

Vaccines for Seniors:
Shingles, Pneumonia, Influenza
Osher Lifelong Learning Institute
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Important Web Sites

Centers for Disease Control & Prevention (CDC)

- <http://www.cdc.gov/index.htm>
- <http://www.cdc.gov/DiseasesConditions/>

Food and Drug Administration (FDA)

- <http://www.fda.gov/>
- <http://www.fda.gov/cber/vaccine/licvacc.htm>

Brief History of Human Vaccines

- **1100's** – Variolation in China
- **1798** – Smallpox (live attenuated)– Edward Jenner
- **1885** – Rabies (live attenuated) –Louis Pasteur
- **1896-7** – Typhoid, cholera, plague (killed whole organisms)
- **1923, 1927** – Diphtheria, tetanus (purified protein)
- **1936** – Influenza (killed whole organisms)
- **After WWII** –
 - Vaccines produced in cell culture (e.g., measles, mumps, rubella)
 - Purified polysaccharide (e.g., pneumococcus, meningococcus)
 - Recombinant proteins (e.g., hepatitis B)
 - Polysaccharide – protein conjugates (e.g., Hib, pneumococcus)

Vaccine Successes

<u>Disease</u>	<u>Annual Cases Baseline 20th Cent.</u>	<u># Cases 1998</u>	<u>% Decrease</u>
Smallpox	48, 164	0	100
Diphtheria	175, 885	1	100
Pertussis	147, 271	7405	95
Tetanus	1,314	41	97
Polio	16,316	1	100
Measles	503,282	100	>99
Mumps	152,209	666	>99
Rubella	47,745	364	>99
Congenital	823	7	>99
<i>H.influenzae b</i>	20,000	61	>99

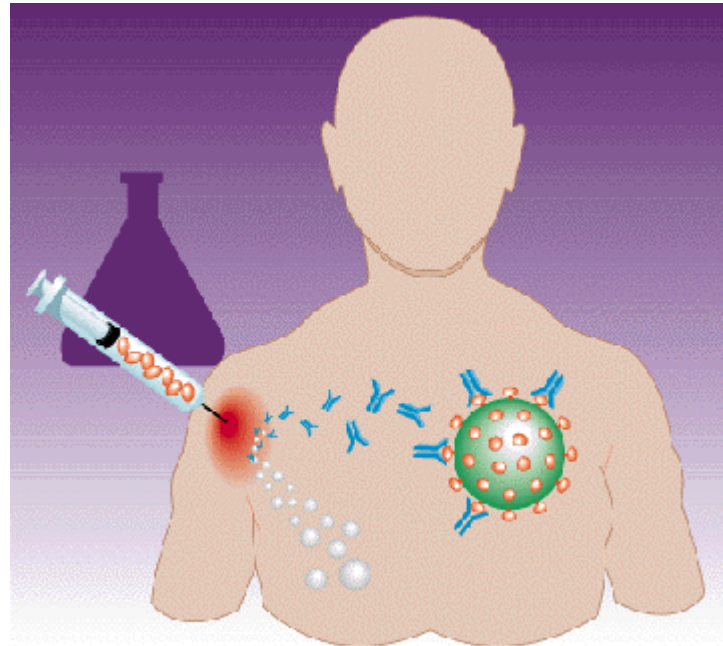
Types Of Infections

- *Bacteria* - Widely distributed group of microscopic prokaryotic **mainly single-celled organisms**, many of which are symbiotic or pathogenic in animals and plants, *e.g.*, pneumococcus, anthrax
- *Virus* - A submicroscopic organism that can **multiply only inside living host cells**, has a non-cellular structure lacking any intrinsic metabolism and usually comprising a single DNA or RNA molecule inside a protein coat, and is frequently pathogenic, *e.g.*, influenza, varicella
- *Parasite* - An animal or plant which **lives in or on another** and draws its nutriment directly from it, harming it in the process, *e.g.*, malaria⁵

Vaccines For Preventive Infectious Disease Indications

- Generally, preparations containing all or a portion of a disease-causing organism or the nucleic acid encoding one or more proteins from that organism
- Vaccines intended to induce an immune response to prevent an infectious disease

How Vaccines Work



The vaccine is made from an antigen isolated or produced from the disease-causing microorganism. The vaccine is injected into the body. The B cells in the blood stream respond to the antigen by producing antibodies. The antibodies bind to the antigen to "neutralize" or inactivate it. In addition, memory cells are produced and remain ready to mount a quick protective immune response against subsequent infection with the same disease causing agent.

