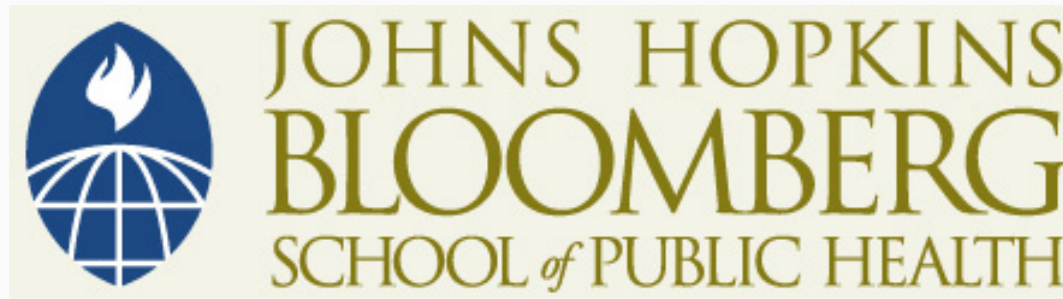


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Vaccines—Impact, Questions, and Challenges

Neal A. Halsey, MD
Johns Hopkins University

- Professor, Johns Hopkins Bloomberg School of Public Health
- Infectious disease prevention with the safest vaccines possible
- Epidemiological studies of vaccine-preventable diseases and phase I, II, and III vaccine trials of hepatitis A and B, inactivated polio virus, pertussis, *Haemophilus influenzae* type B, tetanus, Lyme disease, rotavirus, Argentina hemorrhagic fever, and influenzae vaccine viruses
- Control of measles has been a particular focus of interest



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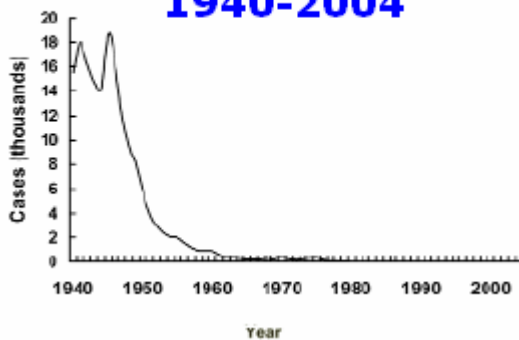
Section A

