Vaccines work!

CDC statistics demonstrate dramatic declines in vaccine-preventable diseases when compared with pre-vaccine era

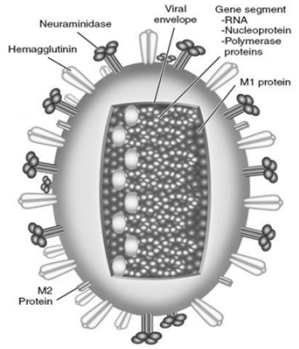
DISEASE	PRE-VACCINE ERA ESTIMATED ANNUAL MORBIDITY*	MOST RECENT REPORTS OR ESTIMATES† OF U.S. CASES	PERCENT DECREASE
Diphtheria	21,053	0†	100%
H. influenzae (invasive, <5 years of age)	20,000	31‡	>99%
Hepatitis A	117,333	2,890§	98%
Hepatitis B (acute)	66,232	18,800§	72%
Measles	530,217	187†	>99%
Mumps	162,344	584†	>99%
Pertussis	200,752	28,639†	86%
Pneumococcal disease (invasive, <5 years of age)	16,069	1,900¶¶	88%
Polio (paralytic)	16,316	1†	>99%
Rotavirus (hospitalizations, <3 years of age)	62,500**	12,500††	80%
Rubella	47,745	9†	>99%
Congenital Rubella Syndrome	152	1†	99%
Smallpox	29,005	0†	100%
Tetanus	580	26†	96%
Varicella	4,085,120	167,490§§	96%

* CDC. JAMA November 14, 2007; 298(18):2155–63.
† CDC. MMWR August 15, 2014; 63(32):702–15.
‡ An additional 10 cases of Hib are estimated to have occurred among the 185 reports of Hib (<5 years) with unknown serotype.
§ CDC. Viral Hepatitis Surveillance – United States, 2011.
** CDC. MMWR, February 6, 2009; 58(RR-2):1–25.
†† CDC. Active Bacterial Core Surveillance, 2013 data (unpublished).
‡‡ CDC. New Vaccine Surveillance Network, 2013 data (unpublished); U.S. rotavirus disease now has a biennial pattern.
§§ CDC. Varicella Program, 2013 data (unpublished).

www.immunize.org/catg.d/p4037.pdf • Item #P4037 (12/14)
Technical content reviewed by the Centers for Disease Control and Prevention
Immunization Action Coalition • Saint Paul, Minnesota • 651-647-9009 • www.immunize.org • www.vaccineinformation.org

Characteristics of Successful Vaccines

- Naturally acquired immunity is solid
- Pathogen is antigenically stable
- Pathogenesis is amenable to immunoprophylaxis
- Benefit/risk ratio is acceptable to vaccinees
- Logistics support deployment



Influenza Vaccine: 2016-2017

Influenza A/California/7/2009(H1N1);
A/Hong Kong/4801/2014 (H3N2)
B/Phuket/3073/2013 (Yamagata);
B/Brisbane/60/2008 (Victoria)

Recommendations: All persons ≥ 6 mos of age who don't have contraindications
: emphasis on high risk, esp elderly, children 6 -59 months, pregnant women

Efficacy rates: 50% protection depending on fit with circulating strains (19-70%)

Inactivated Influenza Vaccine

Egg Grown

- Trivalent Standard Dose (45µg): A/H1N1, A/H3N2, B (Yamagata)
- Quadrivalent Standard Dose (60µg): Trivalent plus another B (Victoria)
- Trivalent High Dose (180µg): A/H1N1, A/H3N2, B (Yamagata)

Efficacy of Inactivated Trivalent High Dose vs. Standard Dose

Study	Population	High Dose	Low Dose	Diff
DiazGranados (RCT)	31,989	1.4% Influenza	1.9% Influenza	24%
Richardson (obs)	25,714	0.3 Influenza or hosp	0.3% Influenza or hosp	N.S.
Izurieta (obs)	2,545,275	1/10,000 person-weeks	1.3/10,000 person-weeks	22%

Other Inactivated Influenza Vaccines

- ☆ Adjuvanted (MF59) trivalent (Fluad)
- Quadrivalent intradermal (Fluzone) – "fine needle" 1.5mm in length for needle phobic
- Trivalent via jet injector (Afluria) – needle free
- Trivalent generated by DNA technology (Flublok) – can be used in bona fide egg allergic in > 18 years of age
- ☆ Quadrivalent generated through cell culture (Flucelvax)

