Public Health Perspectives on Vaccinations

Maureen Tierney, MD, MSc.
HAI Consultant/Coordinator
Epidemiology Unit, Div of Public Health
Nebraska DHHS

Pneumococcal Vaccine

- Pre-vaccine children < 5 (US) including:
  - more than 700 cases of meningitis,
  - 13,000 blood infections,
  - about 5 million ear infections, and
  - about 200 deaths.
- Adults (US): approx. 4,000 deaths

Pneumococcal Vaccine Timeline

- 1983: Pneumovax: 23-valent; polysaccaride vaccine (covers 90% of SP bacteremias)
  - questions re: efficacy; kids don't respond
- 2000: Prevnar7 for kids: conjugated (diphtheria protein) vaccine
  - invasive SP and otitis media
  - By 2009 PCV coverage in 19-35 mos: 92.6% for ≥3 doses/80.4% for ≥4 doses
- 2010: Prevnar13—80-90% of all severe SP infections in US
- Vaccinating kids may protect adults in the vicinity
- 4-dose series at ages 2, 4, 6, and 12--15 months

Conjugate Vaccine in Adults

- Prevnar-13 for >= 65 yo
  - pneumovax uptake: 2/3 of population > 65 yo
  - prevents community-acquried pneumonia (hard to prove this with pneumovax)
- Prevnar13 followed in 6-12 mos by Pneumovax-23
  - will other serotypes emerge???

Pneumococcal Conjugate Vaccine Recommendations

- Routine vaccination of children 2 through 59 months of age
- Doses at 2, 4, 6, months of age, booster dose at 12-15 months of age
- First dose as early as 6 weeks
- Unvaccinated children 7 months of age or older require fewer doses
- Adults 65 years old and older

Conjugate Vaccine High-risk Schedule 6-18 yo

- Single dose if no dose of PCV13 received previously
- Anatomic asplenia (including sickle-cell disease)
- Immunocompromising conditions (e.g. HIV infection)
- Cochlear implant
- Cerebrospinal fluid leak

Conjugate Vaccine for Persons ≥65 yo

- For those who have not received PCV13 previously, administer a dose of PCV13
- A dose of PPSV23 should be administered 6-12 months after the dose of PCV13
- Do not administer the two vaccines simultaneously
- Adults who previously received a dose of PPSV23 should receive PCV13 no earlier than 1 year after the dose of PPSV23

Conjugate Vaccine High-risk Adults 19-64 yo

- Anatomic asplenia (including sickle-cell disease)
- Immunocompromising conditions (e.g. HIV infection)
- Cochlear implant
- Cerebrospinal fluid leak
- PPSV23 should also be recommended, if not received previously
- PCV13 administered first followed by a dose of PPSV23 8 weeks later

Polysaccharide Vaccine Recommendations

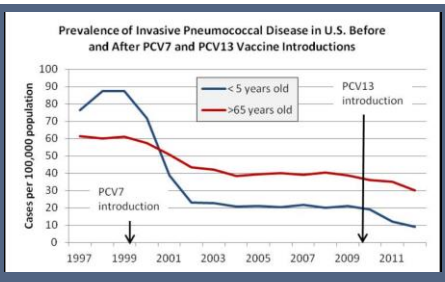
- Adults 65 years and older
- Persons 2 years and older with chronic illness
- anatomic or functional asplenia
- immunocompromised (disease, chemotherapy, steroids)
- HIV infection
- environments or settings with increased risk
- cochlear implant

Polysaccharide Vaccine Revaccination — High-risk Immunocompetent Persons

- Routine revaccination of immunocompetent persons is not recommended
- Revaccination recommended for immunocompetent persons 2 years of age or older who are at high risk of serious pneumococcal infection
  - chronic heart disease
  - pulmonary disease (including asthma, 19 years and older)
  - liver disease
  - alcoholism
  - CSF leaks
  - cochlear implants
  - those who smoke cigarettes (19 years and older)
- Single revaccination dose at least 5 years after the first dose and after the 65th birthday