Background and History

The Most Effective Tool

- Vaccines are the most effective tool we have to control infectious diseases

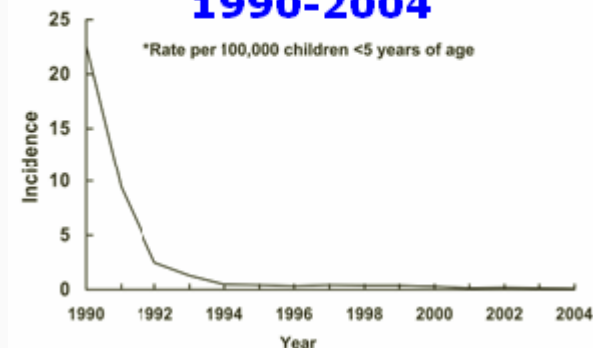
Diphtheria - US 1940-2004



Pertussis - US 1940-2004



Hib - US 1990-2004



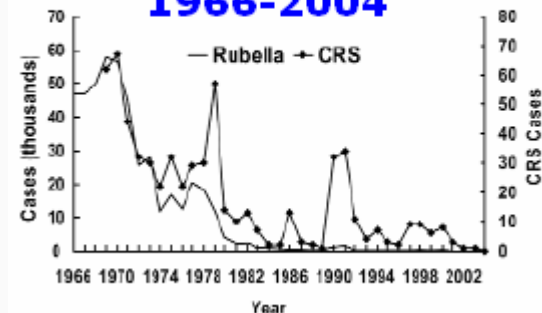
Measles - US 1950-2004



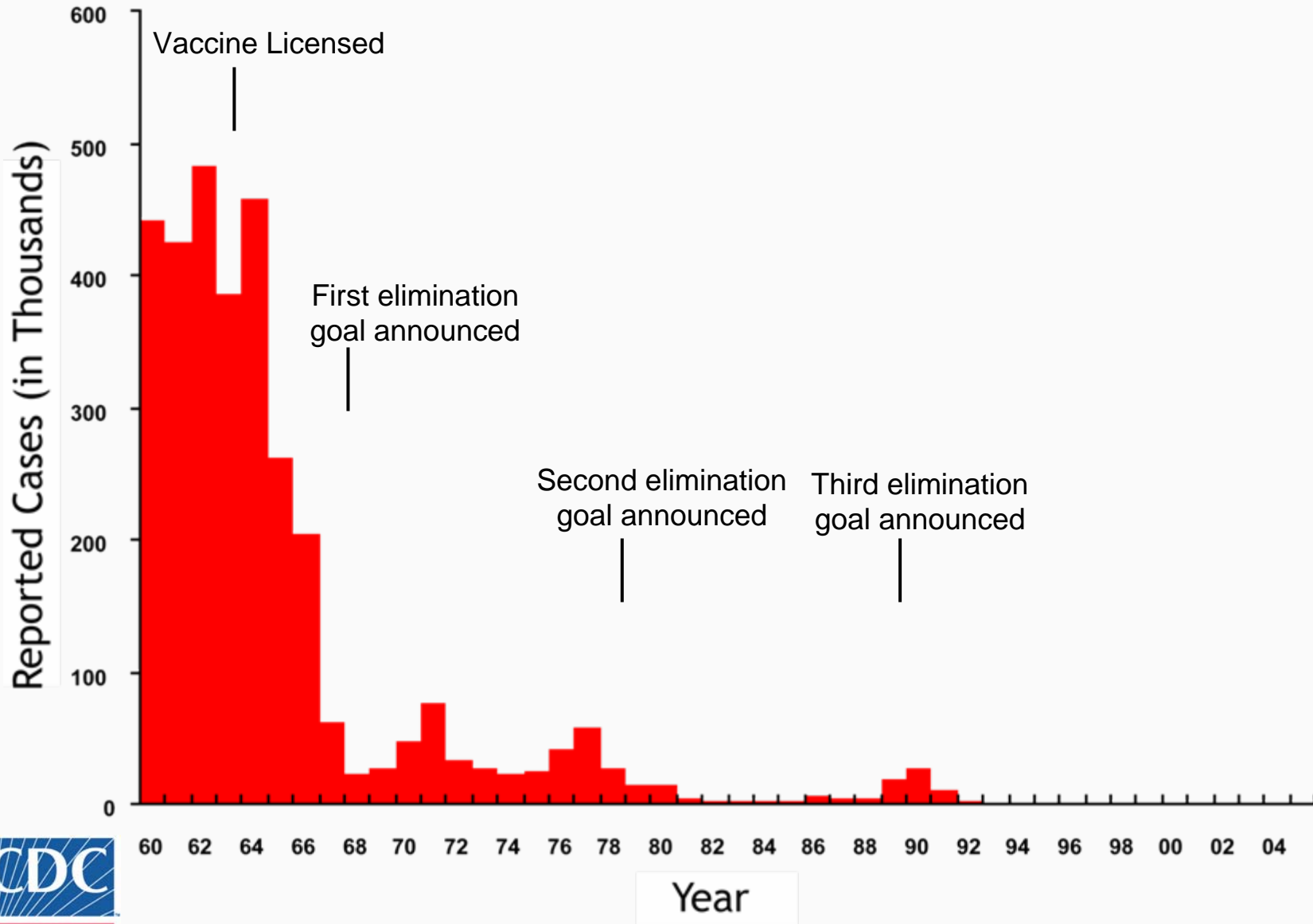
Mumps - US 1968-2004



