Adolescent Vaccines

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What's ahead?

- What do we mean by "adolescent vaccines"?
- Background and recommendations for each:
  - Tdap
  - Meningitis conjugate vaccine
  - Human papillomavirus vaccine

Childhood Vaccine Schedule 2010

- Birth — Hep B
- 2 mo. — Pediarix, PedvaxHIB, Prevnar, RotaTeq
- 4 mo. — Pediarix, PedvaxHIB, Prevnar, RotaTeq
- 6 mo. — Pediarix, Prevnar, RotaTeq *
- 12 mo. — PedvaxHIB, MMR, Varicella, Prevnar *
- 15 mo. — DTaP, Hep A
- 2 yr. — Hep A
- 4-6 yr. — DTaP, IPV, MMR, Varicella

- **11-18 yr. — Tdap, MCV, HPV**

* Influenza for children 6 months to 18 yrs during the Flu season

•Pediarix = DTaP-IPV-HepB

Tdap Vaccine

- Tdap vaccine has replaced Td vaccine for most Adolescents and Adults 11-64 years old.
- Brands in Alaska: Adacel® and Boostrix®
- Groups who still need Td
  - Persons 65 years and older
  - Pregnant women
  - Persons contraindicated for pertussis

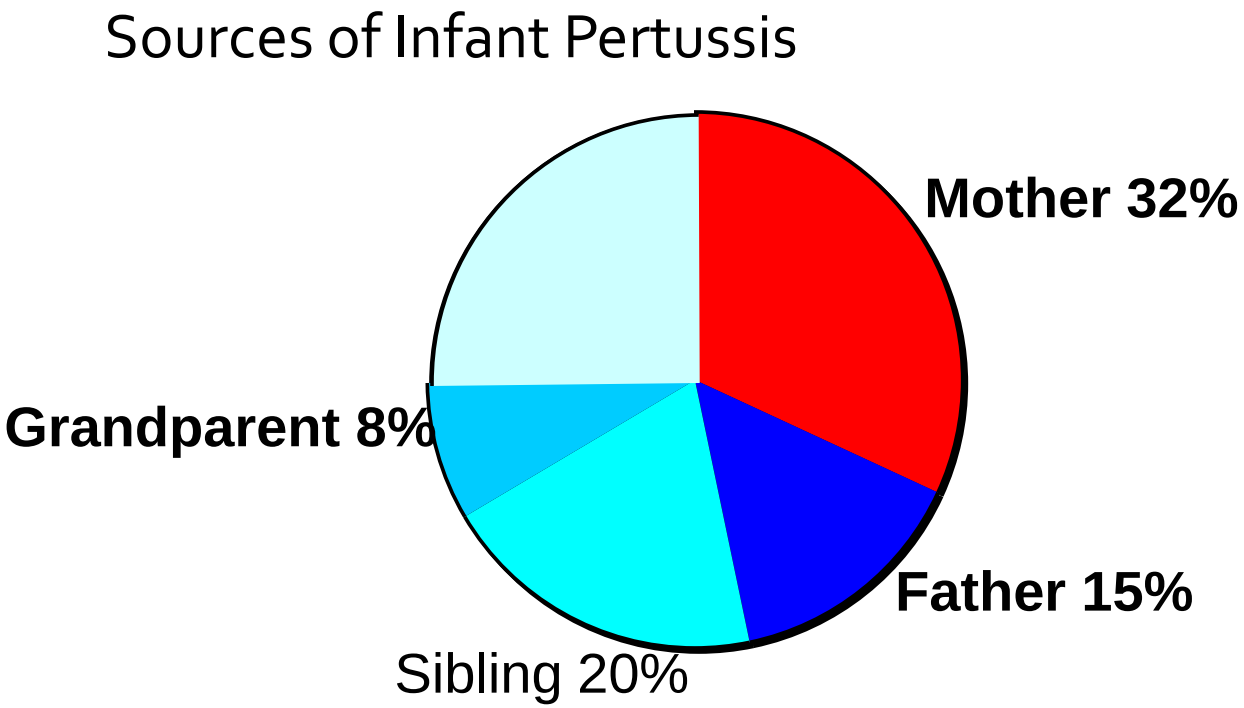
Things to consider:

1. Post-partum Standing Orders
2. Infection Control – vaccinate HCWs
3. Avoid DTaP/Tdap substitutions

http://www.epi.hss.state.ak.us/bulletins/docs/b2006_03.pdf

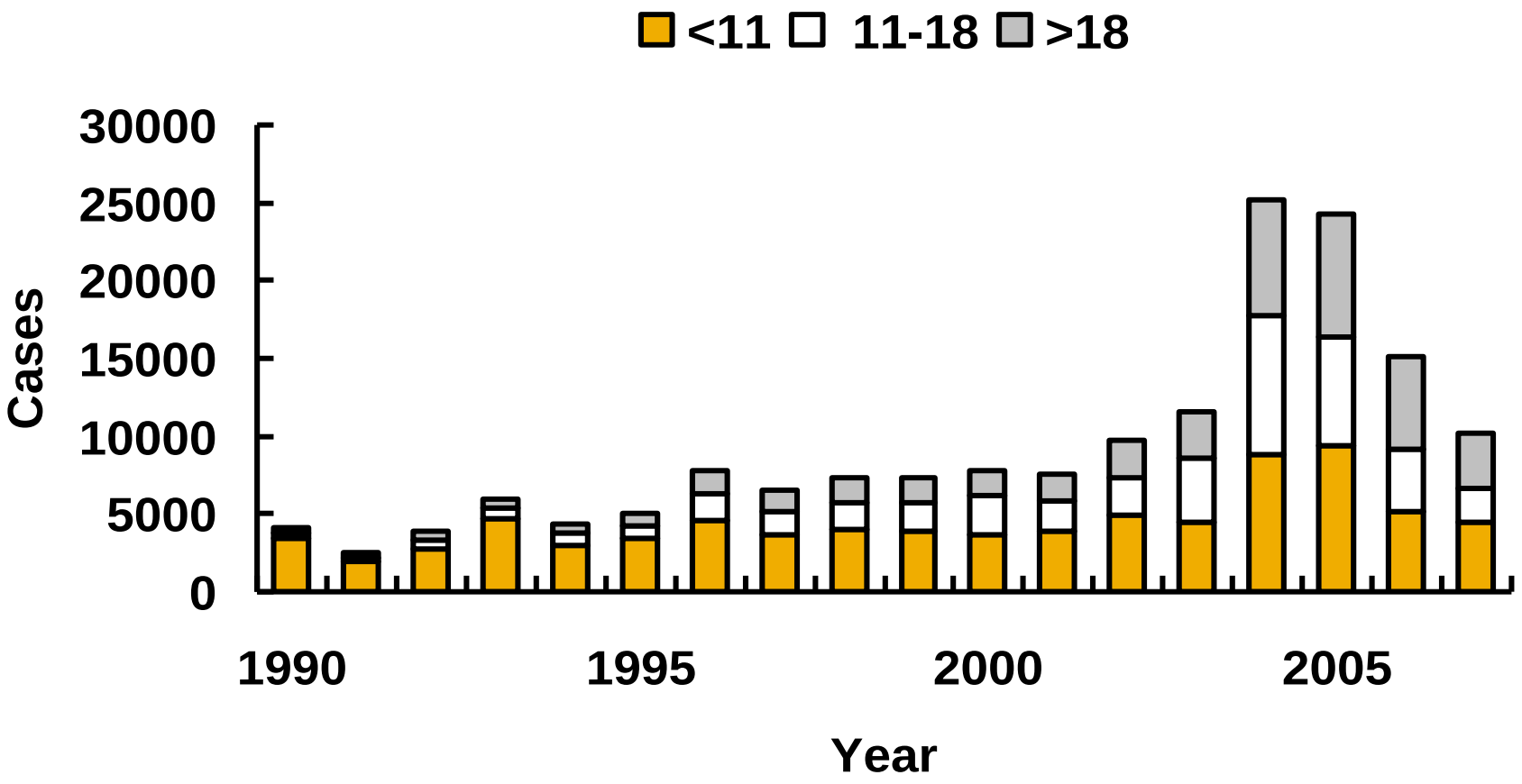
Why Tdap is important

- Pertussis Immunity wanes 5-8 years after DTaP
- Most infants with pertussis get it from a family member

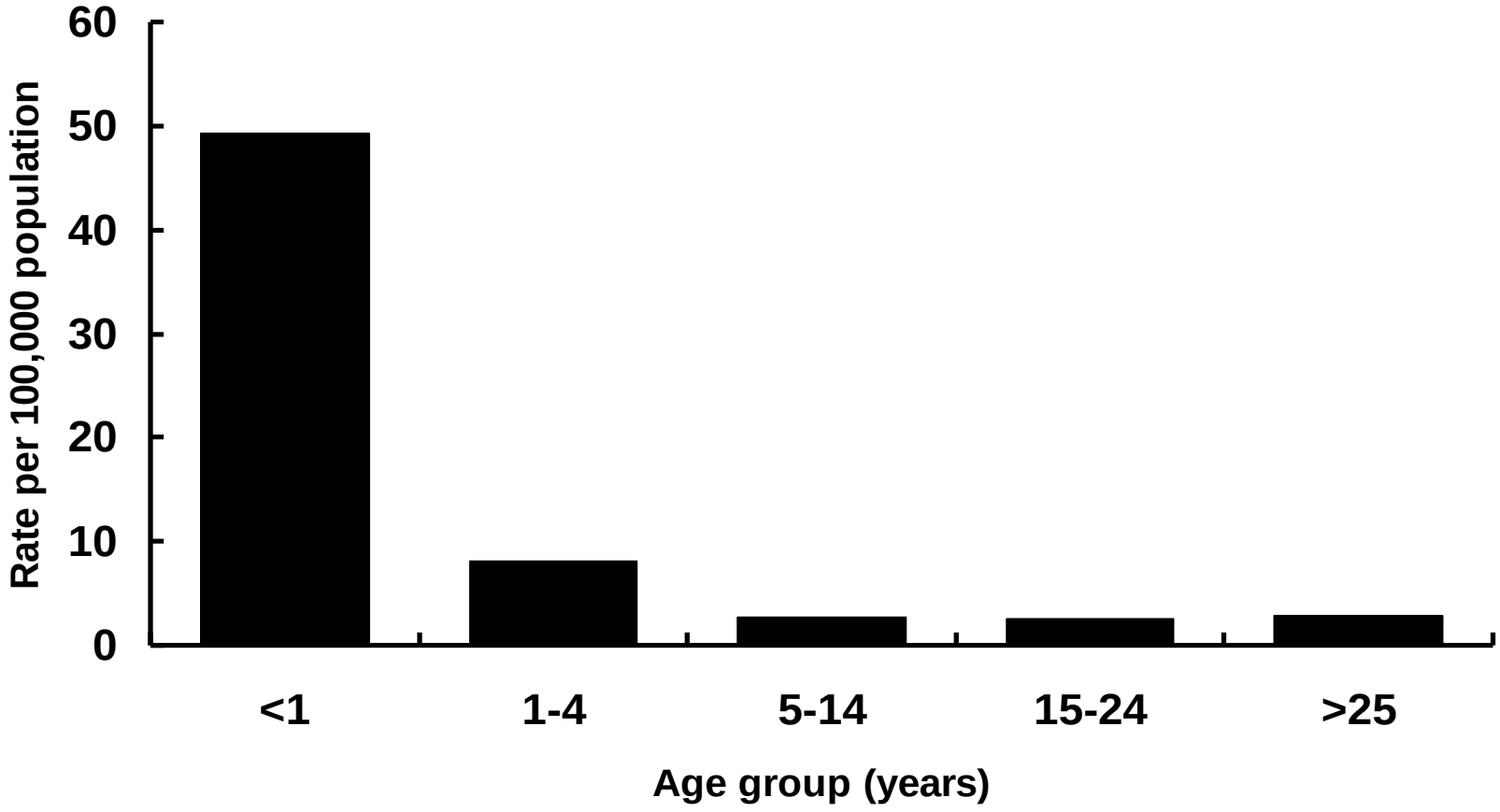


Bisgard, K. PIDJ. 2004;23:985-9.

Reported Pertussis by Age Group, 1990-2007



Pertussis Incidence, 2006



Pertussis Among Adolescents and Adults

- Prolonged cough (3 months or longer)
- Post-tussive vomiting
- Multiple medical visits and extensive medical evaluations
- Complications
- Hospitalization
- Medical costs
- Missed school and work
- Impact on public health system

Adolescent and Adult Pertussis Vaccination

- Primary objective
  - protect the vaccinated adolescent or adult
- Secondary objective
  - reduce reservoir of *B. pertussis*
  - potentially reduce incidence of pertussis in other age groups and settings

Tdap Vaccines

- Boostrix (GlaxoSmithKline)
  - Approved for persons 10 through 64 years of age
- Adacel (sanofi pasteur)
  - Approved for persons 11 through 64 years of age

General Principles for Use of Tdap and Td

- No brand preference
- Tdap preferred to Td to provide protection against pertussis
- Approved only for a single booster dose in persons who have received a full series of pediatric DTaP or DTP

Recommendations for Tdap Vaccination of Adolescents

- Adolescents 11 or 12 years of age should receive a single dose of Tdap instead of Td*
- Adolescents 13 through 18 years who have not received Tdap should receive a single dose of Tdap as their catch-up booster instead of Td*