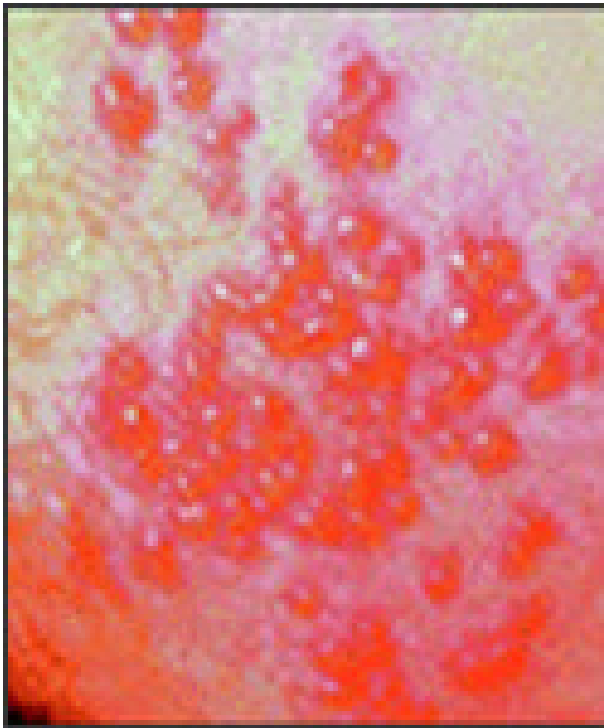
Types of Preventive Vaccines

- **Live, attenuated:** *Measles, Mumps, Rubella, **Varicella**, Yellow Fever, Salmonella Ty21A, Influenza, Smallpox*
- **Inactivated:** *Hepatitis A, **Influenza**, Inactivated Polio, Rabies*
- **Crude or purified antigens derived from living or killed cells:** *Diphtheria and Tetanus Toxoids, Acellular Pertussis, **Polysaccharides**, Anthrax*
- **Conjugate vaccines:** *Meningococcal, Haemophilus and Pneumococcal PS-Protein Conjugate*
- **Recombinant-DNA derived:** *Hepatitis B, Human Papillomavirus (HPV) Vaccine*
- **Vectored and DNA vaccines:** *(Investigational)*

What Is Shingles (herpes zoster)?

- Painful skin rash caused by the varicella zoster virus (VZV), the same virus that causes chickenpox (virus hides in nerve cells until reactivated)
- Rash (one side): blisters that scab after 3-5 days, rash clears within 2-4 weeks
- Before rash: pain, itching, tingling; also fever, headache, chills, upset stomach
- Rarely: pneumonia, hearing problems, blindness, brain inflammation
- Estimated 1 million shingles cases each year

Pictures of Shingles Rash (from CDC website)



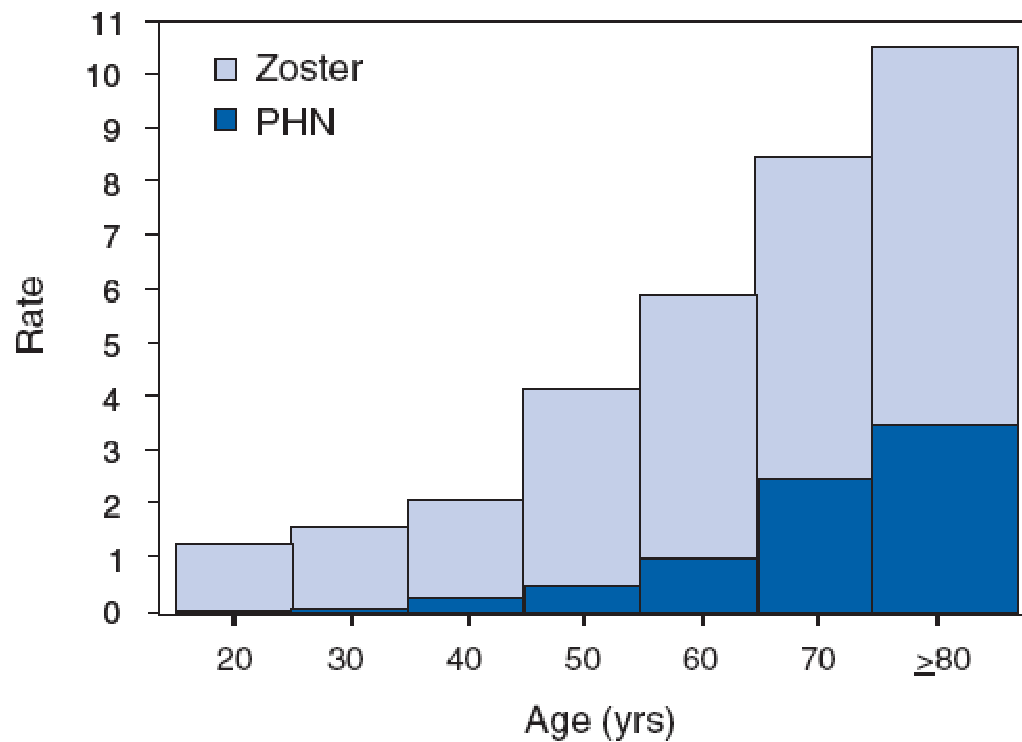
Shingles (cont.)