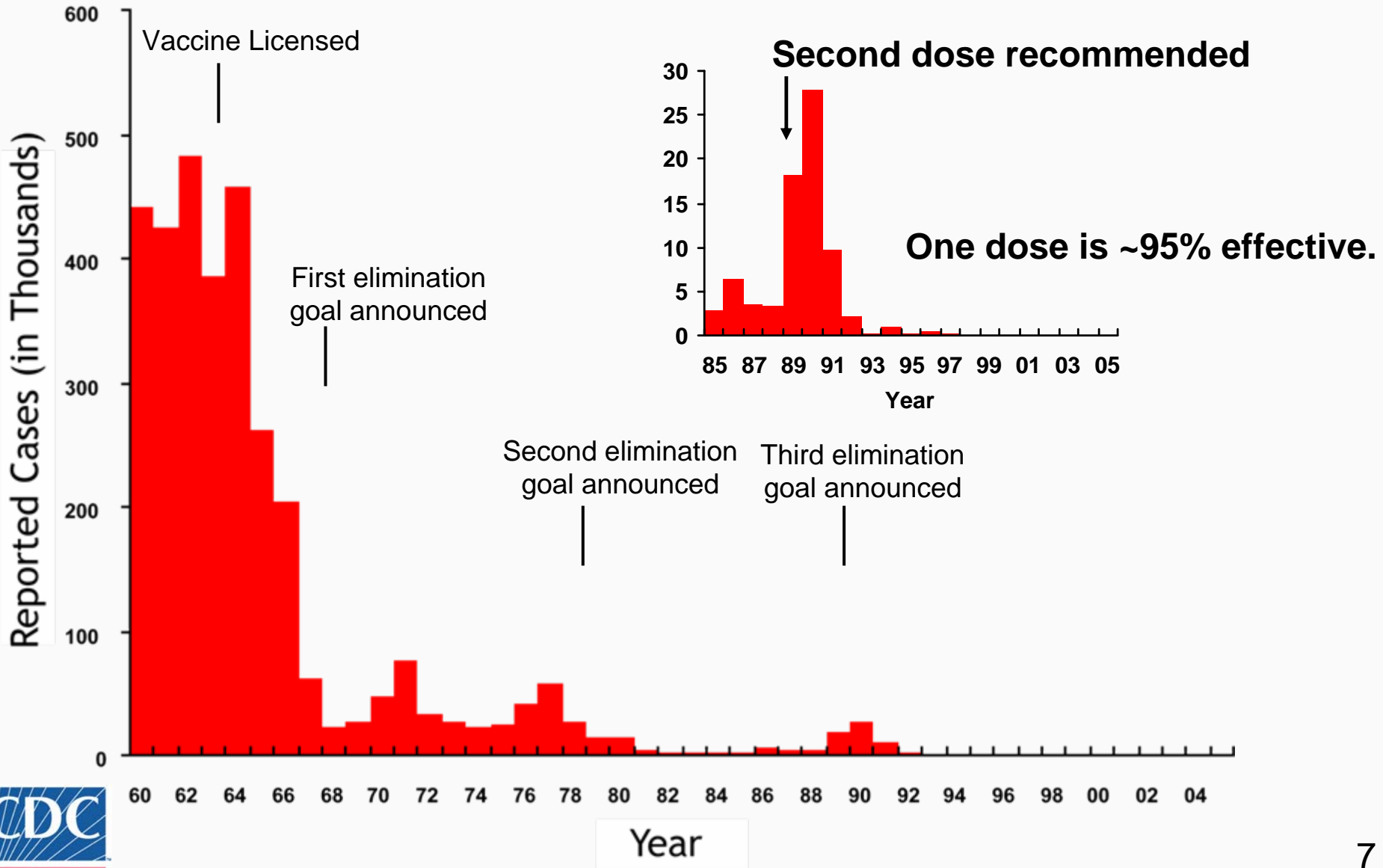
Rubella - US 1966-2004



Reported Measles in the United States

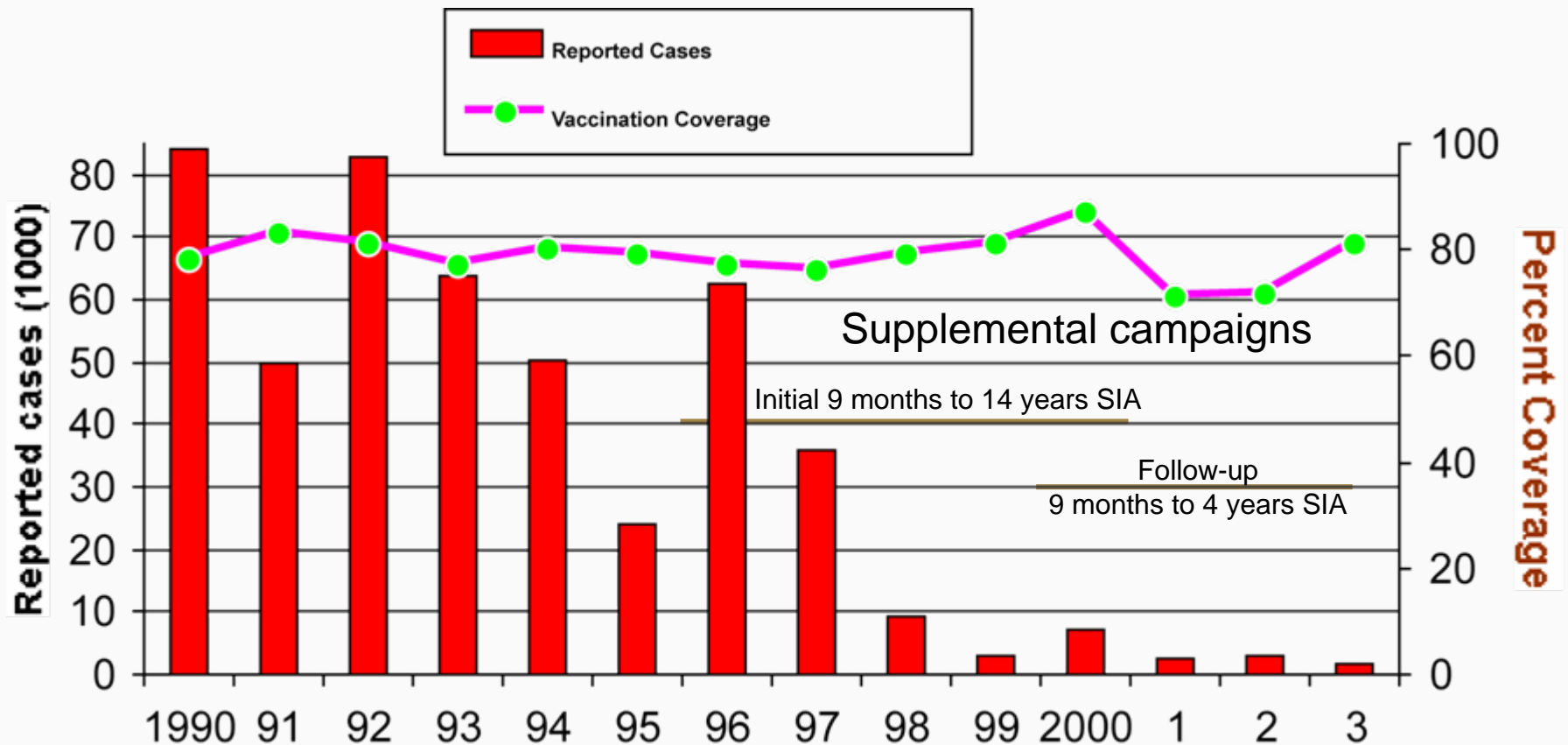


Reported Measles in the United States