Tdap Vaccination of Adults 19 Through 64 Years of Age

- Single dose of Tdap to replace a single dose of Td
- May be given at an interval less than 10 years since receipt of last tetanus toxoid-containing vaccine
- Special emphasis on adults with close contact with infants (e.g., childcare and healthcare personnel, and parents)

Tdap For Persons Without A History of DTP or DTaP

- All adolescents and adults should have documentation of having received a series of DTaP, DTP, DT, or Td
- Persons without documentation should receive a series of 3 vaccinations
- Preferred schedule:
  - Single dose of Tdap*
  - Td at least 4 weeks after the Tdap dose
  - Second dose of Td at least 6 months after the Td dose

Tdap

- Tdap minimum ages
  - 10 years for Boostrix
  - 11 years for Adacel
- Neither brand of Tdap approved for children 7 trough 9 years of age, or persons 65 years or older
- Off-label use of Tdap in these age groups NOT recommended

Minimum Interval Between Td and Tdap

- ACIP did not define an absolute minimum interval between Td and Tdap
- Interval between Td and Tdap may be shorter if protection from pertussis needed
- Decision to administer Tdap based on whether the benefit of pertussis immunity outweighs the risk of a local adverse reaction

Tdap and MCV

- MCV is recommended for all children at the 11 or 12-year visit
- Administer Tdap and MCV during the same visit, if both vaccines are indicated and available
- If simultaneous administration of Tdap and MCV is not possible, these vaccines can be administered at any time before or after each other

Use of Tdap Among Pregnant Women

- Td is generally preferred during pregnancy
- Women who have not received Tdap should receive a dose in the immediate post-partum period
- Any woman who might become pregnant is encouraged to receive a single dose of Tdap
- Clinician may choose to administer Tdap to a pregnant woman in certain circumstances (such as during a community pertussis outbreak)
- Pregnancy is not a contraindication for Tdap

Tdap Adverse Reactions

- Local reactions 21%-75%
  (pain, redness, swelling)
- Temp of 100.4°F 3%-5%
  or higher
- Adverse reactions occur at approximately the same rate as Td alone (without acellular pertussis vaccine)

Tdap Contraindications

- Severe allergic reaction to vaccine component or following a prior dose
- Encephalopathy not due to another identifiable cause occurring within 7 days after vaccination with a pertussis-containing vaccine

Tdap Precautions

- History of a severe local reaction (Arthus reaction) following a prior dose of a tetanus and/or diphtheria toxoid-containing vaccine
- Progressive neurologic disorder until the condition has stabilized
- History of Guillain-Barré syndrome within 6 weeks after a prior dose of tetanus toxoid-containing vaccine
- Moderate or severe acute illness

State Funded HPV Vaccine in Alaska

- HPV vaccine is limited to VFC-eligible 9-18 year olds
- All Alaska Natives < 18 years old are VFC-eligible
- HPV vaccine is now permissible for boys and can now be given to VFC-eligible males <18 years old – but will not forecast

VFC Eligibility Criteria

- **VFC Eligibility Criteria:**
  - AK Native/American Indian
  - Medicaid (Denali KidCare) eligible
  - Uninsured - OR…..
  - Underinsured and receiving care at a FQHC (Federally Qualified Health Clinic)

- No proof of eligibility is required.

Human Papillomavirus (HPV) and HPV Vaccine

Epidemiology and Prevention of Vaccine-Preventable Diseases

National Center for Immunization and Respiratory Diseases

Centers for Disease Control and Prevention

Revised May 2009

Human Papillomavirus (HPV)

- Small DNA virus
- More than 100 types identified based on the genetic sequence of the outer capsid protein L1
- 40 types infect the mucosal epithelium

Human Papillomavirus Types and Disease Association

mucosal/genital(~40 types)

nonmucosal/cutaneous (~60 types)

high-risk types
16, 18, 31, 45
(and others)

low-risk types
6, 11
(and others)

skin warts (hands and feet)

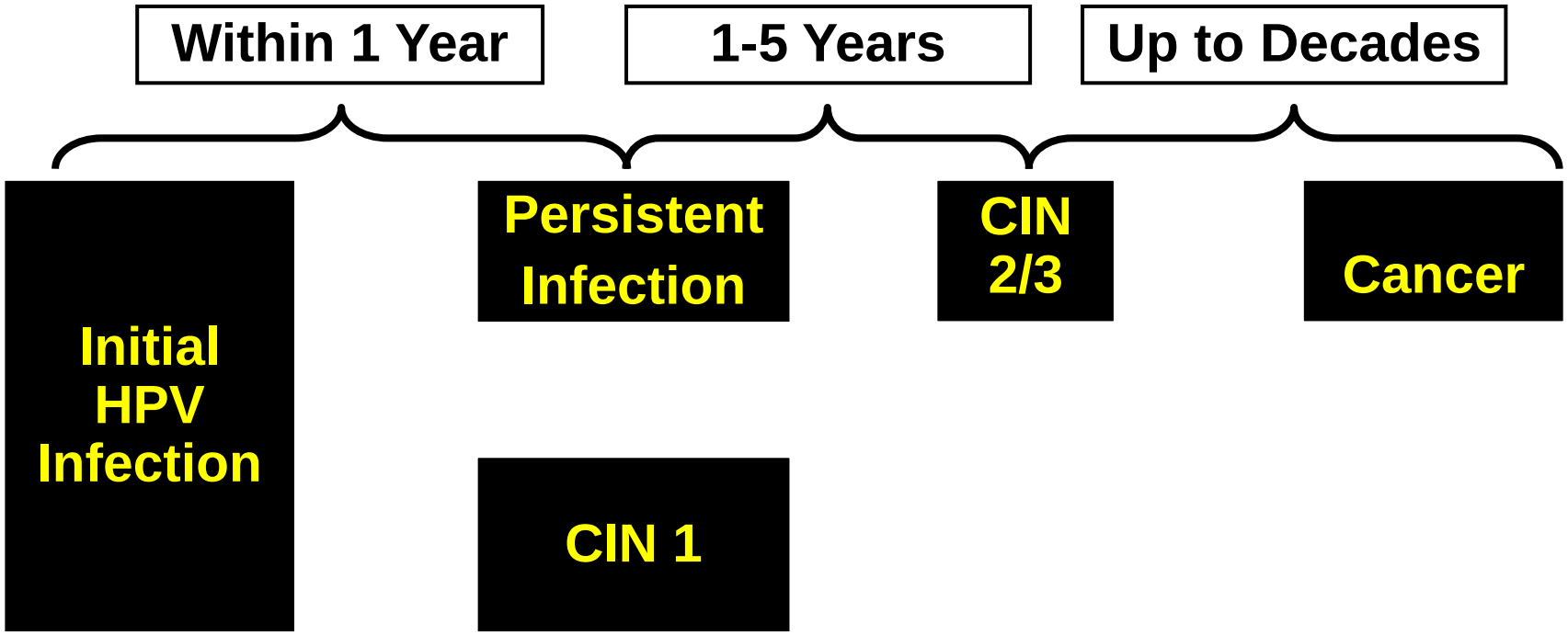
- **low grade cervical abnormalities**
- **cancer precursors**
- **anogenital cancers**

