

Haemophilus influenzae type b Disease and Vaccine: Past and Present

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Leadership for a Healthy Arizona



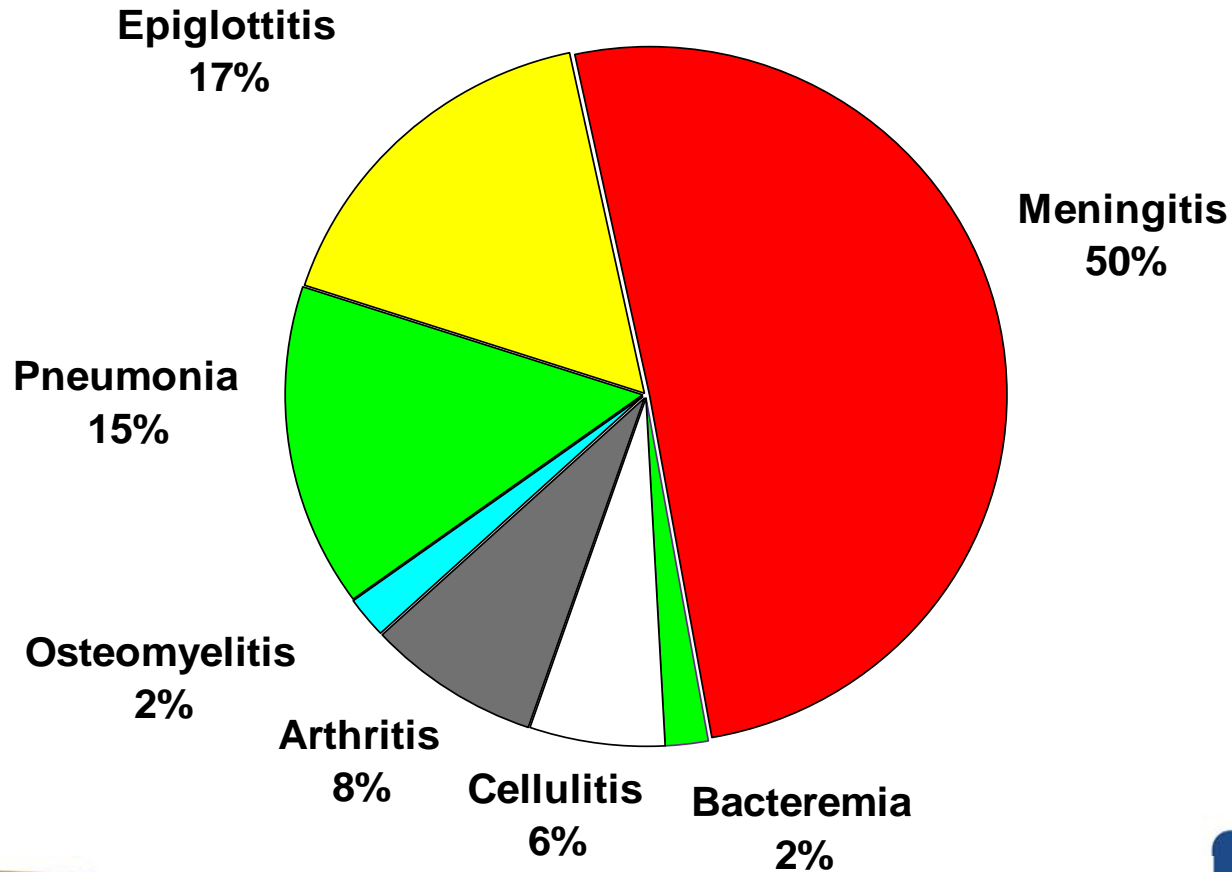
Before Hib Vaccines

- How many cases of invasive Hib disease were there yearly in the US?
- What was the #1 disease from invasive Hib?
- What was the #2 disease from invasive Hib?