- Post-herpetic neuralgia (PHN): severe pain even after rash clears up (~1 in 5 w/ zoster)
- Susceptible: anyone who has recovered from chickenpox, increases with age (50% of those who live to 85 will have shingles)
- Usually only one episode, but second or third case can occur (rarely)
- Treatment: Antiviral drugs
 - Acyclovir (Zovirax); valacyclovir (Valtrex); famcyclovir (Famvir)
- Prevention: varicella zoster vaccine - Zostavax® (Merck; May 2006)

Occurrence of Shingles by Age

(MMWR, June 6, 2008, Vol. 57)

FIGURE 3. Rate* of zoster and postherpetic neuralgia (PHN)[†], by age — United States



*Per 1,000 person-years.

[†]Defined as ≥ 30 days of pain.

The Shingles (Zoster) Vaccine

- Zoster Vaccine, Live (Oka/Merck strain) - ZOSTAVAX[®], approved May 2006
- Attenuated (weakened) through serial growth in cultures – produce immunity w/o disease
- Sterile preparation for subcutaneous injection
- $\geq 19,400$ pfu (viable virus particles) in 0.65ml (14-fold more than in chickenpox vaccine)
- Also: sucrose, hydrolyzed porcine gelatin, salts, residual (small) amounts of cell protein and DNA, trace amounts of neomycin and bovine calf serum

The Shingles Vaccine – Efficacy and Safety

Efficacy:

- In clinical trial, prevented shingles in 51% of people 60 years of age or older
- For individuals 60-69, occurrence reduced 64%
- Reduced post-herpetic neuralgia in 67% of study participants
- Reduced PHN pain for 182 days by 73%

Side Effects:

- Most common: redness, pain, tenderness, swelling at injection site; also itching and headache (usually mild)
- Potential allergic reaction (rare)

Who Should Get the Shingles Vaccine?

- Persons aged ≥ 60 years, to reduce the risk of shingles and its associated pain
- Can be given to people who have already had an episode of shingles
- Not intended to treat people who already have shingles

Who Should NOT Get the Shingles Vaccine?

- Allergic to vaccine ingredients, including gelatin and neomycin
- Have a weakened immune system
 - HIV/AIDS
 - High dose steroids, immunosuppressive drugs
 - Cancer treatment, e.g., radiation or chemotherapy
 - Cancer of the lymph, bone, blood (leukemia or lymphoma)
- Active, untreated tuberculosis
- Pregnant or plan to become pregnant

What Are Special Issues for the Shingles Vaccine?

- Vaccine must be stored and transported frozen and protected from light
- Availability limited?
- Relatively expensive: ~\$125 - \$150/dose
- Not covered by Medicare Part B (covers flu and pneumonia vaccines), instead reimbursed through Medicare Part D

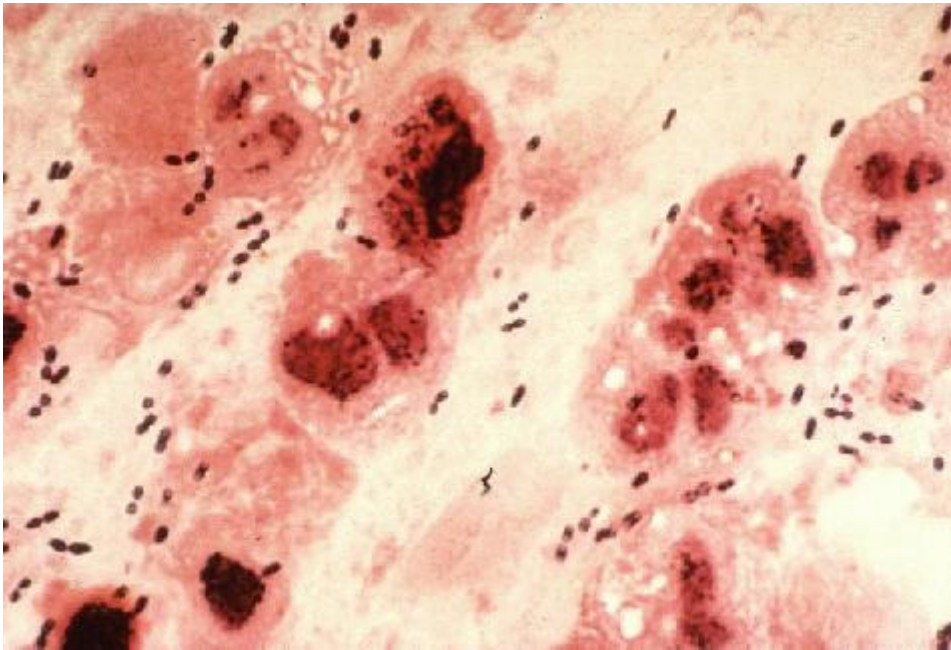
What Is Pneumococcal Disease?