Polysaccharide Vaccine Revaccination — Highest-risk Persons

- Persons 2 years of age or older with:
  - functional or anatomic asplenia
  - immunosuppression
  - transplant
  - chronic renal failure
  - nephrotic syndrome
- A revaccination dose 5 years after the first dose
- For those who receive 2nd dose prior to the 65th birthday, a third dose is recommended after the 65th birthday (and at least 5 years from the second dose)



Invasive Strep pneumo in Nebraska

	Year of Report				
AGEGROUP	2011	2012	2013	2014	2015*
Less than 1 yr	3	5	5	3	0
1 to 5 yrs	9	8	10	12	5
20 to 49 yrs	20	19	35	31	19
50 to 64 yrs	35	45	42	59	33
65 yrs or older	54	62	68	50	33
TOTAL	121	139	160	155	90

* As of August

HPV Clinical Features

- Most HPV infections are asymptomatic and result in no clinical disease
- Clinical manifestations of HPV infection include:
  - anogenital warts
  - recurrent respiratory papillomatosis
  - cervical cancer precursors (cervical intraepithelial neoplasia)
  - cancer (cervical, anal, vaginal, vulvar, penile, and oropharyngeal cancer)

HPV Disease Burden in the United States

- Anogenital HPV is the most common sexually transmitted infection in the US
  - estimated 79 million infected
  - 14 million new infections/year
- Common among adolescents and young adults
- 12,595 cases / 3,968 deaths due to cervical cancer
  - HPV types 16 and 18 are associated with 70% of these cancers.
- 5000 new cases of oropharyngeal cancer
- HPV: 90% of anal ca, 71% of vulvar, vaginal, or penile ca, 72% of oropharyngeal ca.

HPV Vaccines: 3 options

- HPV4 (Gardasil): M/F, 9-26 yo
  - types 16/18 (high risk-cancer) and types 6/11 (low risk-warts)
- HPV2 (Cervarix, GlaxoSmithKline) approved for females 9 through 25 years of age
  - contains types 16/18 (high risk)
- a 9-valent vaccine (Gardasil-9) (Dec 2014)

HPV Vaccine Efficacy

- High efficacy among females vs vaccine HPV types
- Not effective vs strains pre-existing at time of vaccine
- Pre-existing infection with one HPV type: vaccine still works against other HPV types
- No waning of immunity 8-10 years out (for 4-, 2-valent vaccines)

HPV Vaccination Schedule

- Routine schedule is 0, 1 to 2, 6 months
- An accelerated schedule using minimum intervals is not recommended
- Series does not need to be restarted if the schedule is interrupted
- Prevaccination assessments not recommended
- No therapeutic effect on HPV infection, genital warts, cervical lesions

Varicella Zoster Virus (VZV)

- Herpesvirus (DNA)
- Primary infection results in varicella (chickenpox)
- Reactivation of latent infection results in herpes zoster (shingles)
- Short survival in environment

Herpes Zoster (Shingles)

- Reactivation of varicella zoster virus (VZV)
- Associated with: aging
  - immunosuppression
  - intrauterine exposure
  - varicella at younger than 18 months of age

Herpes Zoster

- 500,000 to 1 million episodes occur annually in the United States
- Lifetime risk of zoster estimated to be 32%
- 50% of persons living until age 85 years will develop zoster

Varicella-Containing Vaccines

- Varicella vaccine (Varivax)
  - Live, attenuated
  - >= 12 months
- Measles-mumps-rubella-**varicella** vaccine (ProQuad)
  - 12 months--12 yo
- Herpes zoster vaccine (Zostavax)
  - Same as varicella vaccine, 14-fold greater concentration
  - >= 50 yo

Varicella Vaccine Recommendations Children

- Routine vaccination at 12 through 15 months of age
- Routine second dose at 4 through 6 years of age

Herpes Zoster Vaccine

- Approved for persons 50 years and older
- Don't vaccineat < 60 yo: low risk for shingles
- In UK: recommend vaccination at 70 years (tradeoffs)

