DHHS

Hib: *Haemophilus influenzae* type b, a species of bacteria

IM: Intramuscular, injection into a muscle

IND: Investigational new drug waiver of FDA rules, the status of a medication being tested to determine if it is safe and effective

IOM: Institute of Medicine, a constituent of the National Academy of Sciences

IPV: Inactivated poliovirus vaccine

MHSS: Military health service system

MMR: Measles-mumps-rubella vaccine

MMWR: *Morbidity & Mortality Weekly Report*, a publication of the CDC

MTF: Medical treatment facility

NIH: National Institutes of Health

NIAID: National Institute of Allergy & Infectious Disease

OPV: Oral poliovirus vaccine

PHS: U.S. Public Health Service, a component of the DHHS

SC: Subcutaneous, injection into the fat layer under the skin

Td: Tetanus & diphtheria toxoids, for adult use

USACHPPM: U.S. Army Center for Health Promotion & Preventive Medicine

USAMMDA: U.S. Army Medical Materiel Development Activity

USAMRIID: U.S. Army Medical Research Institute of Infectious Diseases

USDA: U.S. Department of Agriculture

VA: Veterans Administration, more properly the U.S. Department of Veterans Affairs

VAERS: Vaccine Adverse Event Reporting System, operated jointly by FDA and CDC

VFC: Vaccines For Children, a federal program to provide vaccines to children

VICP: Vaccine Injury Compensation Program, a no-fault program operated by the Health Resources & Services Administration of DHHS

VIS: Vaccine Information Statement, a brief summary of vaccine benefits and risks

VSD: Vaccine Safety Datalink, CDC program to assess uncommon adverse events after vaccination

WHO: World Health Organization

WRAIR: Walter Reed Army Institute of Research

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Comparison of Adverse Events After Anthrax Vaccine to Other Vaccines

Symptom	Anthrax vaccine, licensed 1970 Occ. Health (a) Surveys (b)		Influ-enza Vaccine (c)	Corresp-onding placebo (c) ("inert")	Hepatitis A vaccine, lic. 1995	Lyme disease vaccine, lic. 1998	Corresp-onding Lyme placebo ("inert")	Yellow–fever vaccine, lic. 1953	Rabies vaccine (*RabAvert*) lic. 1997	Typhoid polysacch. (*Typhim Vi*), lic. '94	Corresp-onding placebo ("inert")	Typhoid (whole-cell) vaccine, lic. 1944
At Injection Site ("Local")	*											
Soreness / tenderness	30%	60% to 80%	64%	24%	53% to 56%	94%	68%			97%-- 98%	6%-13%	6--40%
Pain		8% to 19%			22% to 51%	22%	7%		34% to 84%	27%--56%	3%--7%	
Hardness ("induration")	20%				1% to 10%					5% to 18%	0%	50-80%
Redness ("erythema")	5% to 30%	8% to 51%			1% to 13%	42%	21%			3% to 11%	0%	50-80%
Swelling	5% to 20%	4% to 13%			1% to 14%	30%	11%					
Swollen lymph nodes									15%			
Itching		5% to 63%										
Lump, knot, nodule	"a few"	29% to 89%										
Beyond Injection Site ("Systemic")	*											
Headache	0.5% to 4%	14% to 25%	11%	14%	14% to 16%	39%	37%	2% to 5%	10% to 52%	11%--27%	13--16%	14-29%
Dizziness / vertigo					< 1%	1%	1%		10% to 15%			
Fatigue		20% to 28%	19%	19%	1% to 10%	41%	33%					
Malaise	< 0.2% to 4%	6% to 17%	16%	18%	1% to 10%			up to 10%	15% to 25%	4% to 37%	3—15%	
Fever > 99.5°					1% to	4%	2%		"uncommon"	0% --1.9%	0%--3%	

F					10%							
Fever, unspecified	<0.2% to 0.5%	1% to 5%	6%	6%		3%	2%	2% to 5%		2% to 11%	0%	
Chills	<0.2% to 0.5%	2% to 6%				2%	1%		"rare"			
Urticaria, other rashes	4%	16%			< 1%	12%	5%					
Nausea		3% to 9%			<1% to 10%	1%	1%		"uncommon"	0% to 8%	0%--4%	
Appetite loss ("anorexia")					1% to 10%				"uncommon"			
Diarrhea		5%			< 1% to 2%				"uncommon"	0% to 3%	4%	
Joint ache ("arthralgia")	0.5% to 4%	12% to 15%			<1% to 6%	26%	16%					
Muscle ache ("myalgia")	0.5% to 4%	3% to 34%	6%	6%	< 1% to 2%	5%	3%	2% to 5%	38% to 53%	2% to 7%	0%	
Insomnia					< 1%							
Photophobia					< 1%							
"Flu"-like symptoms						3%	2%					

(a) Data from Brachman study, 1960s CDC study, 1950s-70s Fort Detrick data, *Federal Register* 1985;50:51002-117, anthrax vaccine product labeling ("package insert").

(b) Data from 1998-99 Tripler Army Medical Study, 1998-99 Korea Study, 1993 Fort Bragg, 1990s Fort Detrick data.

(c) Data from Nichol KL, Lind A, Margolis KL, et al. The effectiveness of vaccination against influenza in healthy, working adults. *N Engl J Med* 1995;333:891.

* Figures report men and women jointly. For surveys that report male and female data separately, temporary adverse events after anthrax vaccination are reported more often among women than men, especially injection-site reactions. This difference is believed to be related to subcutaneous injection.

Data in other columns are derived primarily from product labeling ("package inserts").

Data shown reflect proportion with symptom, without regard to magnitude. Data shown reflect experiences in adult vaccine recipients.

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