- **low grade cervical abnormalities**
- **genital warts**
- **laryngeal papillomas**

HPV-Associated Disease

Type	Women	Men
16/18	70% of Cervical Cancer 70% of Anal/genital Cancer	70% of Anal Cancer Transmission to women
6/11	90% of Genital Warts 90% of RRP lesions	90% of Genital Warts 90% of RRP lesions Transmission to women

Natural History of HPV Infection



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 some head and neck cancer)

HPV Epidemiology

Reservoir	Human
Transmission	Direct contact, usually sexual
Temporal pattern	None
Communicability	Presumed to be high

HPV Disease Burden in the United States

- Anogenital HPV is the most common sexually transmitted infection in the US
  - Estimated 20 million currently infected
  - 6.2 million new infections/year
- Common among adolescents and young adults
- Estimated 80% of sexually active women will have been infected by age 50
- Infection also common in men

Cervical Cancer Disease Burden in the United States

- The American Cancer Society estimates that in 2008
  - 11,070 new cervical cancer cases
  - 3,870 cervical cancer deaths
- Almost 100% of these cervical cancer cases will be caused by one of the 40 HPV types that infect the mucosa

Cervical Cancer Screening

- Cervical cancer screening – no change
  - 30% of cervical cancers caused by HPV types not prevented by the quadrivalent HPV vaccine
  - Vaccinated females could subsequently be infected with non-vaccine HPV types
  - Sexually active females could have been infected prior to vaccination
- Providers should educate women about the importance of cervical cancer screening

Human Papillomavirus Vaccine

- HPV L1 major capsid protein of the virus is antigen used for immunization
- L1 protein expressed in yeast cells using recombinant technology
- L1 proteins self-assemble into virus-like particles (VLP)
- VLPs are noninfectious and nononcogenic

HPV Vaccine Efficacy*

Endpoint	Efficacy
HPV 16/18-related CIN2/3 or AIS	100
HPV 6/11/16/18 related CIN	95
HPV 6/11/16/18 related genital warts	99

*Among 16-26 year old females. CIN – cervical intraepithelial neoplasia; AIS – adenocarcinoma *in situ*

HPV Vaccine Efficacy

- High efficacy among females without evidence of infection with vaccine HPV types
- No evidence of efficacy against disease caused by vaccine types or which participants were infected at the time of vaccination
- Prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types

Routine HPV Vaccination Recommendations

- ACIP recommends routine vaccination of females 11 or 12 years of age
- The vaccination series can be started as young as 9 years of age at the clinician's discretion
- "Catch-up" vaccination recommended for females 13 through 26 years of age

***MMWR* 2007;56(RR-2):1-24**

HPV Vaccination Schedule

- Routine schedule is 0, 2, 6 months
- Third dose should follow the first dose by at least 24 weeks
- An accelerated schedule using minimum intervals is not recommended
- Series does not need to be restarted if the schedule is interrupted

Provisional Recommendations for Vaccination of Females

- The quadrivalent HPV vaccine and bivalent HPV vaccine are each administered in a 3 dose schedule, with the second dose administered 1 to 2 months after the first dose and the third dose 6 months after the first dose.
- The minimum interval between the first and second doses of vaccine is 4 weeks. The minimum interval between the second and third dose of vaccine is 12 weeks. The minimum interval between the first and third dose is 24 weeks.
- If the HPV vaccine schedule is interrupted, the vaccine series does not need to be restarted.
- HPV vaccines are not live vaccines and can be administered either simultaneously or at any time before or after an inactivated or live vaccine.

http://www.cdc.gov/vaccines/recs/provisional/downloads/hpv-vac-dec2009-508.pdf

Provisional Recommendations* for Vaccination of Females

ACIP recommends routine vaccination of females aged 11 or 12 years with 3 doses of HPV vaccine. The vaccination series can be started as young as 9 years of age.

HPV vaccination is also recommended for females aged 13 through 26 years who have not been previously vaccinated or who have not completed the full vaccination series. Ideally, vaccine should be administered before potential exposure to HPV through sexual contact.

- ACIP recommends vaccination with either the bivalent HPV vaccine or the quadrivalent HPV vaccine for prevention of cervical cancers and precancers.
- ACIP recommends vaccination with the quadrivalent HPV vaccine for prevention of cervical cancers, precancers and and genital warts.

http://www.cdc.gov/vaccines/recs/provisional/downloads/hpv-vac-dec2009-508.pdf

Current Understanding of HPV Vaccines in Females

Attribute	Quadrivalent	Bivalent
Protection against HPV 16/18 related CIN2+*	≥98%	≥93%
Protection against HPV 6/11 related genital lesions	~99%	-
Cross-protection against CIN2+ due to high risk types other than HPV 16,18	Some types phylogenetically related to HPV 16?	Some types phylogenetically related to HPV 16 and 18?
Seroconversion to vaccine types	>99%	>99%
Geometric mean antibody titers	bivalent > quadrivalent	
Duration of protection	Unclear if any differences	
Local reactogenicity	bivalent > quadrivalent	
Cost of vaccine dose	$130 private $106 CDC contract**	$128 private Unknown

*Quadrivalent vaccine - also demonstrated protection against VIN2/3 and VaIN2/3

** http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm

Indications for Quadrivalent HPV Vaccine in Females

- Prevention of the following diseases:
  - cervical, vulvar, and vaginal cancer caused by HPV types 16,18
  - genital warts caused by HPV types 6,11
- Prevention of the following diseases caused by HPV types 6,11,16,18:
  - CIN grade 2/3 and adenocarcinoma in situ
  - CIN grade 1
  - VaIN and VIN grade 2 and 3
- Approved for females aged 9 through 26 yrs

http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm094042.htm

Indications for Bivalent HPV Vaccine in Females

- Prevention of the following diseases caused by HPV types 16,18:
  - cervical cancer
  - CIN grade 2 or worse and adenocarcinoma in situ
  - CIN grade 1
- Approved for females aged 10 through 25 yrs

http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm186957.htm

Burden of Disease/Cancers in Males

- Genital warts
- Recurrent respiratory papillomatosis

> 90% HPV 6, 11

- Anal cancers
- Penile cancers
- Oropharyngeal cancers

~30-90% HPV 16, 18

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Statement:

Quadrivalent HPV vaccine may be given to males aged 9 through 26 years to reduce their likelihood of acquiring genital warts. Quadrivalent HPV vaccine would be most effective when given before exposure to HPV through sexual contact.