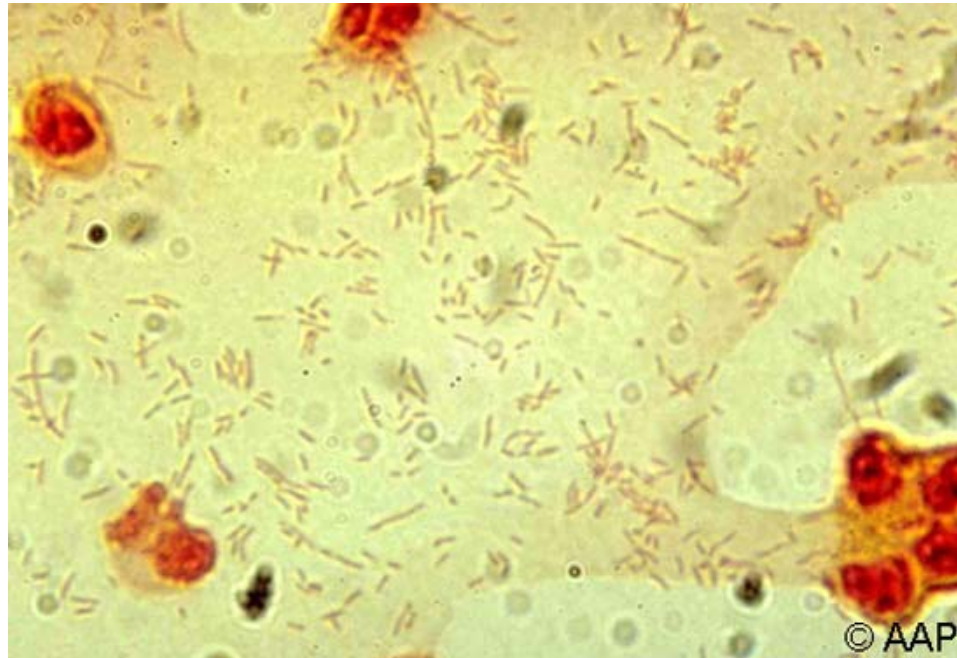
Prevaccination Epidemiology of Hib

- 20,000-30,000 cases/year in US
- Rates of 40-50 cases/100,000 in < 5 yo
- Meningitis
 - 50% of disease
 - #1 cause of childhood bacterial meningitis
 - 15-30% brain damage or hearing loss
 - 2-5% mortality

Haemophilus influenzae type b Prevaccination Clinical Features



Gram Negative Rods (Hib) in Cerebrospinal Fluid



Haemophilus influenzae type b Vaccination Following Invasive Disease

- Children younger than 24 months may not develop protective antibody after invasive disease
 - Vaccinate during convalescence
 - Complete series for age

Prophylaxis for Invasive Hib Disease

- Who gets prophylaxis?
- What prophylaxis is given?
- When are secondary cases of Hib most likely to occur?
- What about day care settings?

Principles for Prophylaxis for Contacts of Hib Disease

- Highest risk in unimmunized household contacts < 4 years old
- Rifampin eradicates 95% nasopharyngeal carriage
- Secondary cases in child care setting unlikely if all contacts are > 2 years old

Give Rifampin to All Household Contacts of Invasive Hib if:

- ≥ 1 household contact < 4 years old who is incompletely immunized or unimmunized
- Household with child < 12 months who has not received primary Hib series
- Household with immune compromised child
 - Irrespective of age and Hib vaccine status

Additional Indications for Rifampin Prophylaxis

- Nursery school and child care center contacts when ≥ 2 cases of invasive Hib within 60 days
- For index case, if
 - Younger than 2 years old, or if
 - Susceptible household contact and index treated with antibiotic besides cefotaxime or ceftriaxone