- Caused by bacterium *Streptococcus pneumoniae*
- Pneumonia – invade lungs
- Bacteremia – invade blood stream
- Meningitis – invade tissues and fluids of the brain and spinal cord

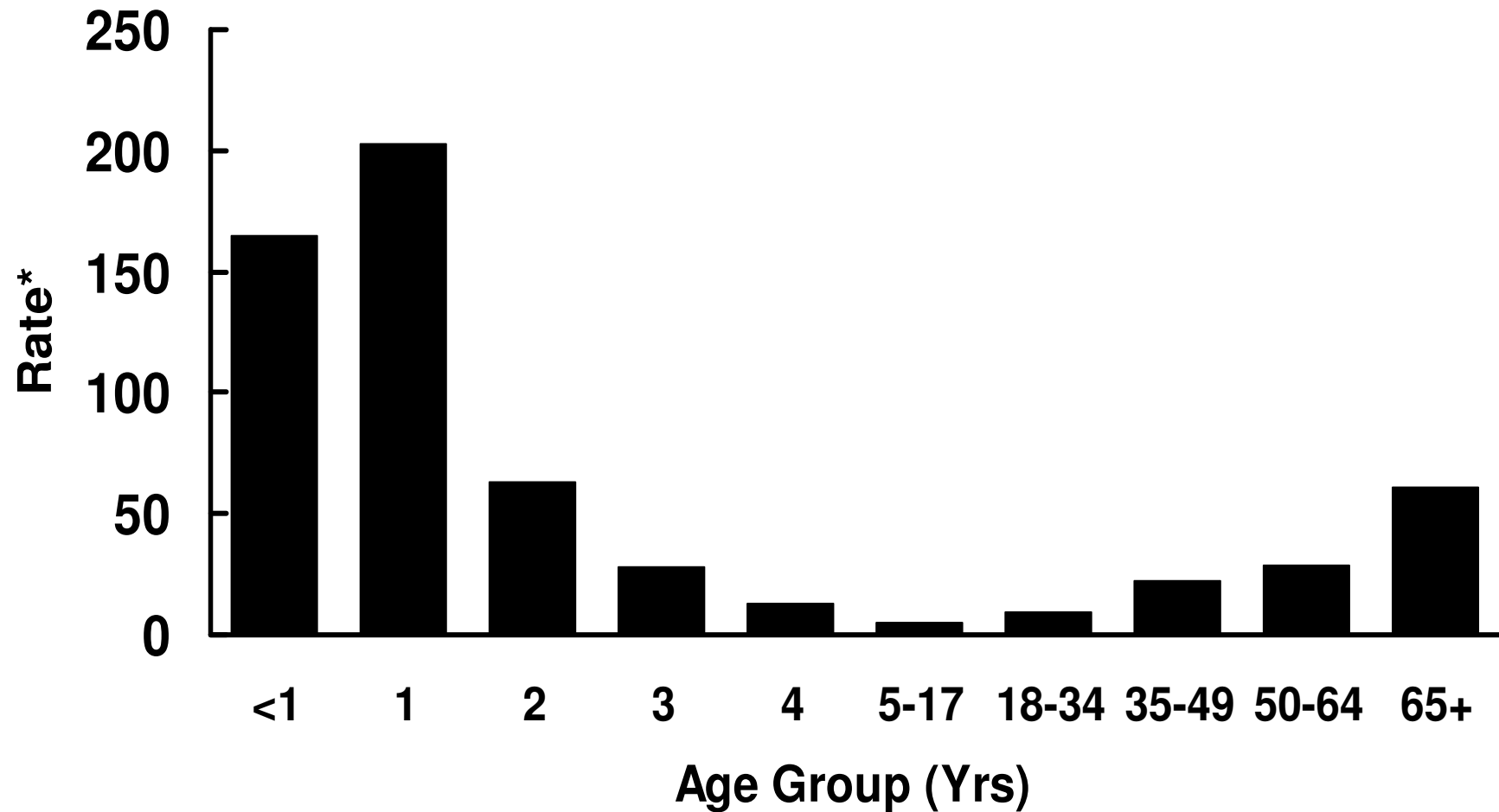
Pneumococcal Disease

- Pneumonia: high fever, cough, shortness of breath, chest pain; deaths 5-7%, higher in elderly
- Bacteremia: fever, feeling poorly, plus joint pain and chills; deaths 20% - 60% (elderly)
- Meningitis: stiff neck, fever, thinking slowly or not clearly, sensitivity to light; deaths 30%-80%
- Major virulence factor: Complex polysaccharide capsule, >90 serotypes