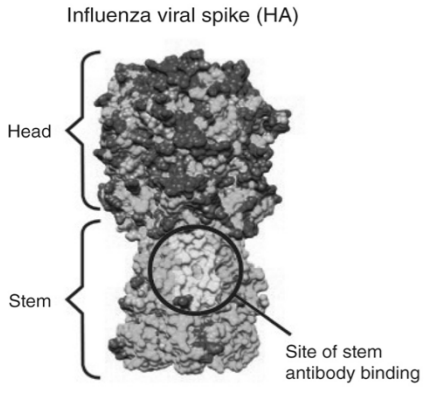
Live Attenuated Influenza Vaccine (LAIV)

- Attenuated through genetic reassortment
- Administrated through nasal spray
- Quadrivalent preparation
- Approved for normals 2–49 years of age
- NO LONGER RECOMMENDED FOR USE IN 2016-2017 SEASON BY ACIP/CDC
  - Based on lack of effectiveness in past two influenza seasons

Which Influenza Vaccine to Choose for the 2016-2017 Season?

- The ACIP and CDC state they have no preference over any of the available inactivated vaccines (!!)
- Choice is between quadrivalent low dose vs. trivalent high dose

Protection Against Pandemics
: Avian Influenza
Universal Influenza Vaccine
: Is it possible?



Pneumococcal Vaccine

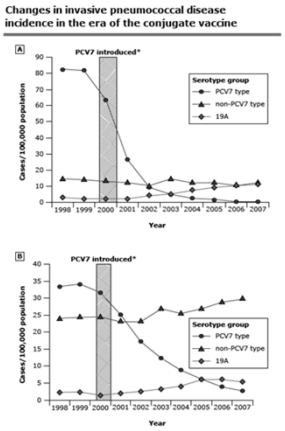
- Capsular polysaccharide (CPS) – 92 types
- Antibody to CPS is correlate of protection
- 23 valent pneumococcal polysaccharide vaccine (PPSV23): Pneumovax
  - Long standing use
  - Covered 85-90% of cases, now 50-60%
  - Effective against bacteremic disease, but controversial in non-bacteremic
  - Poorly immunogenic in ≤ 2 yrs of age
- 13 valent conjugate vaccine (PCV13): Prevnar
  - CPS bound to protein carrier
  - T-cell dependent antigen
  - Immunogenic in infants
  - Stimulates local antibody

Pneumococcal Vaccine Efficacy

- PPSV has efficacy against invasive disease, but less so in elderly and immunocompromised, and uncertain in non-invasive disease
- PCV7 and PCV13 are highly efficacious in children and adults ≥ 65 yrs
  - Reduction in incidence of disease caused by serotypes in vaccine (>90%)
  - CAPITA TRIAL – 85,000 patients >65 years of age
    - 46 % reduction in vaccine-type bacteremic pneumococcal pneumonia
    - 45% reduction in vaccine-type non-bacteremic pneumonia
    - 75% reduction in bacteremic invasive pneumococcal disease

Pneumococcal Vaccine Recommendations - 2015

Individuals ≥ 65 years of age	**PCV13 followed by PPSV23 6-12 months later**
Individuals ≥ 2 years of age with immunocompromise, CSF leak, cochlear implants, asplenia, hemoglobinopathy	PCV13 followed by PPSV23 ≥ 8 weeks later
Individuals 19-64 years of age with intermediate risk – chronic heart or lung disease, diabetes mellitus, chronic liver disease, cigarette smoking	PPSV23 alone



Meningococcal Vaccines

- Quadrivalent Vaccines against serogroups A, C, Y, and WI35
  - Capsular Polysaccharide (Menomune, MPSV4)
  - Conjugate with diphtheria toxoid (Menactra, MenACY)
  - Conjugate with mutant diphtheria toxin (Menveo, MenACY)
- Recommendations
  - Conjugate vaccine for all individuals between 11 and 18 years of age
    - Booster at age 16 if primary dose at 12 years of age or younger
  - Conjugate vaccine for high risk meningococcal disease
    - Complement deficiencies, asplenia, microbiologists exposed, children and adolescents with HIV
    - 2 mos. to 55 years of age
    - ≥ 56, MPSV4 if only one vaccination is anticipated, conjugate vaccine if revaccination is needed