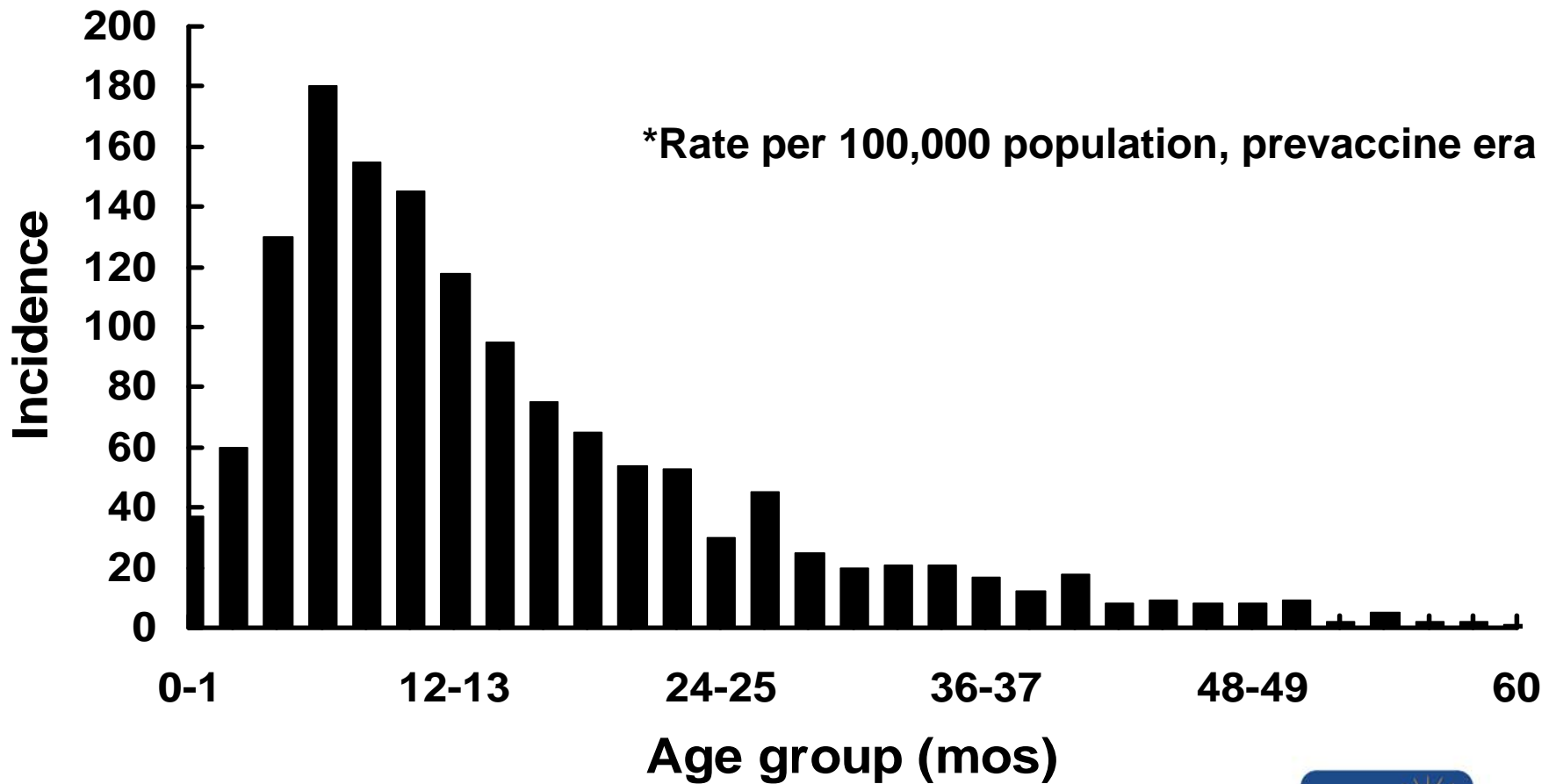
No Need to Give Rifampin Prophylaxis if:

- Household where no child younger than 4 years old, other than index patient
- Households where
 - Contacts 12-48 months have completed Hib vaccine series, and
 - Contacts < 12 months have completed primary Hib vaccine series
- Nursery care contacts of 1 case, esp if > 2 yo
- Pregnant women

Dose of Rifampin for Hib Prophylaxis

- Adult: 600 mg daily for 4 days
- Child: 20 mg/kg daily for 4 days
 - Maximum 600 mg
- Infant < 1 month: 10 mg/kg daily for 4 days

Haemophilus influenzae type b, 1986 Incidence* by Age Group



Incidence of Invasive Hib Disease in Selected Ethnic Groups

Rate per 100,000	Period	Age	Meningitis	Other Dz
Sweden	1971-1980	< 4 y	27	--
		5-9 y	4	--
		10-15 y	1	--
AZ White Mt. Apache	1973-1986	< 5 y	254	--
Alaska Native	1980-1982	< 1 y	871	1702
		< 5 y	282	601
Alaska Nonnative	1980-1982	< 1 y	155	291
		< 5 y	69	129

Relative Risks for Invasive Hib Atlanta, GA 1983-1984

	Age	Relative risk	P value
Day care	2-5 mo	17.7	< 0.001
	6-11 mo	9.4	< 0.001
	12-23 mo	5.0	< 0.001
	24-35 mo	2.7	< 0.04
	36-59 mo	1.4	NS

Relative Risks for Invasive Hib Atlanta, GA 1983-1984

	Age	Relative Risk	P Value
Extreme crowding	0-4 y	2.7	< 0.04
Low Family Income	0-4 y	1.6	NS
Breast Feeding	2-5 mo	0.08	< 0.007
	6-11 mo	0.68	NS

