Poliomyelitis, Pneumococcal and Meningococcal Disease CH 8, 17 &18

Poliomyelitis

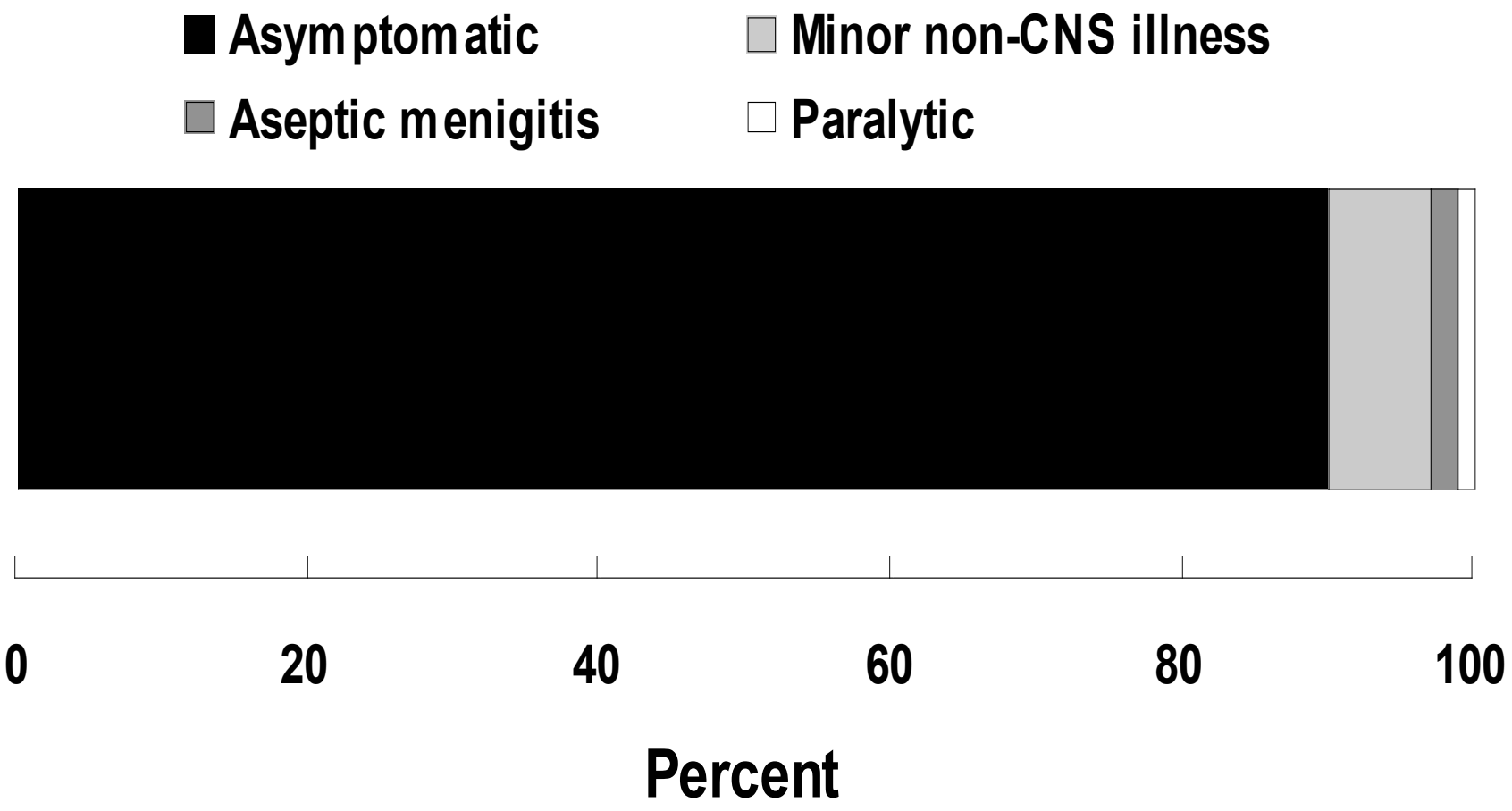
- First described by Michael Underwood in 1789
- First outbreak described in U.S. in 1843
- 21,000 paralytic cases reported in the U. S. in 1952
- Global eradication in near future


MARINA

Poliovirus

- Enterovirus (RNA)
- Three serotypes: 1, 2, 3
- Rapidly inactivated by heat, formaldehyde, chlorine, ultraviolet light
- Entry into mouth
- Replication in pharynx, GI tract, local lymphatics
- Hematologic spread to lymphatics and central nervous system
- Viral spread along nerve fibers
- Destruction of motor neurons