**L) Gram stain of *S. pneumoniae* in film of sputum from a case of lobar pneumonia;
R) Capsule swelling of antibody-treated bacteria**



Invasive Pneumococcal Disease Incidence by Age Group—1998 (from CDC)



Pneumococcal Disease is Serious

- **More deaths (~40,000/yr) than all other vaccine preventable diseases combined**
- **Most common form of community acquired bacterial pneumonia**
- **175,000 hospitalized cases of pneumonia per year**
- **>50,000 cases of pneumococcal bacteremia**
- **3,000-6,000 cases of meningitis annually**
- **Treatment:** Penicillin & other antibiotics
- **Prevention:**
 - **Pneumococcal Polysaccharide Vaccine (PPV23)**
 - **Pneumococcal Conjugate Vaccine (PCV7) (≤ 9 yr)**

The Pneumococcal Polysaccharide Vaccine (PPV23)

- Contains 23 PS serotypes, ~90% of pneumococcal disease
- Pneumovax® 23, Merck, 1983
- 25 mcg of each PS antigen, 0.25% phenol
- Injected intramuscularly or subcutaneously
- Efficacy: 60-70% against invasive disease
- Side Effects: Most common (30-50%): swelling and soreness at injection site (mild, short time)
- Less than 1%: fever and muscle pain
- Potential allergic reaction (rare)

Potential risks from disease much greater than from vaccine

Who Should Get the Pneumococcal Vaccine (PPV23)?

People who are:

- 65 years of age or older
- ≥ 2 yr with chronic illness (serious long-term health problems): e.g., heart or lung disease
- ≥ 2 yr with weakened immune system, e.g., HIV/AIDS, renal failure, transplants, -spleen, cancer treatment
- 2-64 yr in nursing homes or LTC facilities
- 2-64 yr and are Alaska Natives and certain American Indian populations

What Are Special Issues for the Pneumococcal PS Vaccine?

Revaccination/Booster:

- Most people do not need a booster

People who should get a booster (once):

- ≥ 65 yr if received PPV23 before 65 and >5 years ago
- Received a transplant
- Chronic kidney disease, compromised immune system

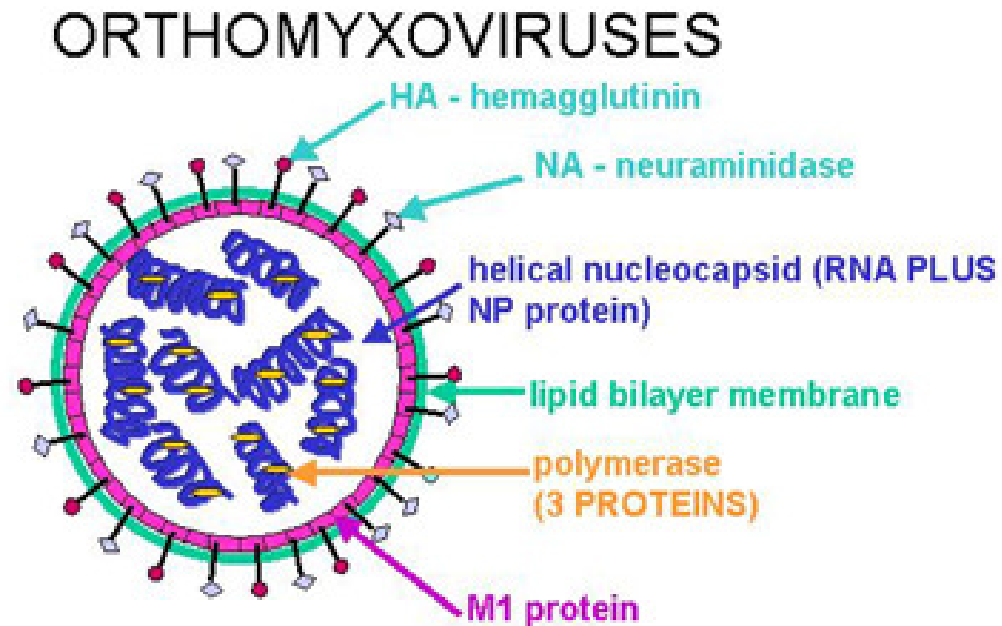
Simultaneous administration:

- OK to get PPV23 at the same time as influenza vaccine

What Is Influenza?