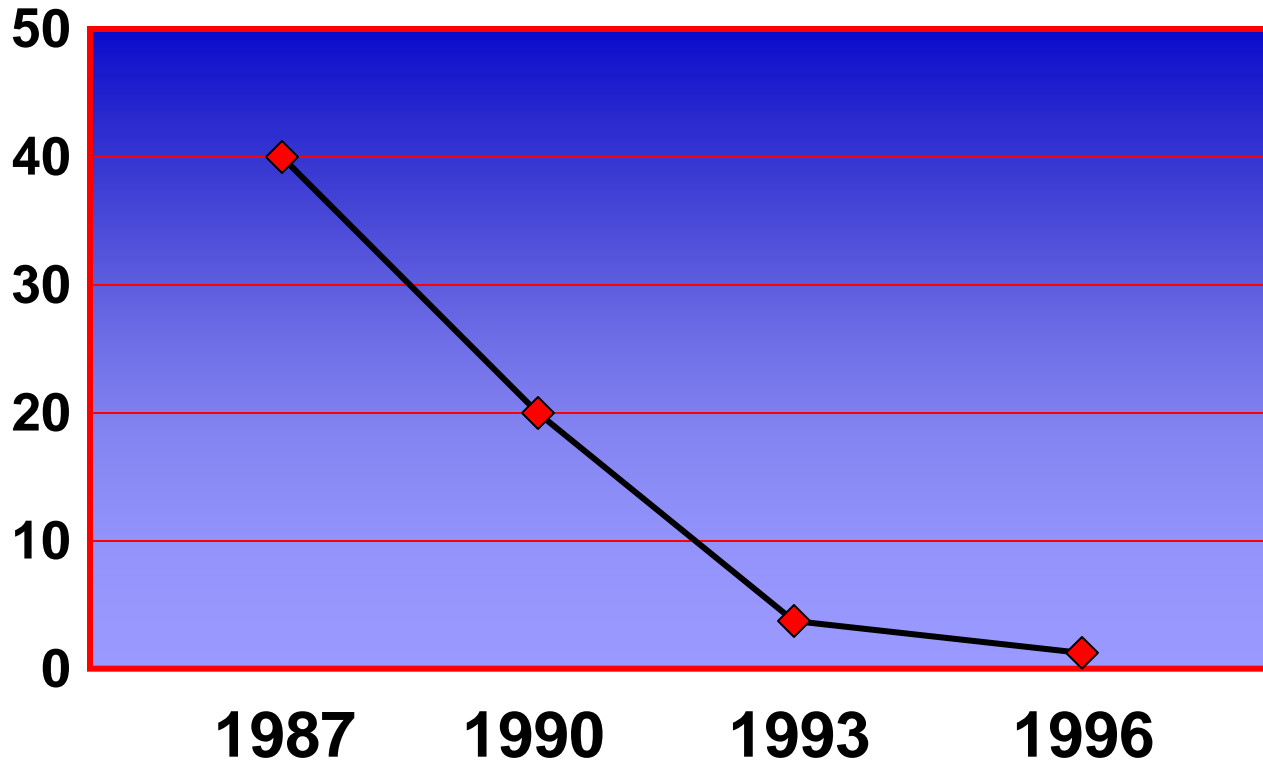
Host Factors Contributing to Increased Hib Disease

- Host factors
 - race/ethnicity
 - HIV
 - Sickle cell
 - Asplenia
 - Malignancy
 - Antibody & complement deficiency