Varicella Vaccination Recommendations Healthcare Personnel

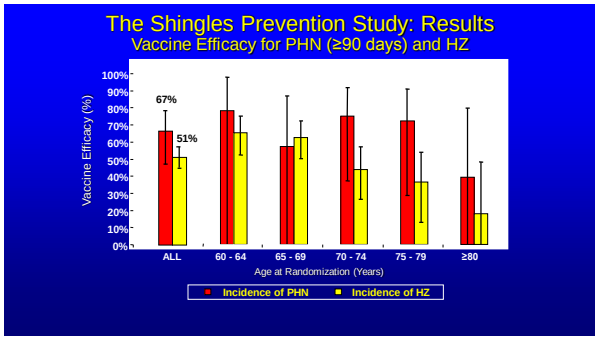
- ACIP recommends all healthcare personnel be immune to varicella
- Prevaccination serologic screening likely cost-effective for persons with uncertain history
- Postvaccination testing not necessary or recommended

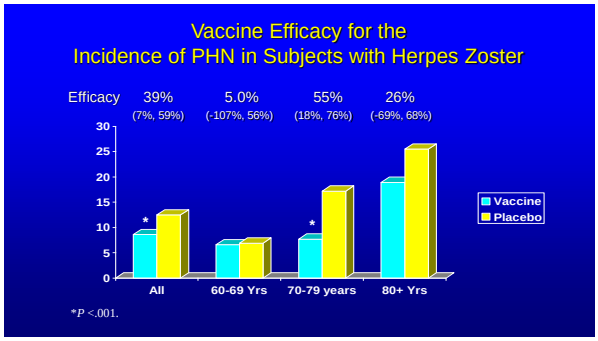
Varicella Vaccine Immunogenicity and Efficacy

- Detectable antibody
  - 97% of children 12 months through 12 years following 1 dose
  - 99% of persons 13 years and older after 2 doses
- 70% to 90% effective against any varicella disease
- 90%-100% effective against severe varicella disease

Herpes Zoster Vaccine Efficacy

- Vaccine recipients 60 to 80 years of age had 51% fewer episodes of zoster
  - efficacy declines with increasing age
  - significantly reduces the risk of postherpetic neuralgia
- Reduces the risk of zoster 69.8% in persons 50 through 59 years of age





New Zoster Vaccine (not yet on the market)

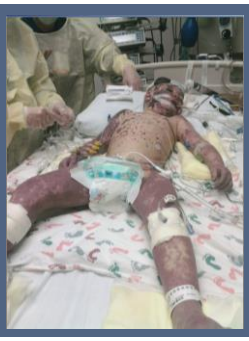
- subunit vaccine: glycoprotein E of VZV (vs live-attenuated Zostavax)
- add two adjuvants
  - **monophosphoryl lipid A** (detoxified lipid A)--same as Cervarix (HPV) vaccine
  - **QS-21**—derived from saponin—a new adjuvant
- Tested in 15,000 older adults: 3 strata: 50-59, 60-69, > years of age, and older than 70 years
- 97 % efficacy over placebo (over 3 yr period): **PHENOMENAL**
- ?: duration of this efficacy
- ?: can we use this new adjuvant in other vaccines

Neisseria meningitidis

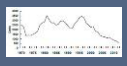
- meningitis, sepsis, and focal disease (e.g. pneumonia and arthritis)
- epidemic disease in sub-Saharan Africa (serogroup A)
- 13 distinct polysaccharide capsules have been described
- almost all invasive disease caused by serogroups A, B, C, Y, and W
- relative importance of serogroups depends on geographic location and other factors (e.g. age)

Neisseria meningitidis Clinical Features

- Incubation period 3-4 days (range 2-10 days)
- Abrupt onset of fever, meningeal symptoms, hypotension, and rash
- Fatality rate 10%-15%, up to 40% in meningococcemia



Meningococcal Disease - US, 1972-2012 (all serogroups)