- Respiratory Illness, abrupt onset
- Cough, sore throat, runny nose, fever, muscle aches, headache, malaise
- Transmission: large particle droplets from cough or sneeze; contact with surface contaminated with droplet
- Incubation period: 1-4 days (avg. 2 days)
- Complications: Influenza viral pneumonia; worsen medical conditions (pulmonary, cardiac); secondary bacterial pneumonia; coinfections
- Not “stomach flu”

Schematic Diagram of Influenza Virus
(<http://pathmicro.med.sc.edu/mhunt/flu.htm>)



type A, B, C : NP, M protein
sub-types: HA or NA protein

The Influenza Vaccines

- Trivalent Inactivated Influenza Vaccine (TIV)
(administered as injection):
Fluzone (≥ 6 mo); Fluvirin (≥ 4 yr);
Fluarix (≥ 18 yr); FluLaval (≥ 18 yr);
Afluria (≥ 18 yr)
- Live, Attenuated Influenza Vaccine (LAIV):
FluMist (2 – 49 yr) – intranasal spray
- Recombinant Hemagglutinin:
FluBlok (made in insect cells; under FDA review)
- Other vaccines are in development

Who Should Get Flu Vaccine?

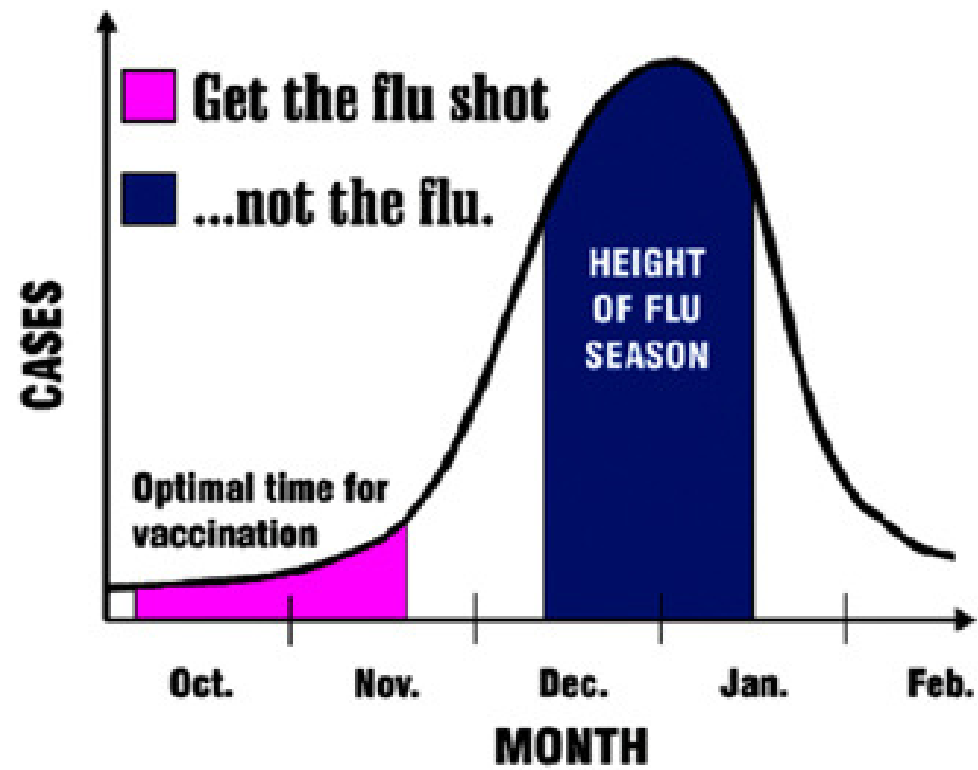
- People 50 yr of age and older
- Children 6 mo – 18 yr
- Pregnant women
- People any age with chronic medical conditions
- People who live in nursing homes and other long-term care facilities
- People who live with or care for those at high risk for complications from flu

Who Should NOT Get Flu Vaccine?

Persons who:

- Had a severe allergic reaction to chickens or egg protein or any vaccine component
- Had a severe allergic reaction to a previous influenza vaccination
- Have a moderate to severe acute febrile illness, until recovered
- Had paralysis due to Guillain-Barre Syndrome

When Should I Get Vaccinated?