Risk Factors for Invasive Hib Disease

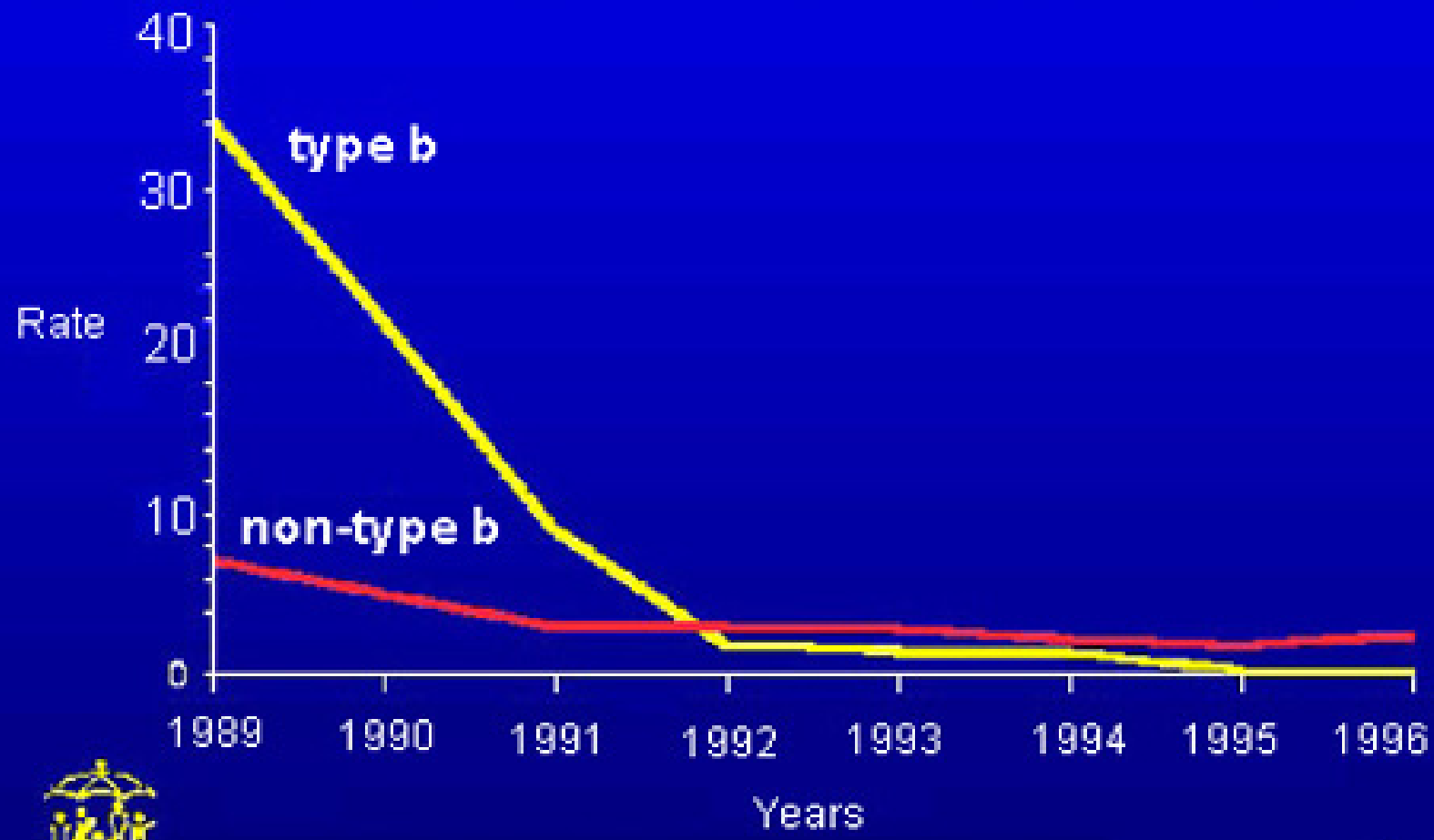
- Child care attendance
- Household crowding
- Large household size
- Low socioeconomic status
- Low parental education
- School-aged siblings

Vaccine protection from *Hemophilus influenzae* type b (Hib)



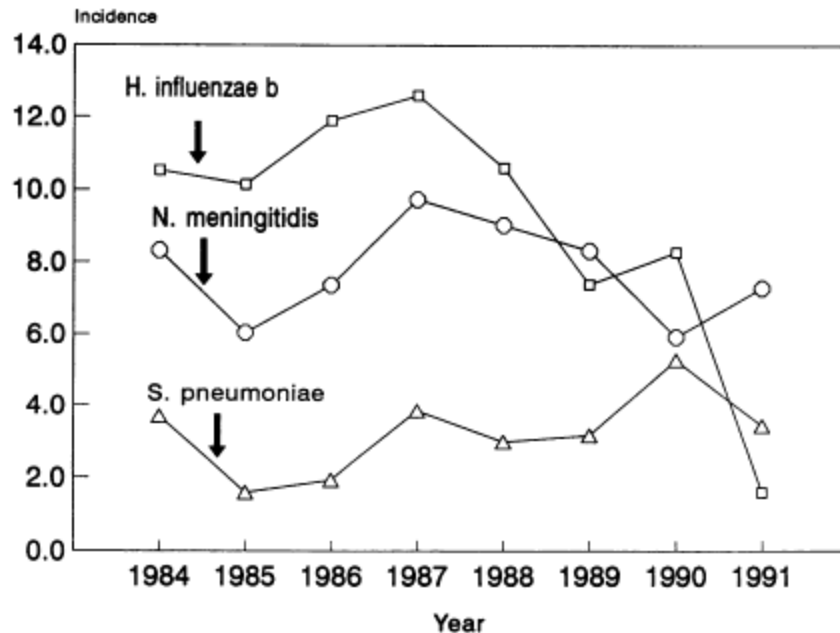
**Estimated annual incidence of invasive Hib per 100,000
Children < 5 years of age, 1987-1996**