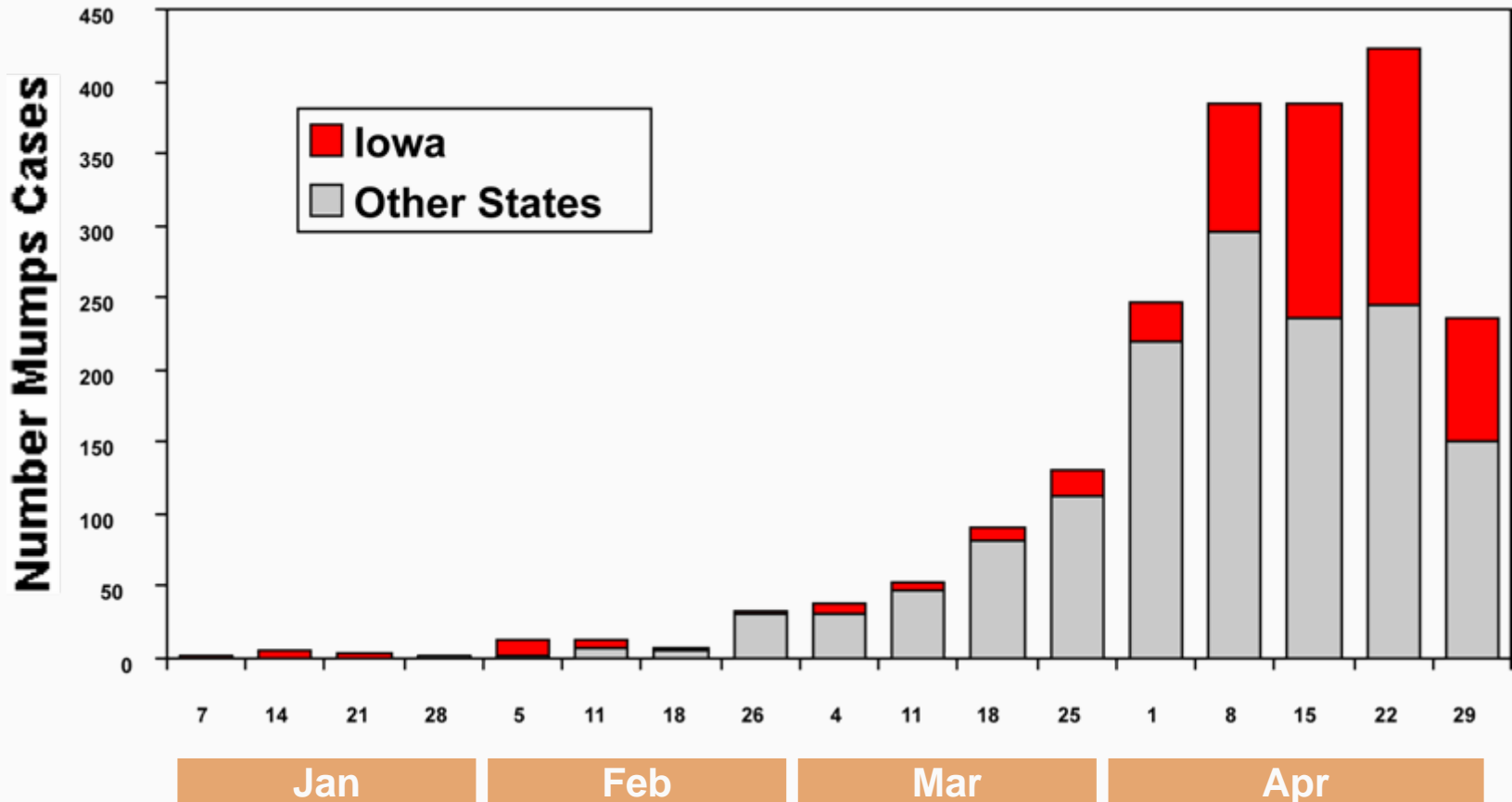
Measles Cases and Weighted Average of Coverage

- Measles cases and weighted average of routine measles vaccination coverage, Southern African countries