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Recommendations and Resolutions

RECOMMENDATION

- Purpose: Describe to providers and programs how the vaccine should be used
- Key question: Is the benefit of the vaccine greater than the risks and costs of the vaccine?
- Evidence used
  - Burden of disease
  - Vaccine efficacy
  - Vaccine safety
  - Cost effectiveness

VFC Resolution

- Purpose: Include a vaccine into the VFC program
- Key question: Does the Committee want to reduce cost as a barrier to VFC-eligible children?
- Cost to VFC should not be the primary consideration, but may be a consideration vis-a-vis public health impact given diversion of scarce public health dollars

HPV Vaccine Special Situations*

- Equivocal or abnormal Pap test
- Positive HPV DNA test
- Genital warts
- Immunosuppression
- Breastfeeding

***Vaccine can be administered**

HPV Vaccine Adverse Reactions

- Local reactions 84%
  (pain, swelling)
- Fever 10%*
- No serious adverse reactions reported

***similar to reports in placebo recipients (9%)**

Syncope Following Vaccination

- An increase in the number of reports of syncope has been detected by the Vaccine Adverse Event Reporting System (VAERS)
- 11-18 year old females have contributed most of the increase
- Serious injuries have resulted
- Providers should strongly consider observing patients for 15 minutes after they are vaccinated

HPV Vaccine Contraindications and Precautions

- Contraindication
  - Severe allergic reaction to a vaccine component or following a prior dose
- Precaution
  - Moderate or severe acute illnesses (defer until symptoms improve)

HPV Vaccination During Pregnancy

- Initiation of the vaccine series should be delayed until after completion of pregnancy
- If a woman is found to be pregnant after initiating the vaccination series, remaining doses should be delayed until after the pregnancy
- If a vaccine dose has been administered during pregnancy, there is no indication for intervention
- Women vaccinated during pregnancy should be reported to the Merck registry (800.986.8999)

***MMWR* 2007;56(RR-2):1-24**

HPV Vaccine Storage and Handling

- Store at 36° F-46° F (2° C-8° C)
- Protect from light
- Do not expose to freezing temperature
- Remove from refrigeration immediately before administration

Meningococcal Disease and Meningococcal Vaccines

Neisseria meningitidis

- Severe acute bacterial infection
- Cause of meningitis, sepsis, and focal infections
- Epidemic disease in sub-Saharan Africa
- Current polysaccharide vaccine licensed in 1978
- Conjugate vaccine licensed in 2005

Neisseria meningitidis

- Aerobic gram-negative bacteria
- At least 13 serogroups based on characteristics of the polysaccharide capsule
- Most invasive disease caused by serogroups A, B, C, Y, and W-135
- Relative importance of serogroups depends on geographic location and other factors (e.g. age)

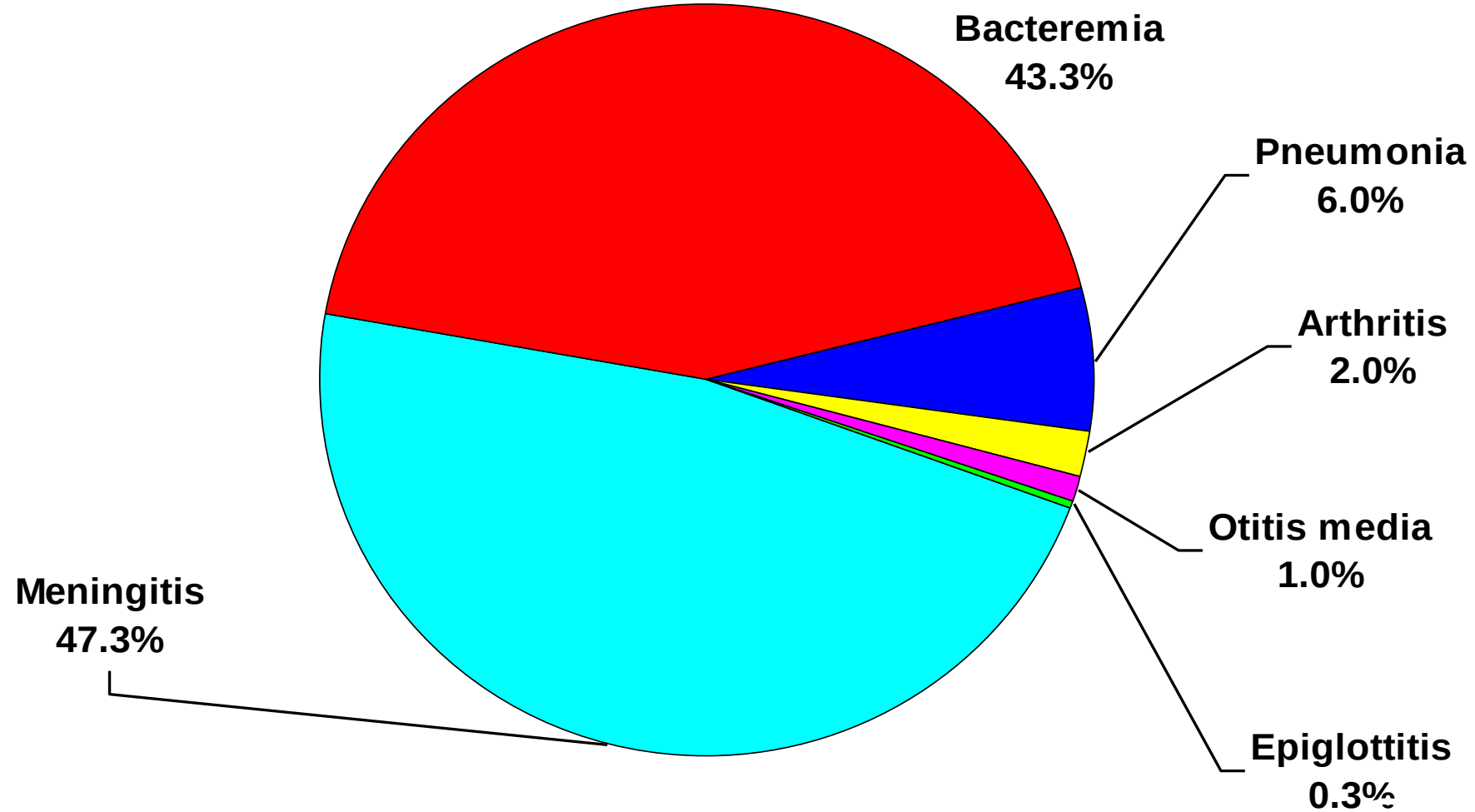
Meningococcal Disease Pathogenesis

- Organism colonizes nasopharynx
- In some persons organism invades bloodstream and causes infection at distant site
- Antecedent URI may be a contributing factor