Haemophilus influenzae type b (Hib) and non-type Invasive Disease, per 100,000 Population, United States, 1989-1996*



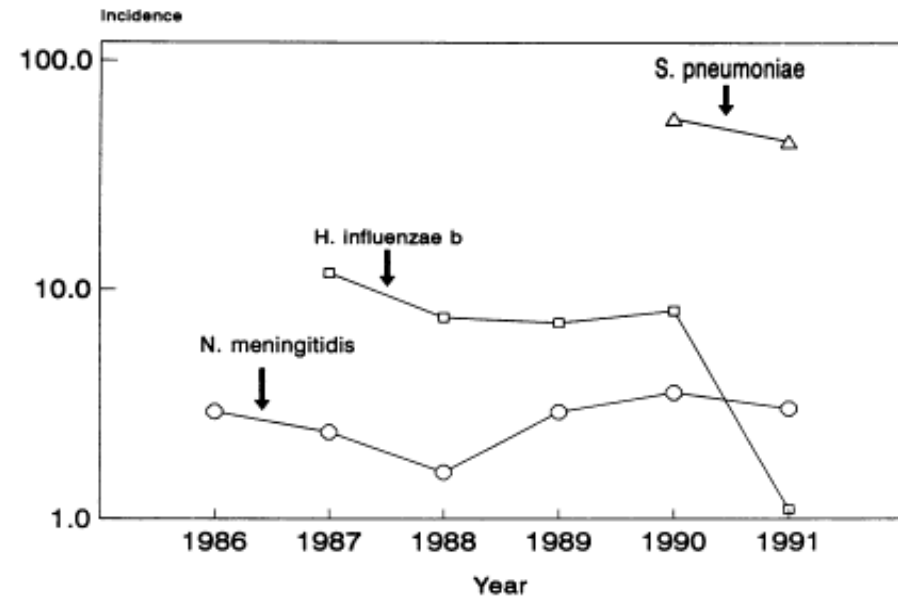
*For children aged <6 years; calculated from four active laboratory-based surveillance areas.

Rapid Fall in Invasive Hib Disease with Hib Vaccination



Note. Age-adjusted incidence per 100 000 children.