N. meningitidis in Nebraska

Year of Report	Frequency
2006	5
2007	5
2008	13
2009	11
2010	6
2011	11
2012	3
2013	4
2014	0
2015	1
Total	78

Meningococcal Meningitis

- Most common presentation of invasive disease
- Results from hematogenous dissemination
  - fever
  - headache
  - stiff neck

Meningococcal Outbreaks in the United States

- Outbreaks account for less than 2% of reported cases
- Most recent outbreaks caused by serogroup C and B

Meningococcal Vaccines

- 1981: quadrivalent (ACYW) polysaccharide vaccine
- 2005: 2 conjugate vaccines (ACYW)
- 2014: 2 serogroup B vaccines

Routine MenACWY Vaccination Recommendations

- Best: 11/12 yo, then booster dose at 16 years of age
- Or: 1 dose at 13-15 yo, plus 1 booster at 16/18 yo
- If 1st dose at or after 16 yo: no booster dose
- No routine vaccination after 21 yo

Select High-risk Groups: use ACWY and B vaccines

- Functional or Anatomic Asplenia*
- Persistent Complement Complement Deficiency
- Lab workers
- Military recruits
- Travellers to sub-Sahara meningitis belt

Meningococcal Outbreak Definition

- Outbreak definition:
  - at least 3 confirmed or probable primary cases of the same serogroup
  - period of 3 months or less
  - primary attack rate of more than 10 cases per 100,000 population
- Both MenACWY, and MPSV4 recommended for use in control of outbreaks caused by A, C, W, and Y
- HibMenCY-TT may be used for age-appropriate persons in outbreaks specifically caused by C and Y

Serogroup B Mening Vaccine (2014)

- use in persons aged 10–25 years
- in the United States, only approximately 50 people will get group B mening disease in that age
- Target: high risk groups (immunocompromised, asplenia, lab workers, etc)
- Outbreaks:
  - Princeton University (5000 vaccinees)
  - UC Santa Barbara (20,000 vaccinees)

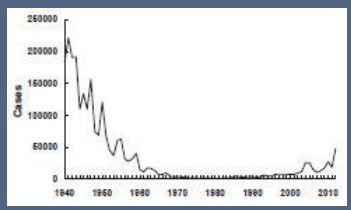
Pertussis

- Acute infectious disease caused by *Bordetella pertussis*
- A disease of antiquity: outbreaks first described in 16th century
- *Bordetella pertussis* isolated in 1906
- Estimated 195,000 deaths worldwide in 2008

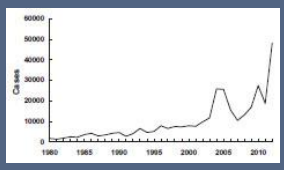
Pertussis Among Children, Adolescents and Adults

- Disease often milder than in infants and young children
- Infection may be asymptomatic, or may present as classic pertussis
- Persons with mild disease may transmit the infection
- Older persons often source of infection for children