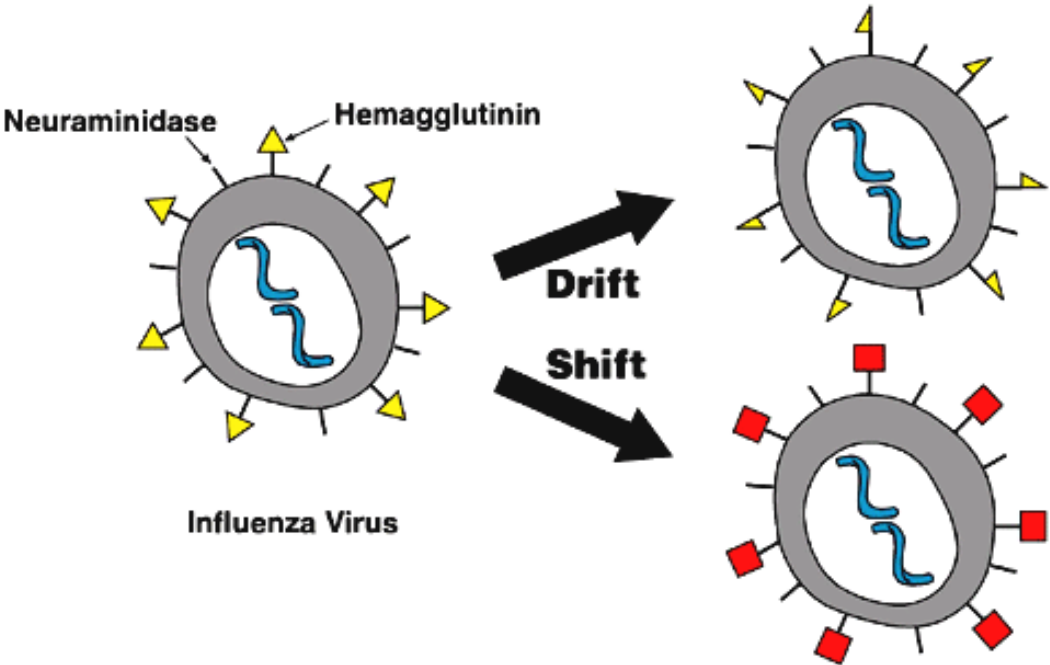
I got the vaccine—why did I still get sick with flu-like symptoms?

- Exposed to influenza virus shortly before getting vaccine or during the 2 weeks to gain protection
- Ill from other (non-flu) viruses that circulate during flu season, e.g., rhinovirus
- Exposed to an influenza virus not included in the vaccine
- Some people are not protected from flu despite getting the vaccine (e.g., weakened immune systems)

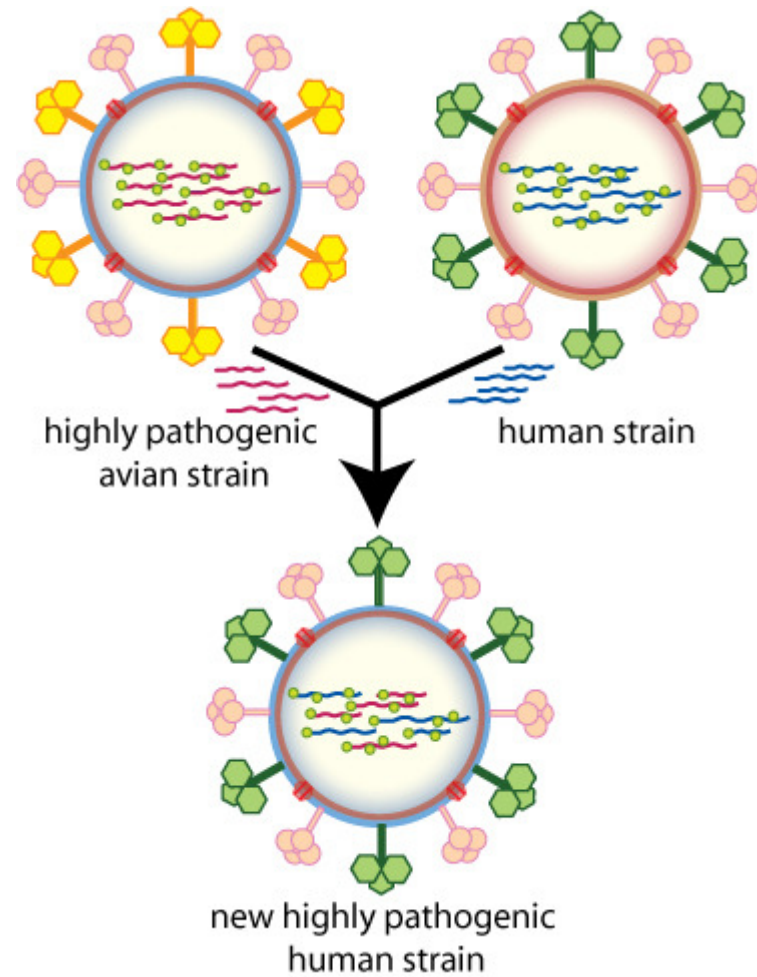
What Are Special Issues for Flu Vaccine?