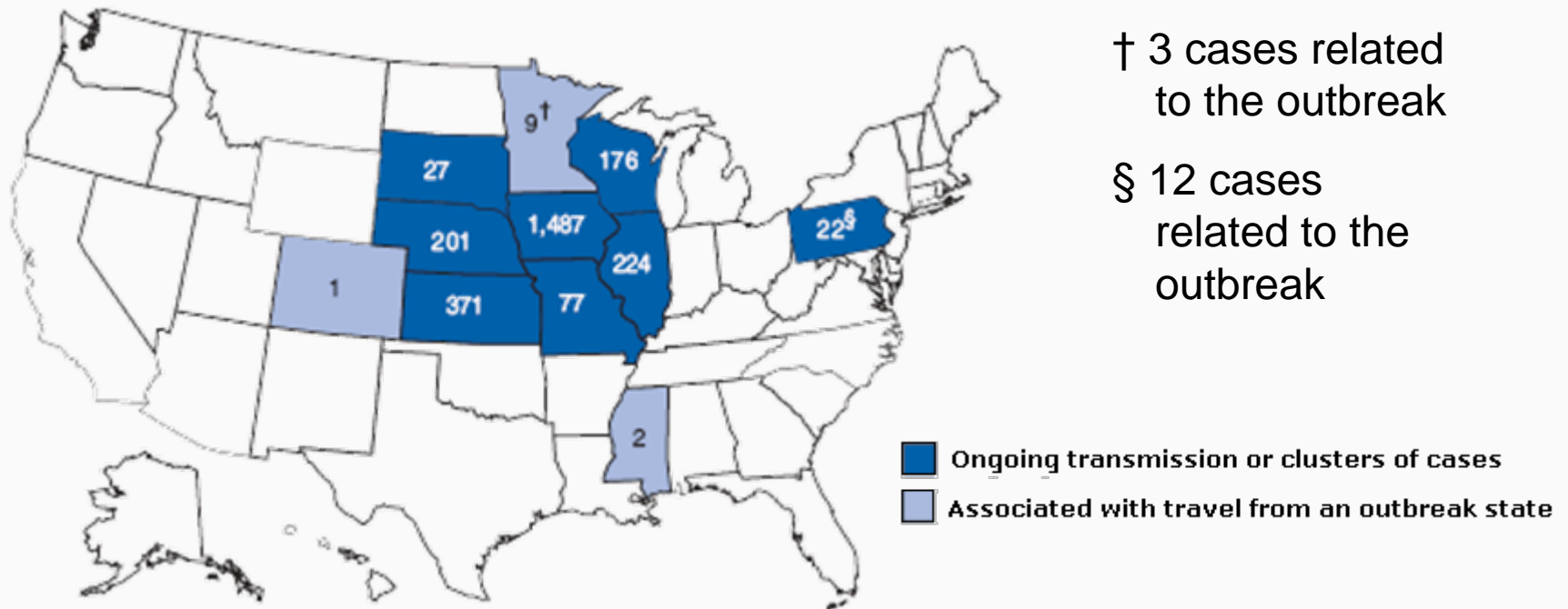
Mumps Cases Linked to Multi-State Outbreak

- Number of reported mumps cases linked to multi-state outbreak, January 1 to May 2, 2006