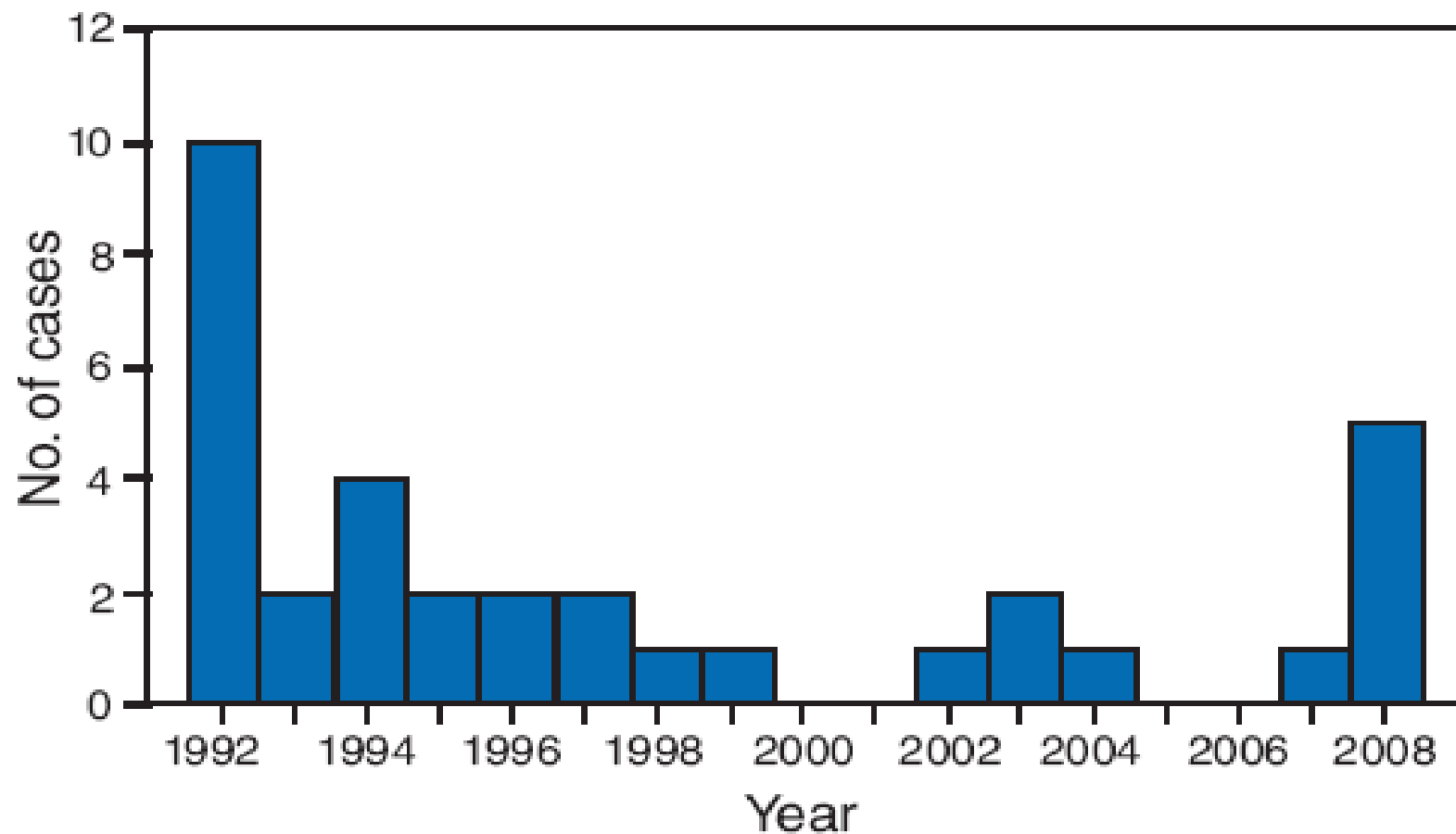
FIGURE 1—Incidence of meningitis resulting from *Haemophilus influenzae* type b, *Neisseria meningitidis*, and *Streptococcus pneumoniae* in children aged newborn to 5 years in Massachusetts, 1984 through 1991.



Note. Age-adjusted incidence per 100 000 children, logarithmic (base 10) scale.

FIGURE 2—Incidence of invasive disease other than meningitis resulting from *Haemophilus influenzae* type b, *Neisseria meningitidis*, and *Streptococcus pneumoniae* in children aged newborn to 5 years in Massachusetts, 1986 through 1991.

FIGURE 1. Number of reported cases of invasive *Haemophilus influenzae* type b (Hib) disease in persons aged <5 years — Minnesota, 1992–2008