Pertussis—United States, 1940-2012



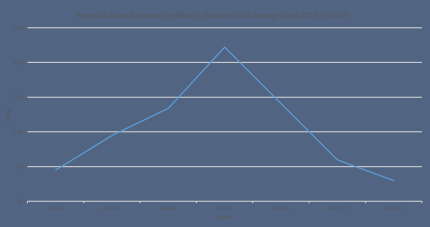
Pertussis—United States, 1980-2012



Pertussis cases by Year of Report

	Year					
JURISDICTION_NAME	2011	2012	2013	2014	2015*	5 Year Ave
Central District HD	5	1	3	4	4	3.4
Dakota County Health Department	0	2	0	1	0	0.6
Douglas County HD	17	124	67	27	26	52.2
East Central HD	1	0	14	5	1	4.2
Elkhorn Logan Valley HD	2	7	3	3	2	3.4
Four Corners HD	0	2	25	25	15	13.4
Lancaster County HD	2	26	47	**174**	**245**	98.8
Loup Basin HD	1	1	0	3	0	1
North Central District Health Department	0	4	2	3	0	1.8
Northeast Nebr Public HD	0	7	0	0	0	1.4
Panhandle Public HD	0	0	10	20	0	6
Public Health Solutions	0	1	2	6	7	3.2
Sandhills District Health Department	0	0	0	1	0	0.2
Sarpy Cass Counties DH & W	3	35	25	21	19	20.6
Scotts Bluff County HD	0	0	10	7	0	3.4
South Heartland District HD	21	2	1	3	2	5.8
Southeast District HD	1	5	3	37	**148**	38.8
Southwest Nebraska Public HD	1	1	1	0	0	0.6
Three Rivers HD	2	15	12	15	8	10.4
Two River HD	1	7	14	12	4	7.6
West Central District HD	0	1	1	3	0	1
TOTAL	57	241	240	370	481	277.8

* As of August 2015



Whole-Cell Pertussis Vaccine

- Developed in 1930s and used widely in clinical practice through mid-1940s
- DTP - 70%-90% effective after 4 doses
- Little to no protection after 5-10 years
- Local adverse reactions common

Acellular Pertussis Vaccines

- DTaP (pediatric): 6 weeks--6 yo (to age 7)
- Tdap (adolescent and adult): 10 >= 10 yo (Boostrix); 10-64 yo (Adacel)

Tdap Recommendations

- A single dose of Tdap is recommended for
  - adolescents 11 through 18 years of age
  - adults 19 through 64 years of age
  - children 7-10 years of age who are not fully vaccinated against pertussis
  - adults 65 years of age and older who have or anticipate having close contact with an infant less than 12 months of age

Tdap in Pregnancy
(if no prior Tdap)

- administer Tdap in each pregnancy: 27-36 weeks

OR

- immediately postpartum

Influenza Vaccine 2015–16

- Trivalent:
  - A/California/7/2009 (H1N1)-like virus
  - A/Switzerland/9715293/2013 (H3N2)-like virus
  - B/Phuket/3073/2013-like (Yamagata lineage)
- Quadrivalent (same as above, plus):
  - B/Brisbane/60/2008-like (Victoria lineage)

Inactivated influenza vaccine, quadrivalent (IIV4), standard dose

Trade name	Manufacturer	Age indications	Route
Inactivated influenza vaccine, quadrivalent (IIV4), standard dose			
Fluarix Quadrivalent	GlaxoSmithKline	≥3 yrs	IM†
FluLaval Quadrivalent	ID Biomedical Corp. of Quebec (distributed by GlaxoSmithKline)	≥3 yrs	IM†
Fluzone Quadrivalent	Sanofi Pasteur	6 through	IM†
		35 mos	
		≥36 mos	IM†
		≥36 mos	IM†
		≥6 mos	IM†
Fluzone Intradermal¶	Sanofi Pasteur	18 through 64 yrs	ID**

Inactivated influenza vaccine, trivalent (IIV3), standard dose

Trade name	Manufacturer	Age indications	Route
Afluria	bioCSL	≥9 yrs††	IMT
		≥9 yrs†† via needle;≤18 through 64 yrs via jet injector	IMT
Fluvirin	Novartis Vaccines and Diagnostics	≥4 yrs	IMT
		≥4 yrs	IMT
Fluzone	Sanofi Pasteur	≥6 mos	IMT

Inactivated influenza vaccine, cell-culture-based (ccIIV3), standard dose

Trade name	Manufacturer	Age indications	Route
Flucelvax	Novartis Vaccines and Diagnostics	≥18 yrs	IMT

Inactivated influenza vaccine, trivalent (IIV3), high dose

Trade name	Manufacturer	Age indications	Route
Fluzone High-Dose***	Sanofi Pasteur	≥65 yrs	IMT

Recombinant influenza vaccine, trivalent (RIV3), standard dose

Trade name	Manufacturer	Age indications	Route
Flublok	Protein Sciences	≥18 yrs	IM†

Live attenuated influenza vaccine, quadrivalent (LAIV4)

Trade name	Manufacturer	Age indications	Route
FluMist Quadrivalent†††	MedImmune	2 through 49 yrs	IN