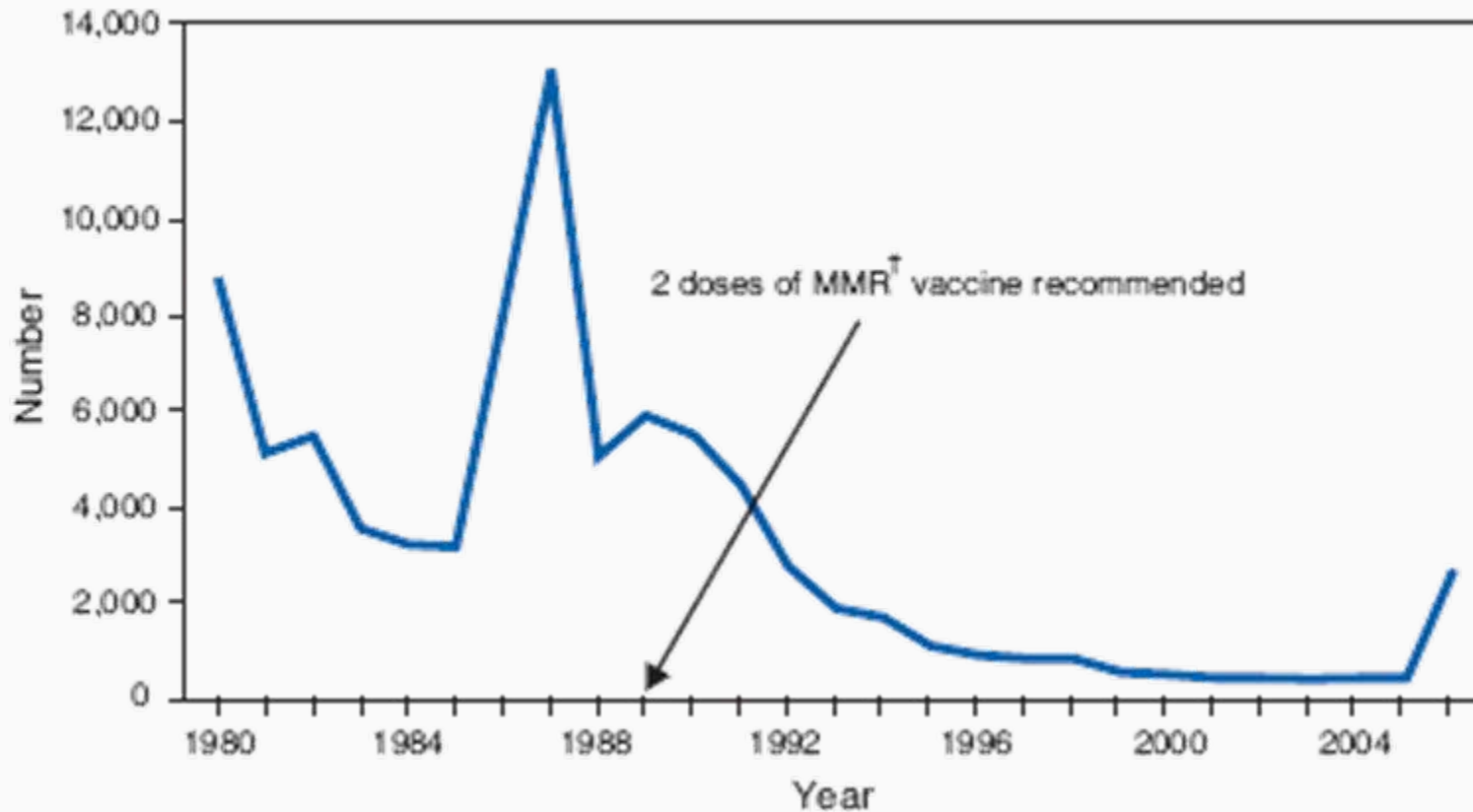


Mumps Cases Linked to Multi-State Outbreak

- Number of reported mumps cases linked to multi-state outbreak, January 1 to May 2, 2006



Number of Reported Mumps Cases, U.S., 1980–2006



Questions

1. How did scientists figure out how to make vaccines?
2. Why aren't some vaccines more effective?
3. Why can't we eradicate more disease?
4. What new vaccines might be approved in the future?
5. What diseases other than infections might be prevented with vaccines?
6. Why do we have so many misunderstandings about vaccine safety?