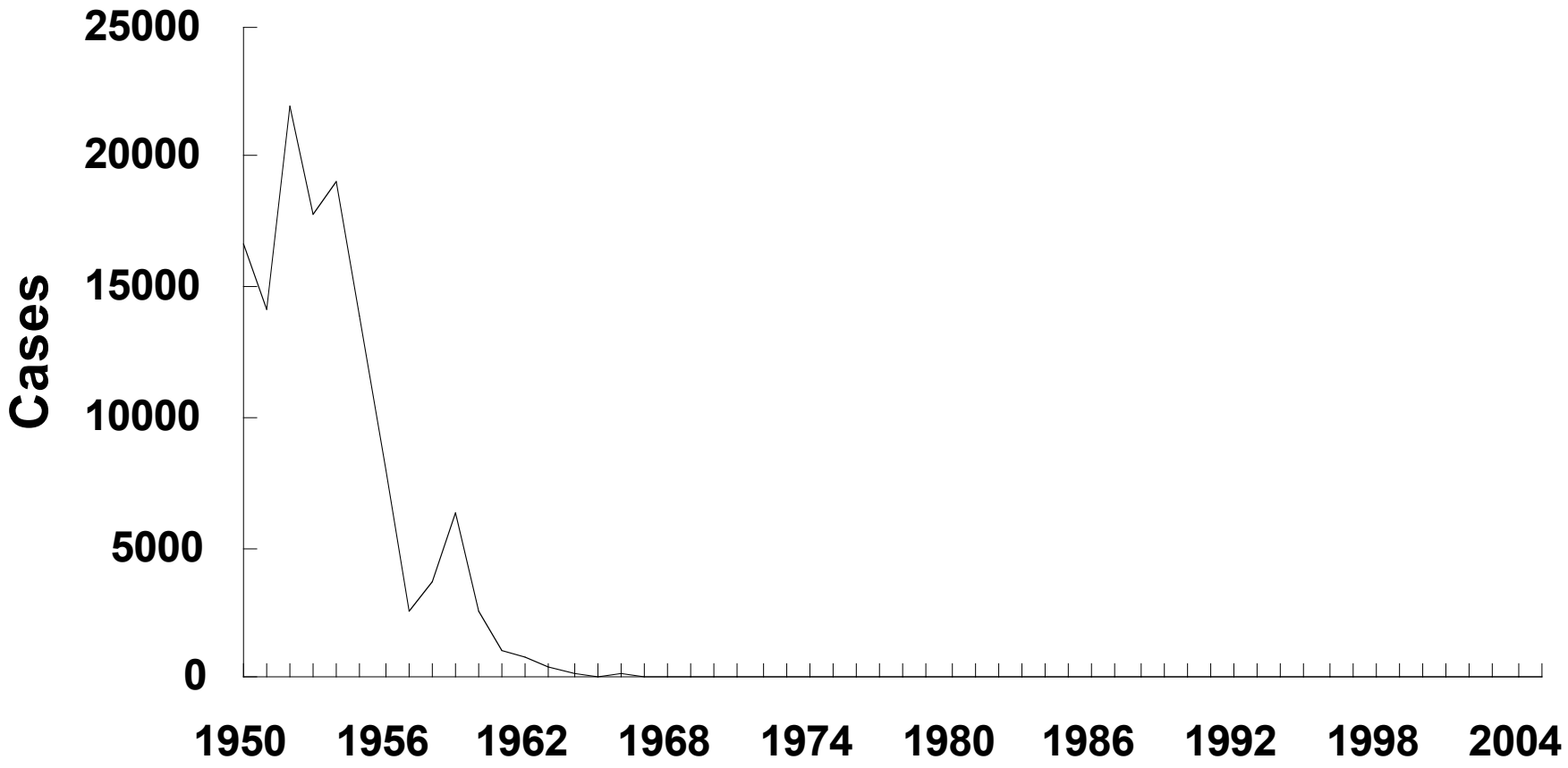
Outcomes of poliovirus infection



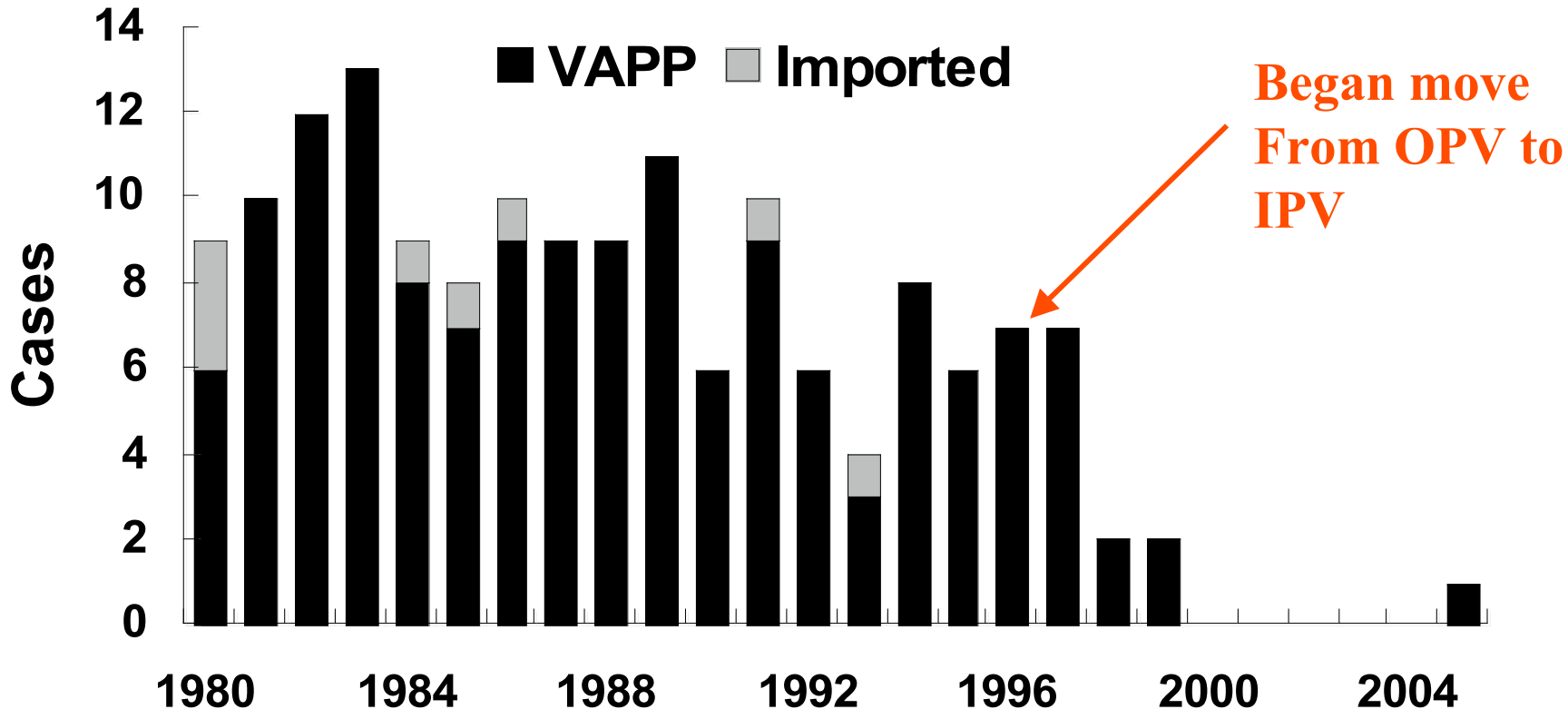
Poliovirus Epidemiology

- Reservoir — Human
- Transmission — Fecal-oral
  Oral-oral possible
- Communicability — 7-10 days before onset
  Virus present in stool
  3-6 weeks

Poliomyelitis—United States, 1950-2005



Poliomyelitis—United States, 1980-2005



Vaccine-Derived Poliovirus Infections - MN, 2005

- 7-month-old infant with a severe immunodeficiency
- Infected with type 1 poliovirus that was derived from the vaccine strain
- 7 additional infections in the community
- None of the infected children were paralyzed or had other symptoms

Inactivated Polio Vaccine

- Contains 3 serotypes of vaccine virus
- Grown on monkey kidney (Vero) cells
- Inactivated with formaldehyde
- Contains 2-phenoxyethanol, neomycin, streptomycin, polymyxin B
- Highly effective in producing immunity to poliovirus
- >90% immune after 2 doses
- >99% immune after 3 doses
- Duration of immunity not known with certainty

Polio Vaccination Schedule

Age	Vaccine	Minimum Interval
2 months	IPV	---
4 months	IPV	4 wks
6-18 months	IPV	4 wks
4-6 years*	IPV	4 wks

*the fourth dose of IPV may be given as early as 18 weeks of age

Schedules that Include Both IPV and OPV

- Only IPV is available in the United States
- Schedule begun with OPV should be completed with IPV
- Any combination of 4 doses of IPV and OPV by 5 years constitutes a complete series

