INFORMATION PAPER

DHA-IHD
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SUBJECT: Influenza Infection and Influenza Vaccines

1. Purpose. To describe influenza disease and supporting vaccines to prevent its spread.

2. Facts.

    a. Microbiology. Influenza viruses are divided into three genera, *Influenzavirus* A, *Influenzavirus* B, and *Influenzavirus* C based on antigenic differences. *Influenzavirus* A and *Influenzavirus* B cause the most serious human disease. Influenza A viruses are further divided on the basis of the two main surface structures, hemagglutinin (HA) and neuraminidase (NA). Hemagglutinin is the major antigen (structure) against which the host's protective antibody response is directed and is responsible for attachment of influenza viruses to the cell surface during early stages of infection. Neuraminidase is less abundant on the viral surface and facilitates release of mature virus from infected cells. Antibody to NA is believed to restrict virus spread and reduce severity of the influenza infection. The capacity of influenza A and B viruses to undergo gradual mutation in their HA and NA proteins, complicates vaccination against the disease. This ongoing process of "antigenic drift" produces continual novel influenza strains that ensure a constant pool of susceptible hosts, resulting in seasonal influenza. Annual review is required to keep up with continually changing influenza viruses and ensure the seasonal influenza vaccine formulation includes the most recently circulating influenza strains.

    b. Disease. Influenza is a contagious respiratory illness caused by influenza viruses. The virus is spread through aerosolized respiratory droplets during close contact with an infected person or animal or through contact with a contaminated object. The incubation period is commonly 2 days, but ranges from 1-4 days. Due to this short incubation period, influenza outbreaks may escalate very quickly, especially in highly susceptible populations. Influenza illness is characterized by the abrupt start of fever, sore throat, headache, myalgia, non-productive cough and extreme fatigue with major symptoms lasting an average of 2-3 days. Fever usually ranges between 100° and 104°F. Illness typically improves within a week, but cough and malaise may persist for 2 or more weeks. The most common complications of influenza is pneumonia but may include exacerbation of underlying chronic pulmonary and cardiopulmonary

diseases, such as chronic obstructive pulmonary disease, asthma, and congestive heart failure.

c. Epidemiology. In temperate climates, influenza activity occurs during the late autumn and winter months. However, in tropical climates, influenza can occur year round. During influenza seasons, an estimated 5-20% of the U.S. population can develop influenza; within institutions such as nursing homes an infection rate of 40-50% is not unusual. In communities, influenza cases often appear first among school-age children. Infection rates usually are the highest in this group; whereas rates of serious disease and complications are highest among the elderly, the very young, and those with certain underlying chronic conditions. In the U.S., influenza results in an estimated 25 million reported cases, over 150,000 hospitalizations due to serious complications, and up to 30,000 deaths annually.

d. Strains. Influenza season is an annually recurring time period characterized by the prevalence of outbreaks of influenza. The season occurs during the cold half of the year in each hemisphere. In the Northern Hemisphere, the flu season is generally October through May, usually peaking in February. In the Southern Hemisphere, the flu season is generally May through October, usually peaking in August. Each year the strains prevalent in laboratory samples from the Southern and Northern hemispheres are submitted and scientists at the World Health Organization estimate which strains of influenza virus will most likely circulate during the next influenza season. The identified strains are then used in the annual influenza vaccine formulation. Since 2000, the vaccine strain composition between the Southern and Northern Hemisphere vaccines have varied by at least one strain 55%-63% of the time. The influenza vaccine strains used during the current year for the Northern Hemisphere can be found at the CDC's Influenza webpage (see https://www.cdc.gov/flu/season/index.html under the Flu Season tab). The strains recommended for the Southern Hemisphere can be found at the WHO's Influenza webpage (see https://www.who.int/influenza/vaccines/virus/en/ under "vaccine viruses")

e. Vaccines. Multiple varieties of Northern Hemisphere influenza vaccine and one vaccine for Southern Hemisphere influenza are available in the United States. All influenza vaccines must be stored in a refrigerator between 2-8°C (36-46°F) upon receipt and used before the expiration date on the package/vial/sprayer label.

(1) Injectable: All trivalent and quadrivalent inactivated influenza vaccine (IIV3/IIV4), cell culture-based (ccIIV4), recombinant hemagglutinin (RIV3/RIV4), and adjuvanted (aIIV3) vaccines are administered by intramuscular injection.

(2) Intranasal: Live, attenuated (weakened) influenza vaccine, quadrivalent (LAIV4) vaccine is administered 0.1 mL (1/2 syringe sprayer) into each nostril of the nose for a total dose of 0.2 mL.

f. FDA-licensed Influenza Vaccines are listed in the following table. To see this year's DOD-procured influenza vaccines, go to https://health.mil/flu.