Invasive Hib in Minnesota

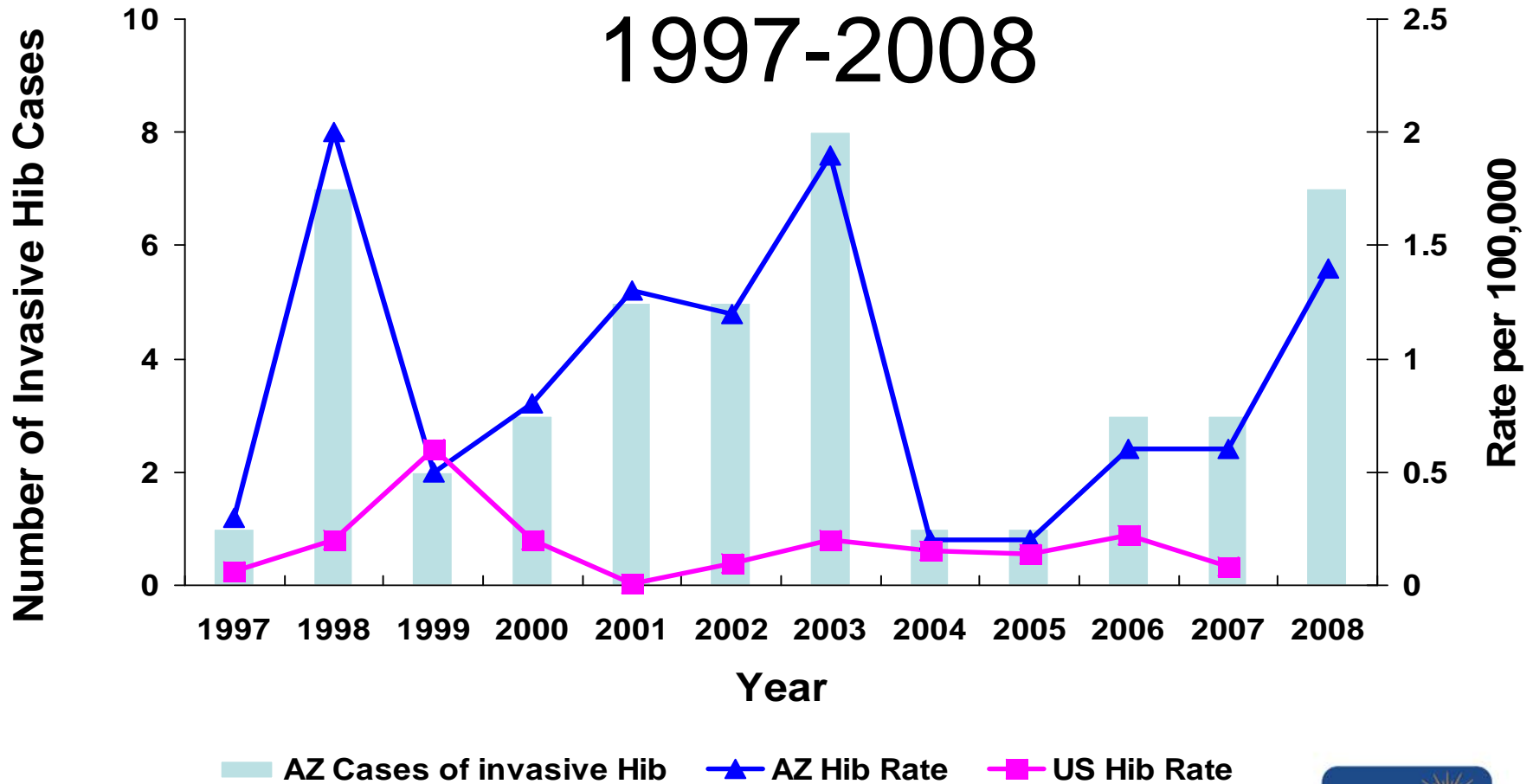
	Age	Clinical	Outcome	Vaccine	Other
1	15 mo	Meningitis	Survived	PRP-OMP 2 & 5 mo	Low IgG
2	3 y	Pneumonia	Survived	0	Healthy
3	7 mo	Meningitis	Died	0	Healthy
4	5 mo	Meningitis	Survived	PRP-TT 2 & 4 mo	Healthy
5	20 mo	Epiglottitis	Survived	0	Healthy

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Other Recent Hib Disease in the US

- 5 cases in PA since October 2008
 - Two deaths
 - 4 yo with Hib meningitis
 - All unvaccinated or under-vaccinated children
- Maine 2009
 - 3 yo partially vaccinated
 - Meningitis & bacteremia

Invasive Hib Cases in AZ in Children < 5 years old 1997-2008



Haemophilus influenzae type b Polysaccharide Vaccine

- Available 1985-1988
- Not effective in children < 18 months old
- Variable effectiveness in older children

Polysaccharide **Conjugate** Vaccines → 1987

- Stimulate T-dependent immunity
- Enhanced antibody production, especially in young children
- Repeat doses elicit booster response

Hib Vaccines In US

Abbreviation	Trade name	Components	Drug Co.
PRP-T	ActHib	Hib	sanofi pasteur
	TriHIBit	Hib & DTaP	
	Pentacel	Hib-DTaP-IPV	
PRP-OMP	PedVaxHIB	Hib	Merck
	Comvax	Hib-Hep B	

Hib Vaccine Scheduling

- What is the minimum age to start Hib vaccination? **6 weeks**
- Why is there a minimum age for Hib?
 - **Possible induction of immune tolerance**
- What is the recommended interval for primary series Hib doses? **8 weeks**
- What is the minimal interval between primary Hib vaccine doses? **4 weeks**

Age Limits for Hib Vaccine?

- What is the upper age limit for which Hib vaccine is not generally recommended?
 - 60 months (5 years) and above
- Which unvaccinated adults need a dose of pediatric conjugated Hib vaccine?
 - Consider for those with asplenia, HIV infection, or immunodeficiency
- When do adults and older children need 3 doses of Hib vaccine?
 - After a bone marrow transplant