Polio Vaccine Adverse Reactions

- Rare local reactions (IPV)
- No serious reactions to IPV have been documented
- Paralytic poliomyelitis (OPV only)

Polio Vaccine
Contraindications and Precautions

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

IPV vs. OPV

- Trivalent
- Inactivated viruses
- Highly effective vaccine
- >90% immune after 2 doses
- >99% immune after 3 doses
- Duration unknown

- Trivalent
- Live, attenuated viruses
- Highly effective vaccine
- ~50% immune after 1 dose
- >95% immune after 3 doses
- Immunity probably lifelong

IPV Vaccine Formulation

Component, per 0.5 ml dose	IPV (IPOL) Sanofi Pasteur	DTaP-HepB-IPV (Pediarix) GSK
Type 1 polio virus	40 D antigen Units (DU)	40 DU
Type 2	8 DU	8 DU
Type 3	32 DU	32 DU
2-Phenoxyethanol	0.5%	2.5 mg
Formaldehyde	<0.2%	<100 μg
Neomycin	< 5 ng	
Streptomy cin	200 ng	
Polymyxin B	25 ng	<0.05 ng
Diphtheria toxoid		25 Lf
Tetanus toxoid		10 Lf
Pertussis toxin, inactivated		25 μg
Filamentous hemagglutinin		25 μg
Pertactin		8 μg
HBsAg		10 μg
Aluminum adjuvant		<0.85 mg
Tween 80		<100 μg
Thimerosal		<12.5ng

IPV production

- VERO cells established on microcarriers with MEM and fetal calf serum
- Cells infected with Polioviruses types 1, 2 or 3, medium changed to serum-free M199
- Viral suspensions clarified, filtered, concentrated
- Purification: anion exchange, gel filtration, anion exchange chromatography
- Adjust titers and inactivate at 37C, 12 days with formalin

Cutter Incident

- April, 1955 - Six manufacturers licensed to sell IPV
- Massive immunization of U.S. population initiated
- Cases of paralytic polio began to appear
  - All from Cutter Lab's IPV
  - ~260 cases of type 1 polio, 192 paralytic
  - Due to incomplete inactivation of virus

Polio eradication by 2000

- Adopted in 1988
  - 350,000 cases paralytic polio/year
  - polio endemic in 125 countries
- 2003 status
  - 784 confirmed cases
  - 6 endemic countries
- 2005 status
  - 61,606 cases paralytic polio
  - polio endemic in 4 countries

Wild Poliovirus 1988

Wild Poliovirus 2004

Pneumococcal Disease

- Leading cause of morbidity and mortality for all ages, worldwide
- U.S. annual incidence:
  - 15-30 cases/100,000
  - case fatality rate 15-20%
- Major cause of :
  - invasive infections: bacteremia, meningitis
  - pneumonia, upper respiratory disease, acute otitis media, sinusitis

Streptococcus pneumoniae

- Gram + coccus
- Increasingly resistant to antimicrobial agents
- Commonly occurs as carrier state
- Both capsulated and non-capsulated
- ~90 serotypes

Pneumococcal Disease

- *S. pneumoniae* first isolated by Pasteur in 1881
- Confused with other causes of pneumonia until discovery of Gram stain in 1884
- More than 80 serotypes described by 1940
- First U.S. vaccine in 1977

Pneumococcal Pneumonia
Clinical Features

- Abrupt onset
- Fever
- Shaking chills
- Pleuritic chest pain
- Productive cough
- Dyspnea, tachypnea, hypoxia

Pneumococcal Pneumonia

- Estimated 175,000 hospitalizations per year in the United States
- Up to 36% of adult community-acquired pneumonia and 50% of hospital-acquired pneumonia
- Common bacterial complication of influenza and measles

Pneumococcal Disease in Children

- Bacteremia without known site of infection most common clinical presentation
- *S. pneumoniae* leading cause of bacterial meningitis among children younger than 5 years of age
- Highest rate of meningitis among children younger than 1 year of age
- Common cause of acute otitis media