Vaccine	Abbreviation	Manufacturer	Supplied as*	Age Indication	Dosage
Afluria	(IIV4)	Seqirus	PFS (0.5 mL) MDV (5 mL)	6-35 mos	0.25mL
				36 mos-8 yrs	0.5 mL
				≥9 yrs	0.5 mL
Fluad	(aIIV3)	Seqirus	PFS (0.5 mL)	≥65 yrs	0.5 mL
Fluarix Quad	(IIV4)	GSK	PFS (0.5 mL)	≥6 mos	0.5 mL
Flublok Quad	(RIV4)	Sanofi Pasteur	PFS (0.5 mL)	≥18 yrs	0.5 mL
Flucelvax Quad	(ccIIV4)	Seqirus	PFS (0.5 mL) MDV (5 mL)	≥4 yrs	0.5 mL
Flulaval Quad	(IIV4)	GSK	PFS (0.5 mL) MDV (5 mL)	≥6 mos	0.5 mL
FluMist	(LAIV4)	AstraZeneca	PFS (0.2 mL)	2-49 yrs	(0.1cc each nostril)
Fluzone Quad (Northern and Southern Hemisphere)	(IIV4)	Sanofi Pasteur	PFS (0.25 mL) PFS (0.5 mL) MDV (0.5 mL) MDV (5 mL)	6-35 mos	0.25 mL or 0.5 mL+
				≥6 mos	0.5 mL
Fluzone - HD	(IIV3-HD)	Sanofi Pasteur	PFS (0.5 mL)	≥65 yrs	0.5 mL

* MDV = Multi-Dose Vial, PFS = Prefilled Syringe; MDVs may contain thimerosal.
\+ Children 6-35 mos of age may receive either 0.25 mL or 0.5 mL of Fluzone.
All flu vaccines require refrigeration between 2-8°C; do not freeze

g. Immunization. ACIP continues to recommend annual influenza vaccinations for all persons 6 months of age and older. Protection of persons at higher risk for influenza related complications should continue to be a focus of vaccination efforts to include children 6 months through 4 years, those aged 50 years and older, pregnant women, those with chronic health conditions and/or who are immunosuppressed.

h. Adverse Events. Local reactions are the most common side effects after administration of IIV. Reactions include soreness, redness and swelling and generally last 1-2 days. Systemic reactions include fever, chills, muscle aches and fatigue. Side effects after receipt of LAIV include cough, runny nose, nasal congestion, sore throat, and chills. Hypersensitivity (allergy) to vaccine components is rare, but may occur.

i. DoD Policy. Influenza vaccination is mandatory for all Active Duty, Guard, and Reserve component personnel and will be administered in accordance with Service-specific guidelines and immunization regulation.

In general, Northern Hemisphere influenza vaccine will be administered to all Active Duty, Guard, and Reserve personnel permanently or temporarily assigned to an area designated as a Northern Hemisphere influenza zone during Influenza season, generally between October and April. Vaccination against Northern Hemisphere strains may continue until expiration date on the vaccine vial. Southern Hemisphere influenza vaccine will be administered to all Active Duty, Guard, and Reserve personnel, permanently or temporarily assigned to an area designated as a Southern Hemisphere influenza zone during Influenza season, generally between April and October. Vaccination against Southern Hemisphere strains may continue until expiration date on the vaccine vial. Northern and Southern Hemisphere-designated countries will be identified by the Defense Health Agency or the Type/Combatant Command to which an individual may be permanently or temporarily assigned.
Personnel traveling to either the Northern or Southern Hemisphere during that hemisphere's influenza season should be vaccinated at least two weeks prior to entry into the region. Northern and Southern Hemisphere Influenza vaccines should be separated by at least 28 days.

While on-base immunization is preferable for Readiness tracking purposes, should an active duty service member receive FluMist or an injectable influenza vaccine at an off-base site, it will count as a valid vaccination for readiness purposes. Verification of vaccination from a local provider is required for documentation. In accordance with DoD Instruction 6205.02, all health-care personnel (HCP) working in DoD medical treatment facilities are required to receive the annual seasonal influenza immunization or obtain an exemption (i.e., medical or administrative). For HCP working under contract to any DoD Component, seasonal influenza immunizations may be provided by the DoD medical treatment facilities, if stated in the contract agreement. Otherwise, contracting companies will provide influenza vaccines to their employees. [Note; Service guidance and local policies may outline more specific influenza vaccination requirements for healthcare personnel.

3. References.

   a. Multiple resources (e.g., package inserts, Vaccine Information Statements, DOD and Service-specific policies) assembled by the Immunization Healthcare Division: www.health.mil/flu.
   b. Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States