- Current vaccines produced in embryonated hens eggs
 - Potential limitation on supply
 - Contraindicated for egg-allergic persons
 - Need for high growth reassortants
- Three strains included in vaccine and content of the vaccine (strain of influenza) may change every year
- Vaccine demand can be unpredictable
- Issues for Pandemic

Changes in Influenza Virus



Influenza Virus Reassortment – Antigenic Shift



Influenza Vaccine Supply/Demand

- **2002** – 95M doses prepared; insufficient demand, manufacturers discarded 12 million doses in US
- **2003** – Vaccine orders down, indicating demand would be less; production based on pre-book orders plus manufacturers safety margin
- **2003-04 Season**
 - 3rd Q 2003, 83-87M doses, considered ample
 - Early influenza outbreaks (>130 children died) created unprecedented surge in vaccine demand late Nov/Dec, exhausting supplies
 - Companies worked with CDC to allocate vaccine to states

Influenza Vaccine Supply/Demand (2)

- **2004-05 Season**
 - **Approx. 100M doses predicted for US**
 - **End of Aug – Chiron announces vaccine delay**
 - **By early Oct AvPast shipped approx. 33M of planned 50M doses**
 - **Oct 5 – Chiron announces vaccine not available**
 - **AvPast increases production to total of 58M doses for 2004-05**
 - **CDC distribution plan, AvPast ships vaccine to prioritized customers**

Influenza Vaccine Timeline

FDA / CDC
Manufacturing and Distribution

Jan...Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

planning & preparation

receive candidate seed viruses

prepare high-growth reassortants

↑ start 1st 2nd 3rd strain
monovalent concentrate production

potency test reagent preparation

↑ ↑
strain selection

vaccine formulation

vaccine filling

↑
license issued

vaccine distributed

Headline (WP 10/17/04): How U.S. Got Down To Two Makers of Flu Vaccine

- 2002-03, Wyeth made 21M doses of influenza vaccine
 - Discarded 7M doses, loss of \$30 million (\$50 million over 3 seasons)
 - Quit making vaccine, closed facility
- Global market for vaccines is \$6 billion/yr, vs. \$340 billion/yr for drugs; low profit margin
- Number of manufacturers for U.S. has dwindled:
 - 1975 – 6; 1999 – 4; 2004 – 2; 2008 – 5 + 1
- Three strains in vaccine; in general, 1 strain must be replaced each year to match mutated flu virus
- Vaccine produced in eggs; labor-intensive; one egg yields enough virus for 4-5 doses of vaccine
- Potential to switch to more efficient cell culture-based production methods; reluctance to invest in egg-based vaccine

Pandemic Influenza:

- **Caused by an emerging strain to which the population has not been exposed and has little if any immunity**
- **Types of influenza viruses infecting humans:**
 - **Type A**
 - Hemagglutinin (HA, 15 subtypes)
 - Neuraminidase (NA, 9 subtypes)
 - **Type B**
- **Current vaccine contains:**
 - **H1N1, H3N2, B**
- **Previous pandemics:**
 - **1918-1919, H1N1, 50M deaths worldwide, 675,000-US**
 - **1957, H2N2 – 70,000 deaths in US**
 - **1968, H3N2 – 50,000 deaths in US**
- **Concern for avian influenza strains:**
 - **H5N1, H7N7, H9N2**

**Victims Crowded Into An Emergency Hospital
At Camp Funston, Fort Riley, Kansas, 1918**



Headline (WP 4/16/06): U.S. Plan For Flu Pandemic Revealed

- Vaccination prioritization
- Expand Internet capacity for work at home
- Treasury Dept – other countries produce currency
- VA – drive-through medical exams and vaccinations
- 12-18 month crisis; 210,000 - 1.9M deaths in US
- Contracts for vaccine manufacture
- Priorities for anti-viral drugs
 - 1st responders and health care workers vs. persons with symptoms and others in same household

Headline (WP 4/16/06): U.S. Plan For Flu Pandemic Revealed (2)

- Use drugs from Strategic National Stockpile
- Cancel large gatherings
- Encourage school closings
- Bring back retired federal workers
- Dispatch National Guard if necessary
- Introduce travel restrictions
- 40% of work force may be out
- Contingency plans for payrolls
- VA – Stockpile medicines, equipment, food, water
- Role of containment/quarantine? (Editorial, WP 10/16/05)

- Web site: www.pandemicflu.gov

Resources

- **Websites:**

- www.pandemicflu.gov
- www.fda.gov
- <http://www.fda.gov/cber/summaries/sci042006jg.pdf>
- <http://www.fda.gov/cber/vaccine/licvacc.htm>
- www.nih.gov
- www.cdc.gov/mmwr
- www.hhs.gov
- www.bt.cdc.gov
- <http://www.who.int/en/>
- <http://www.fda.gov/cdrh/ppe/fluoutbreaks.html>
(personal protective equipment)