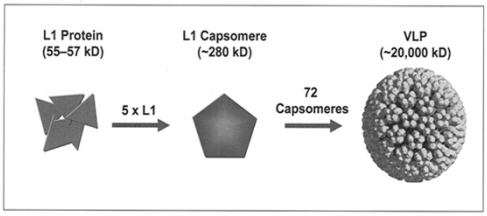
Meningococcal Serogroup B Vaccine

- Trumenba (MenB-FHbp) – 3 dose series
- Bexsero (MenB-4C) – 2 dose series
- Recommendations
  - High risk 10 years of age or older
  - To individuals in outbreaks of Serogroup B disease
  - “Optional” for normals ages 16-23, to be discussed with physician

Human Papilloma Virus (HPV)

- > 100 HPV types
- HPV 16 and 18 associated with 70% of cervical cancers
- HPV 31, 33, 45, 52, and 58 associated with 19% of cervical cancers
- HPV 6 and 11 associated with 90% of genital warts
- Anal cancer – 88% associated with HPV (mostly 16 and 18)
- Association also with penile cancer and oropharyngeal cancers

Human Papillomavirus Vaccine



Neutralizing antibody and protection is type specific.

Human Papilloma Virus Vaccines

Types	Regimen
• Nonavalent vaccine (Gardasil 9): 6,11,16,18,31,33,45,52,58	IM 0,2,6 months
• Quadrivalent vaccine (Gardasil): 6,11,16,18	IM 0,2,6 months
• Bivalent vaccine (Cervarix): 16,18	IM 0,1,6 months

Recommendations
- Females age 11-12 (as early as 9) – catch up 13-26
- Males ages 12-12 (as early as 9) – catch up 13-21
- Pregnancy – not recommended (limited data)
- Immunocompromised – recommended through age 26

HPV Vaccine Efficacy

- Quadrivalent or nonavalent vaccine
  - 97-100% efficacy in prevention of CIN2 or more severe cervical disease caused by vaccine HPV types in HPV naïve
  - 44% efficacy in group with or without previous HPV infection (reflects rate of previous infections)
  - Anal or oropharyngeal disease – less extensive data, but efficacy appears to be similar to that against cervical disease
- Duration of efficacy
  - At least 4.5 years and probably up to 10 years

HPV Vaccines Utilization

Safety
- Generally well tolerated
- Mild injection site reactions most common
- Possible increased risk of syncope (Quadrivalent vaccine)

Cost
- Nonavalent $163/dose

Problems with low utilization

Pertussis Vaccine

- Epidemiology of *Bordetella Pertussis* infection is changing
  - Most cases occur in adolescents and adults
  - Spread to infants is major problem
- acellular Pertussis vaccines have replaced previous cellular Pertussis vaccines
- DTaP recommended for children (birth, 2, 4, 6, 15-18 months, 4-6 years)
- For older children and adults: Tdap
  - Bostrix
  - Adacell
- Children 11-12 up to 18 years of age: one booster dose
- 19 yrs to 64 years of age: one dose if not vaccinated with Pertsussis vaccine earlier
- All persons ≥65 years of age should receive one dose of Tdap
  - Bostrix is preferred, but Adacell is acceptable

Pertussis Vaccines
Special Populations

- Pregnant women: Tdap between 27 and 36 weeks of each pregnancy
- Health Care Personnel who have direct patient contact and who have not received TdaP as an adult
  - Emphasis for personnel in contact with children ≤12 months of age
  - Childcare providers
  - Grandparents
- Generally well tolerated in adults

Zika Virus Vaccine

- Flavivirus – single serotype
- Natural Acquired Immunity
- Experimental vaccines developed
  - Inactivated virus particle
  - Plasmid (nucleic acid) vaccine
  - Viral vectors
- High degree of protection in animal models
  - Single dose
  - Antibodies are correlates of immunity
- Phase 1 clinical trials underway
- Anticipate Phase 2 deployment in endemic areas

Ebola Vaccine

- rVSV-ZEBOV
  - Glycoprotein of Zaire Ebola Strain in Vesicular Stomatitis Virus vector
  - Field trial in Guinea*
    - 7,651 exposed subjects
    - Immediate vaccination: 0 cases
    - Delayed vaccination (21 days later): 16 cases
  - Preliminary efficacy: 100% for immediately vaccinated group (p=0.0036)
  - Reactogenicity
- ChAd3 – Zaire
  - Good immune responses in phase 2 study
  - Excellent protection in non-human primates, but no human efficacy data

* Henao-Restrepo AM, Longini IM, Egger M, et al. Lancet. 2015 Aug 29;386(9996):857-66.

HIV Vaccine Challenges

- No natural acquired immunity
- Marked strain diversity
- No entirely satisfactory animal model
- Commitment to commercial development is unclear