Burden of Pneumococcal Disease in Children*

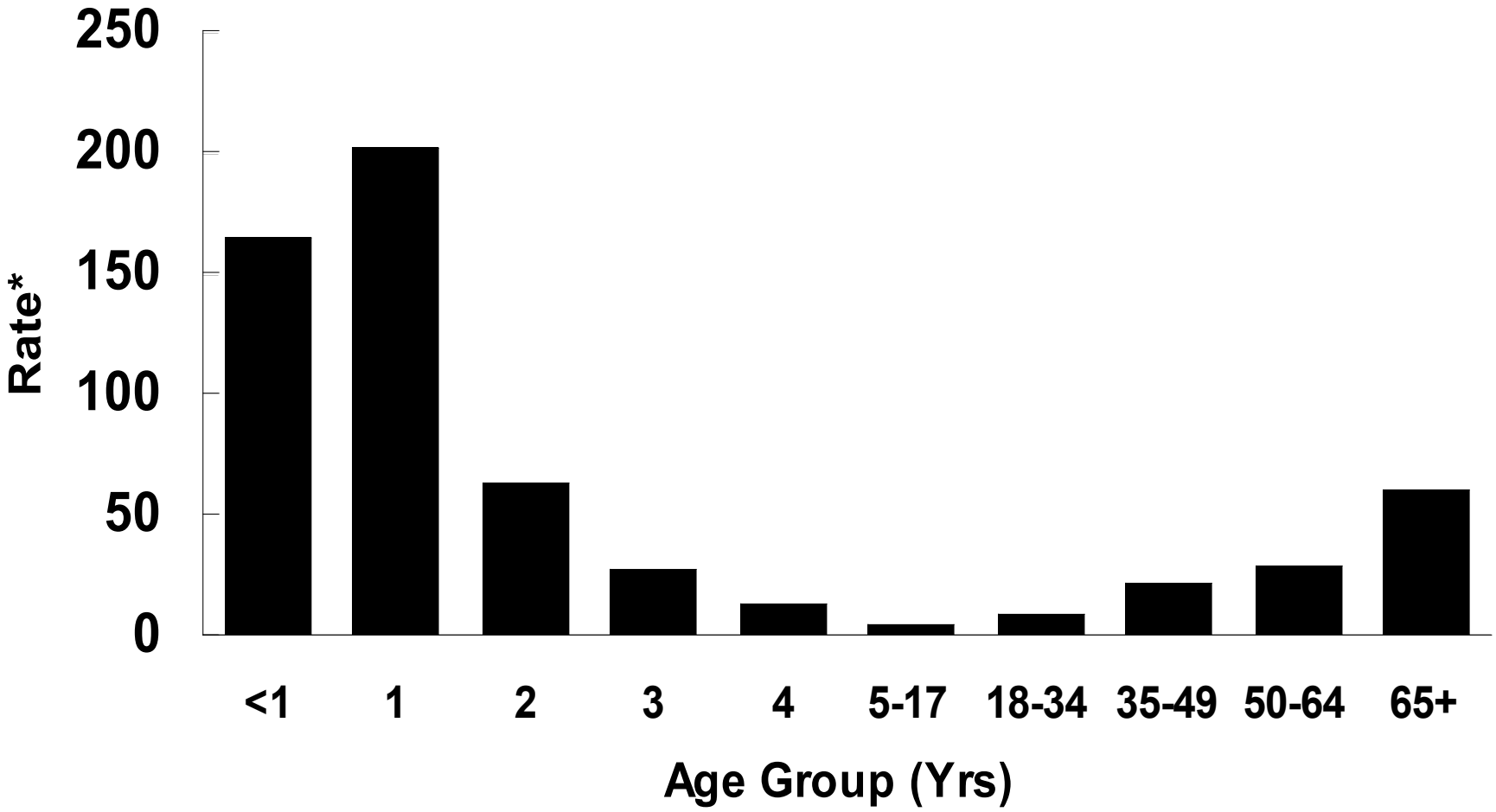
Syndrome	Cases
Bacteremia	13,000
Meningitis	700
Death	200
Otitis media	5,000,000

***Prior to routine use of pneumococcal conjugate vaccine**

Pneumococcal Disease Epidemiology

- Reservoir — Human carriers
- Transmission — Respiratory
- Temporal pattern — Winter and early spring
- Communicability — Unknown
  Probably as long as organism in respiratory secretions

Invasive Pneumococcal Disease Incidence by Age Group—1998



Children at Increased Risk of Invasive Pneumococcal Disease

- Functional or anatomic asplenia, especially sickle cell disease
- HIV infection
- Recipient of cochlear implant
- Out-of-home group child care
- African American children
- Alaska Native and American Indian children who live in Alaska, Arizona, or New Mexico
- Navaho children who live in Colorado and Utah

Pneumococcal Disease Outbreaks

- Outbreaks not common
- Generally occur in crowded environments (jails, nursing homes)
- Persons with invasive disease often have underlying illness
- May have high fatality rate

Pneumococcal Vaccines

1977 14-valent polysaccharide vaccine licensed

1983 23-valent polysaccharide vaccine licensed (PPV23)