Meningococcal Disease
Clinical Features

- Incubation period 3-4 days (range 2-10 days)
- Abrupt onset of fever, meningeal symptoms, hypotension, and rash
- Fatality rate 9%-12%; up to 40% in meningococcemia

Neisseria meningitidis Clinical Manifestations*



Meningococcal Meningitis

- Most common pathologic presentation
- Result of hematogenous dissemination
- Clinical findings
  - fever
  - headache
  - stiff neck

Meningococcemia

- Bloodstream infection
- May occur with or without meningitis
- Clinical findings
  - fever
  - petechial/purpuric rash
  - hypotension
  - multiorgan failure

Meningococcal Disease Laboratory Diagnosis

- Bacterial culture
- Gram stain
- Non-culture methods
  - Antigen detection in CSF
  - Serology

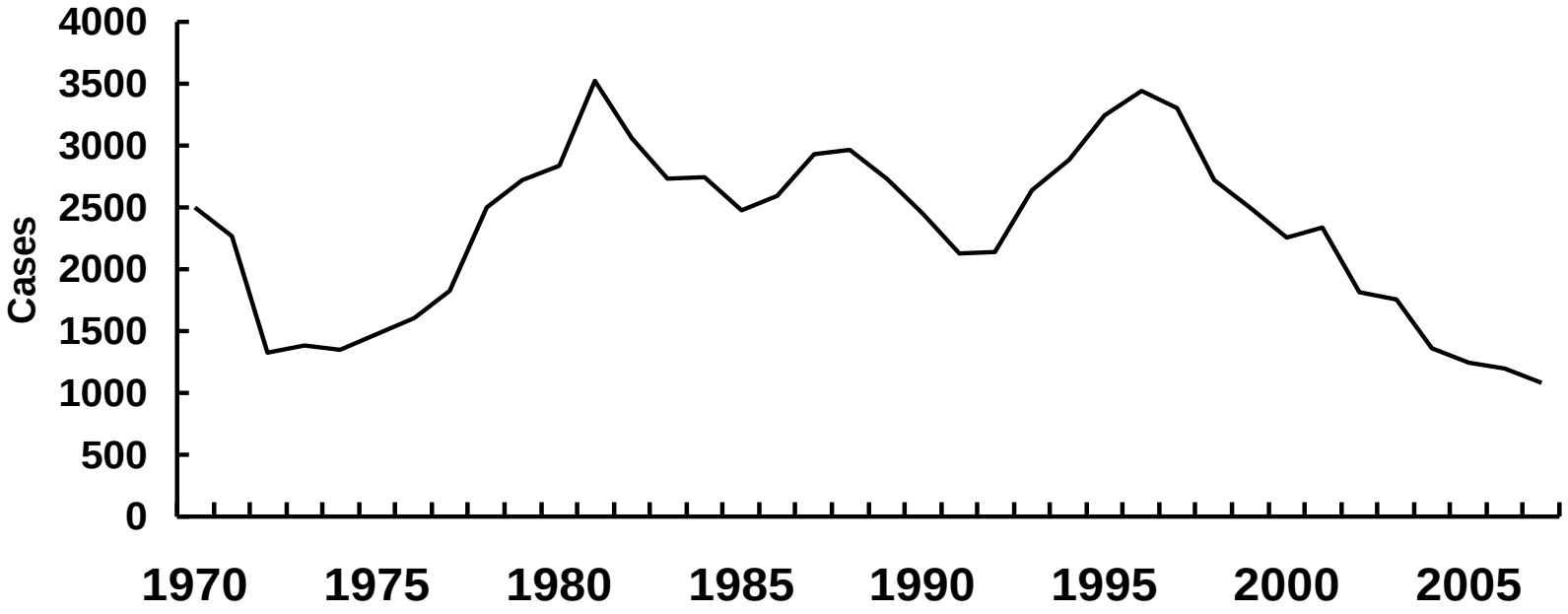
Neisseria meningitidis Medical Management

- Initial empiric antibiotic treatment after appropriate cultures are obtained
- Treatment with penicillin alone recommended after confirmation of *N. meningitidis*