2000 7-valent polysaccharide conjugate vaccine licensed (PCV7)

Pneumococcal Polysaccharide Vaccine

- Purified capsular polysaccharide antigen from 23 types of pneumococcus
- Account for 88% of bacteremic pneumococcal disease
- Cross-react with types causing additional 8% of disease

Pneumococcal Conjugate Vaccine

- Pneumococcal polysaccharide conjugated to nontoxic diphtheria toxin (7 serotypes)
- Vaccine serotypes account for 86% of bacteremia and 83% of meningitis among children younger than 6 years of age

Pneumococcal Polysaccharide Vaccine Recommendations

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

Pneumococcal Conjugate Vaccine Recommendations

- All children younger than 24 months of age
- Unvaccinated children 24-59 months with a high-risk medical condition

Pneumococcal Conjugate Vaccine Recommendations

- Doses at 2, 4, 6, months of age, booster dose at 12-15 months of age
- Unvaccinated children ≥7 months of age require fewer doses

Pneumococcal Conjugate Vaccine

- Children aged 24-59 months at high risk and previously vaccinated with PPV23 should receive 2 doses of PCV7
- Children at high risk who previously received PCV7 should receive PPV23 at age 2 years of age

Pneumococcal Polysaccharide Vaccine Revaccination

- Routine revaccination of immunocompetent persons is not recommended
- Revaccination recommended for persons age ≥2 years at highest risk of serious pneumococcal infection
- Single revaccination dose ≥5 years after first dose

Pneumococcal Vaccines Adverse Reactions

- Local reactions
  - polysaccharide 30%-50%
  - conjugate 10%-20%
- Fever, myalgia
  - polysaccharide <1%
  - conjugate 15%-24%
- Severe adverse reactions rare

Pneumococcal Vaccines Contraindications and Precautions

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

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)

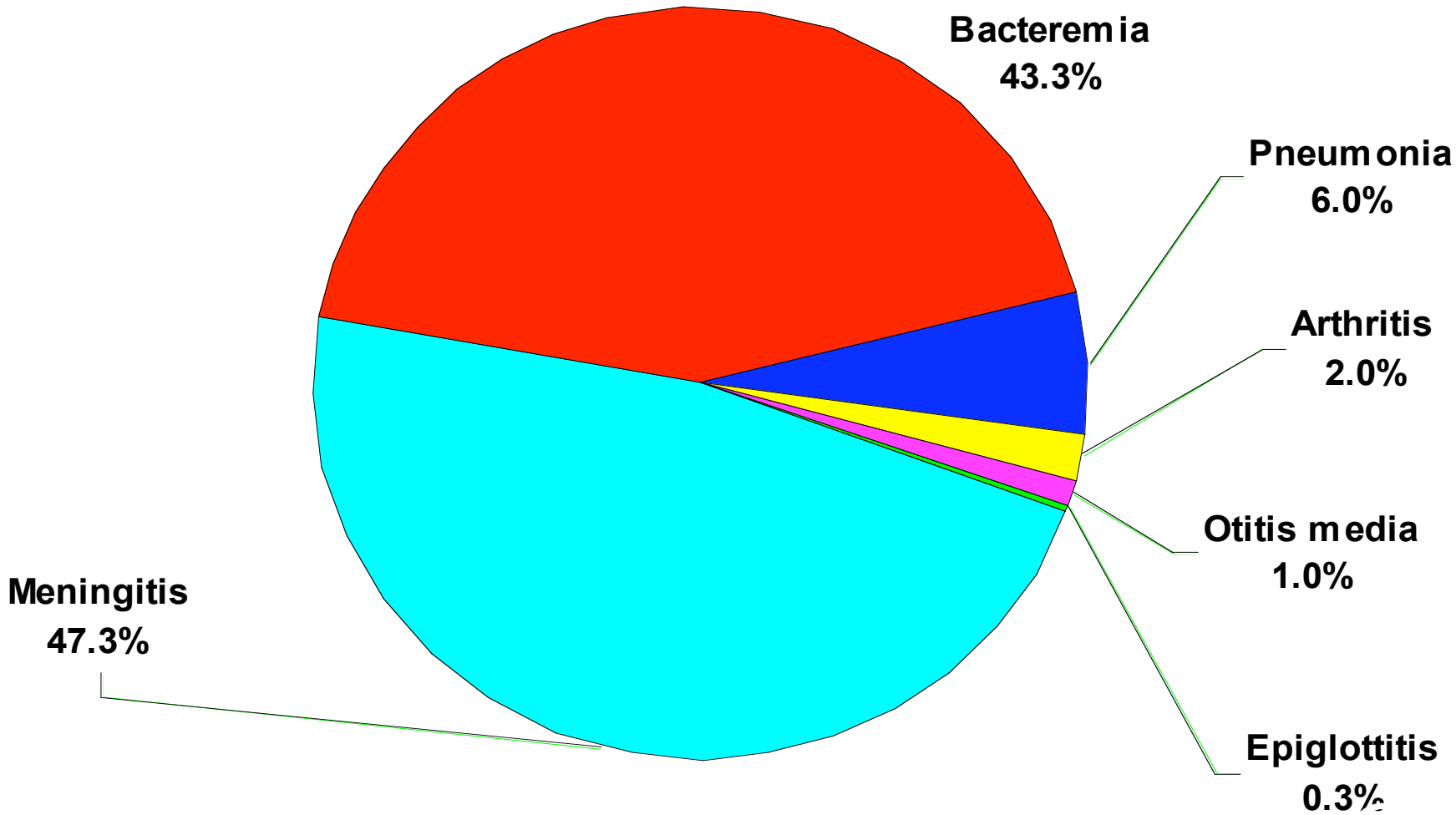
Meningococcal Disease Pathogenesis

- 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*



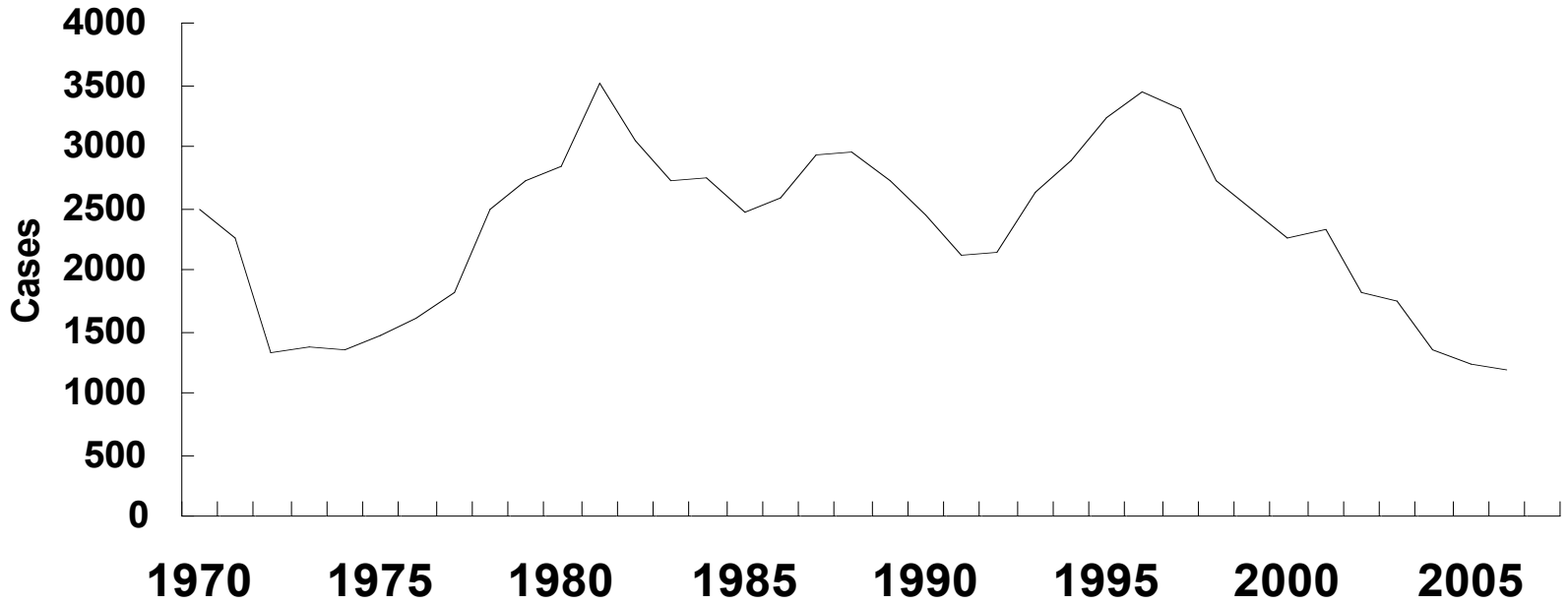
Meningococcal Meningitis

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

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 - United States, 1972-2006



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

Bruce et al, *JAMA* 2001;286;688-93

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

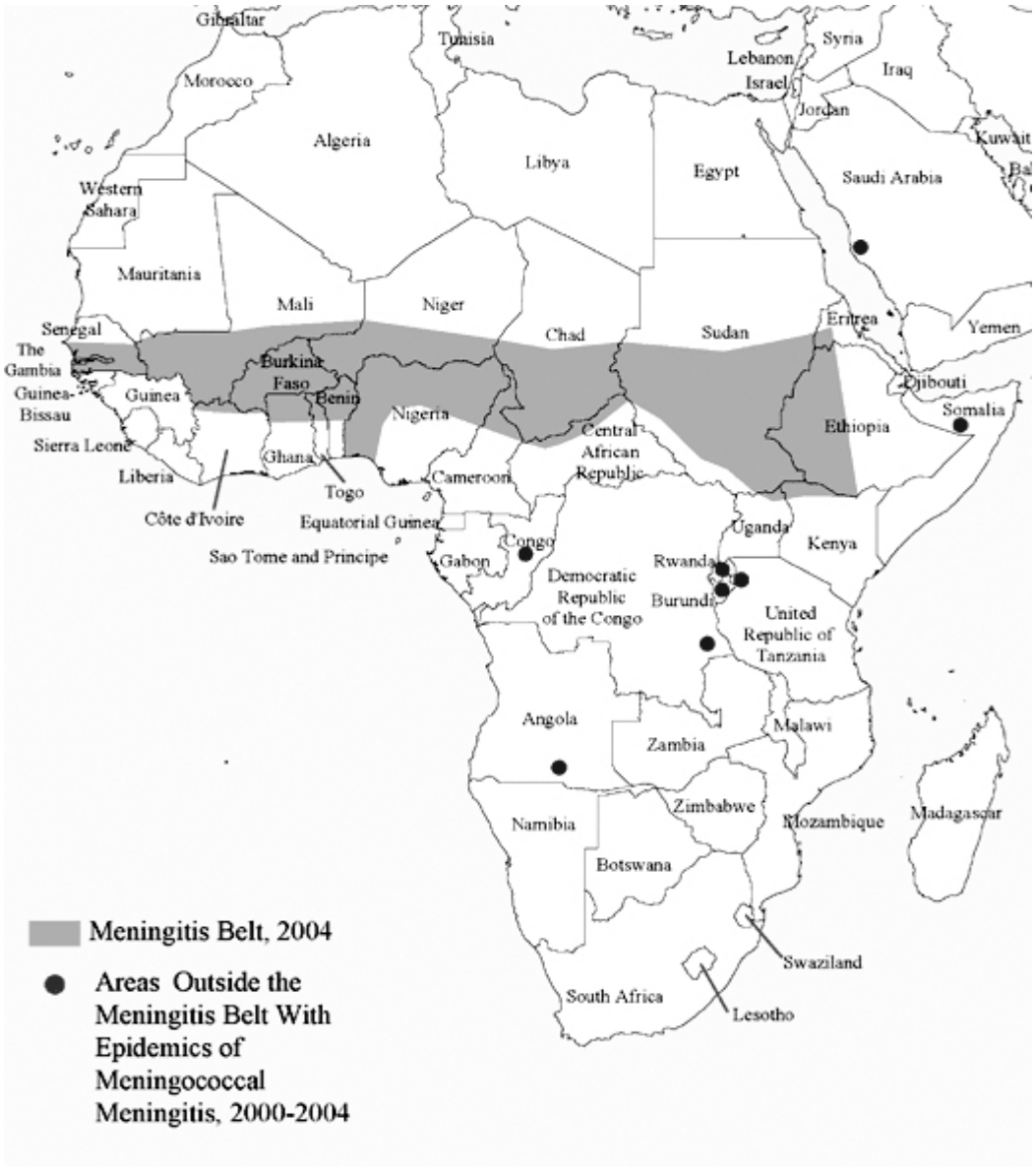
MPSV Recommendations

- Approved for persons 2 years of age and older
- Not recommended for routine vaccination of civilians
- Should be used only for persons at increased risk of *N. meningiditis* infection who are 56 years of age or older, or if MCV is not available

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 Endemic Areas 2004



Meningococcal Conjugate Vaccine and Guillain-Barré Syndrome (GBS)

- 25 confirmed case reports* of GBS within 6 weeks after receipt of MCV vaccine
  - 20 of the reports are in persons 15-19 years of age
- Available data cannot determine if MCV increases the risk of GBS
- No change in vaccination recommendations except that persons with a history of GBS who are not in a high risk group for invasive meningococcal disease should not receive MCV

Meningococcal Vaccines Contraindications and Precautions

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