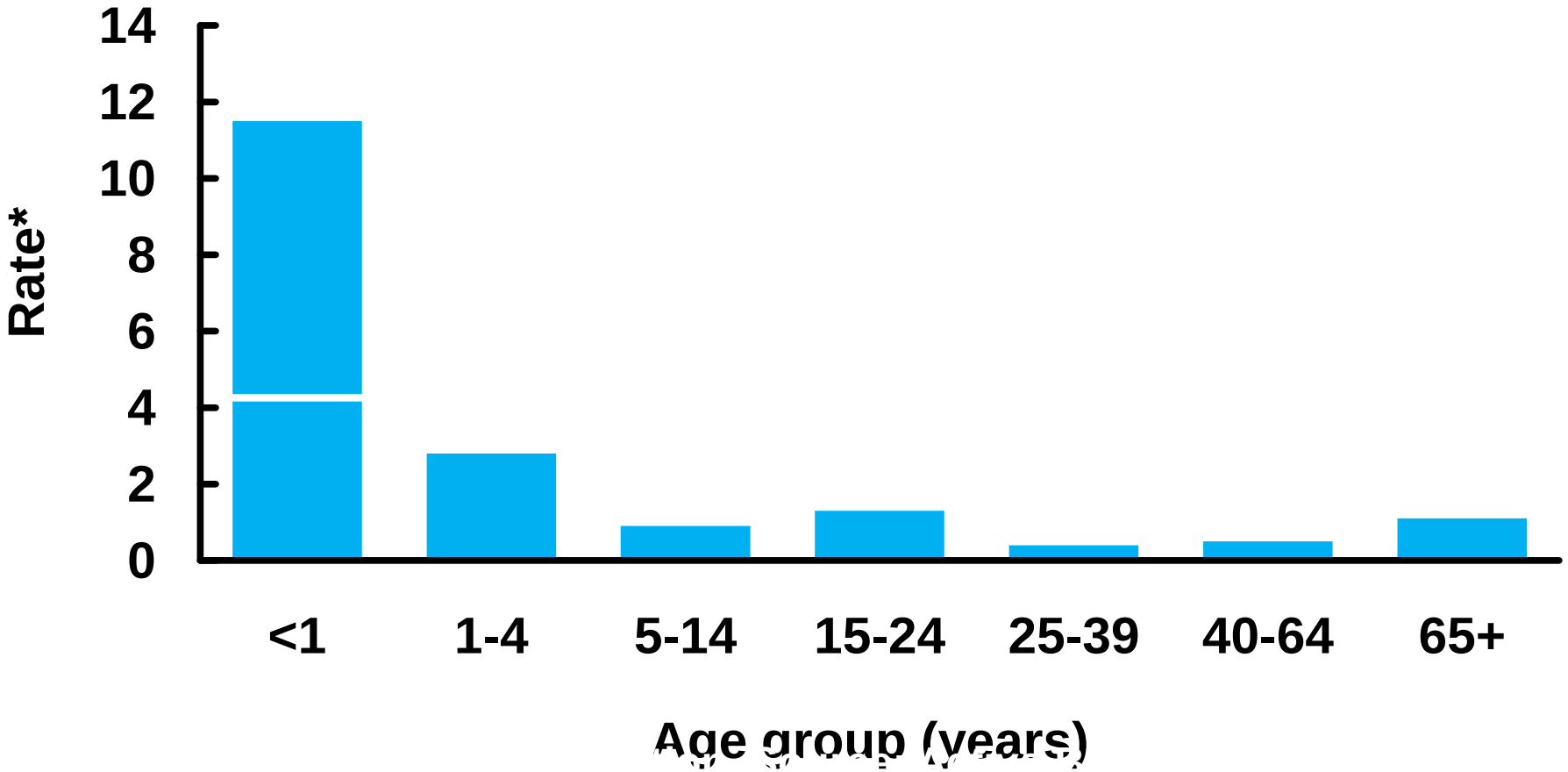
Meningococcal Disease Epidemiology

- Reservoir — Human
- Transmission — Respiratory droplets
- Temporal pattern — Peaks in late winter–early spring
- Communicability — Generally limited

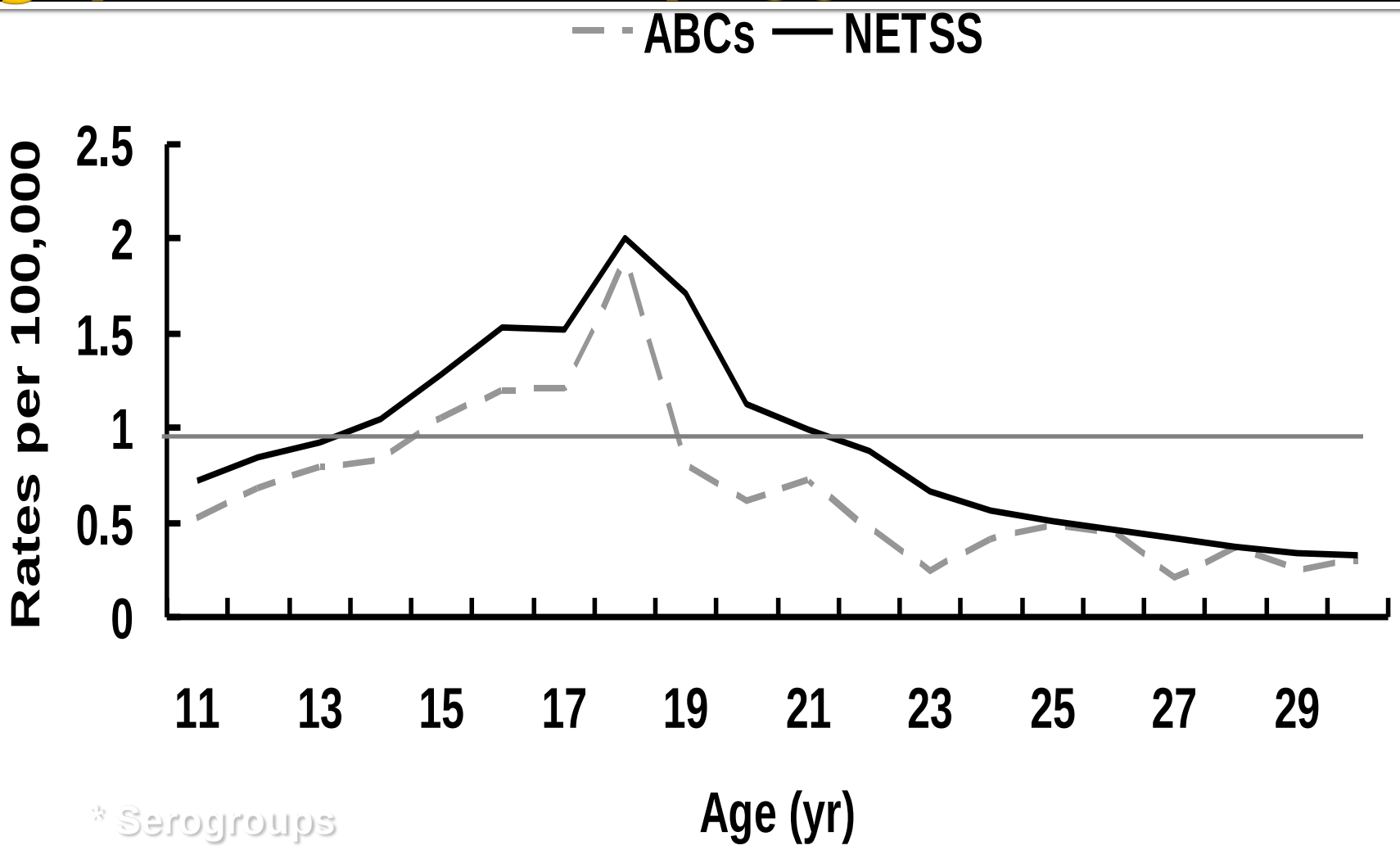
Meningococcal Disease - United States, 1972-2007



Meningococcal Disease, 1998
Incidence by Age Group



Rates of Meningococcal Disease* by Age, United States, 1991-2002



* Serogroups

Meningococcal Disease in the United States

- Distribution of cases by serogroup varies by time and age group
- In 1996-2001:
  - 31% serogroup B
  - 42% serogroup C
  - 21% serogroup Y
  - 65% of cases among children younger than 1 year of age caused by serogroup B

Neisseria meningitidis Risk factors for invasive disease

- Host factors
  - Terminal complement pathway deficiency
  - Asplenia
  - Genetic risk factors
- Exposure factors
  - Household exposure
  - Demographic and socioeconomic factors and crowding
  - Concurrent upper respiratory tract infection
  - Active and passive smoking

Meningococcal Disease Among Young Adults, United States, 1998-1999

18-23 years old	1.4 / 100,000
18-23 years old not college student	1.4 / 100,000
Freshmen	1.9 / 100,000
Freshmen in dorm	5.1 / 100,000

Meningococcal Outbreaks in the United States

- Outbreaks account for less than 5% of reported cases
- Frequency of localized outbreaks has increased since 1991
- Most recent outbreaks caused by serogroup C
- Since 1997 outbreaks caused by serogroup Y and B organisms have also been reported

Meningococcal Polysaccharide Vaccine (MPSV)

- Menomune® (sanofi pasteur)
- Quadrivalent polysaccharide vaccine (A, C, Y, W-135)
- Administered by subcutaneous injection
- 10-dose vial contains thimerosal as a preservative

Meningococcal Conjugate Vaccine (MCV)

- Menactra® (sanofi pasteur)
- Quadrivalent polysaccharide vaccine (A, C, Y, W-135) conjugated to diphtheria toxoid
- Administered by intramuscular injection
- Single dose vials do not contain a preservative

MCV Recommendations

- Routinely recommended for:
  - All children at 11-18 years of age
  - All college freshmen living in a dormitory
  - Other persons 2 through 55 years of age at increased risk of invasive meningococcal disease

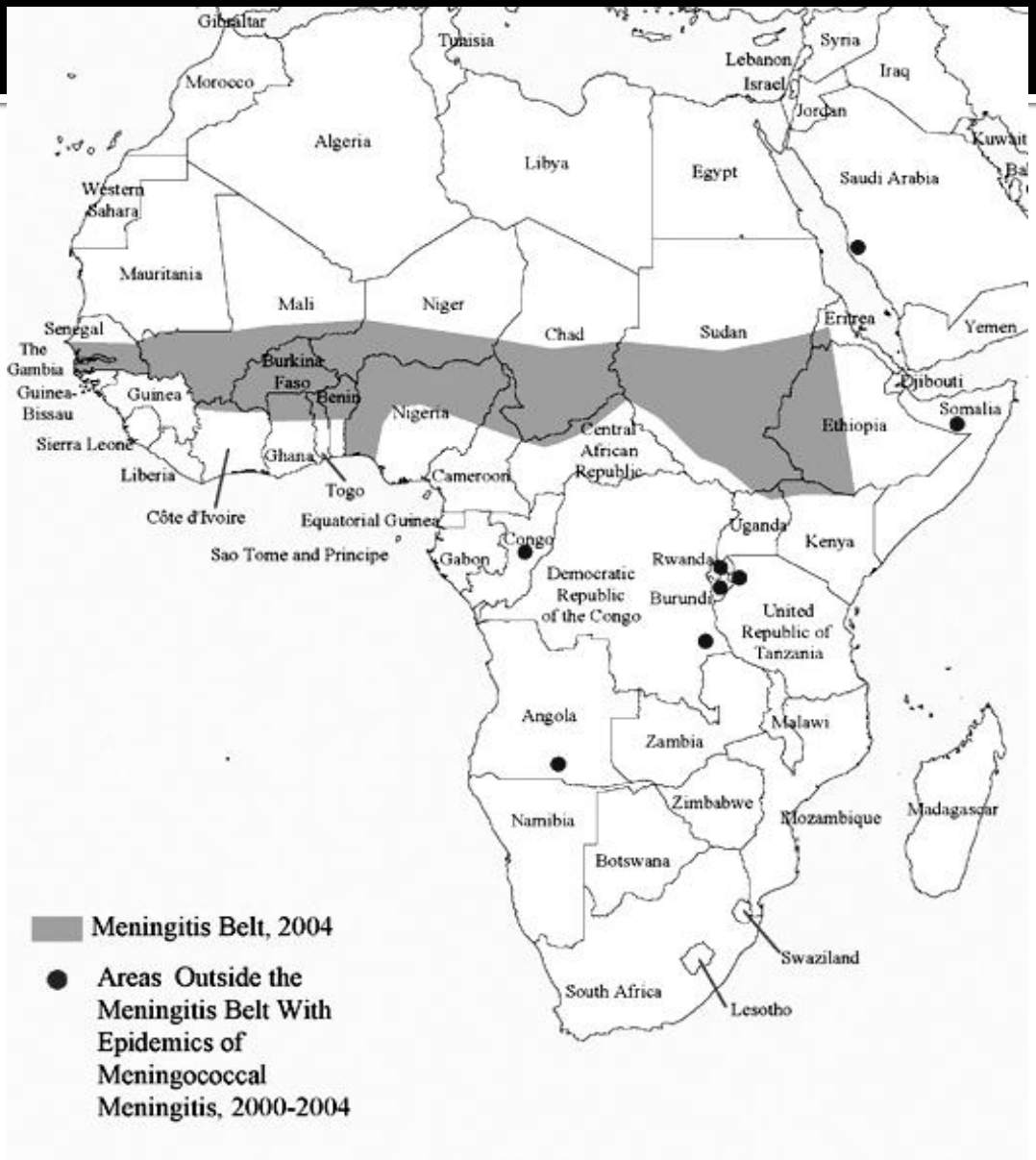
Meningococcal Vaccine Recommendations

- Use of MCV is preferred for persons 2 through 55 years of age for whom meningococcal vaccine is recommended
- MPSV should be used for persons 56 years and older

Meningococcal Vaccine Recommendations

- Recommended for persons at increased risk of meningococcal disease:
  - Microbiologists who are routinely exposed to isolates of *N. meningitidis*
  - Military recruits
  - Persons who travel to and U.S. citizens who reside in countries in which *N. meningitidis* is hyperendemic or epidemic
  - terminal complement component deficiency
  - functional or anatomic asplenia

Meningococcal Endemic Areas 2004



Meningococcal Vaccine Recommendations

- Both MCV and MPSV recommended for control of outbreaks caused by vaccine-preventable serogroups
- Outbreak definition:
  - 3 or more confirmed or probable primary cases
  - Period <3 months
  - Primary attack rate >10 cases per 100,000 population*

Meningococcal Vaccine Revaccination

- Revaccination may be indicated for persons at increased risk for infection*
- Revaccination may be considered 5 years after receipt of the MPSV
- MCV is recommended for revaccination of persons 2 through 55 years of age although use of MPSV is acceptable
- Revaccination after receipt of MCV is not recommended at this time

Meningococcal Vaccines Adverse Reactions

Local reactions for 1-2 days	4%-48%	11%-59%
Fever ≥100°F	3%	5%
Systemic reactions (headache, malaise fatigue)	3%-60%	4%-62%

Meningococcal Vaccines Contraindications and Precautions

- Severe allergic reaction to vaccine component or following prior dose of vaccine
- Moderate or severe acute illness

CDC Vaccines and Immunization Contact Information

- Telephone 800.CDC.INFO
- Email nipinfo@cdc.gov
- Website www.cdc.gov/vaccines

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Vaccine Resources

- Resources:
  - www.immunize.org
  - www.cdc.gov/vaccines/
  - www.immunizationinfo.org
- Parent resources
  - http://www.aap.org/healthtopics/Autism.cfm
  - http://www.cispimmunize.org/fam/fam_main.html