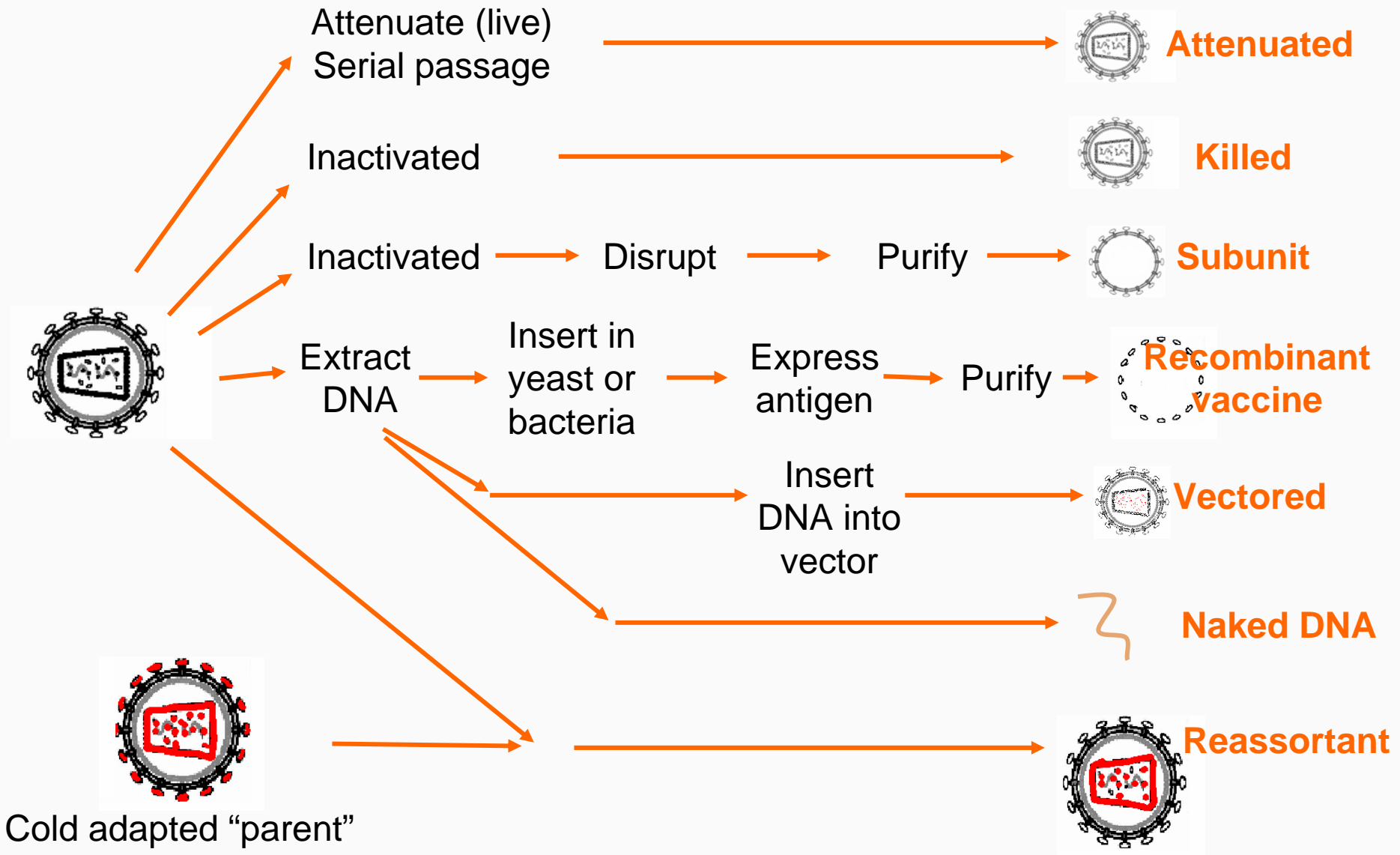
1879 Laboratory Attenuation

1. Chicken cholera culture exposed to air over a holiday
2. Infected chickens
3. Chickens protected from challenge
4. “Induced immunity”

1890s: Killed Typhoid Vaccines

- Richard Pfeiffer, Wilhelm Kolle (Germany)
- Almoth Wright (England)
- 1899 Boer War—mass immunization in military
 - Great opposition, dumped vaccine overboard
 - 58,000 cases, 9,000 deaths in military

How Are Vaccines Made?



Routine Vaccines in U.S. and Developing Country EPI Programs

Vaccines for Routine Use in U.S. and in Developing Country Expanded Programme on Immunization (EPI) Programs

U.S.

1. Diphtheria
2. Tetanus
3. Pertussis
4. Polio (IPV)
5. Hepatitis B
6. *H. influenzae* type b
7. *S. pneumoniae*
8. *N. meningitidis*
9. Measles
10. Mumps
11. Rubella
12. Varicella
13. Rotavirus
14. Influenza
15. HPV

EPI

1. BCG
2. Diphtheria
3. Tetanus
4. Pertussis
5. Polio (OPV)
6. Measles
7. (Yellow Fever)
8. Hepatitis B
9. (*H. influenzae* type b)
10. (Rubella)

Vaccines for Selective Populations

- Smallpox
- Anthrax
- Argentine hemorrhagic fever
- Typhoid fever
- Rabies
- Japanese encephalitis
- Plague
- *Clostridium perfringens* “pig bell”



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Section B

Modern Vaccine Issues

Needed Vaccines

Viruses

- Herpes simplex
- Dengue
- HIV
- RSV
- Hepatitis C
- Cytomegalovirus
- EBV
- West Nile
- Parainfluenza

Under development

Bacteria

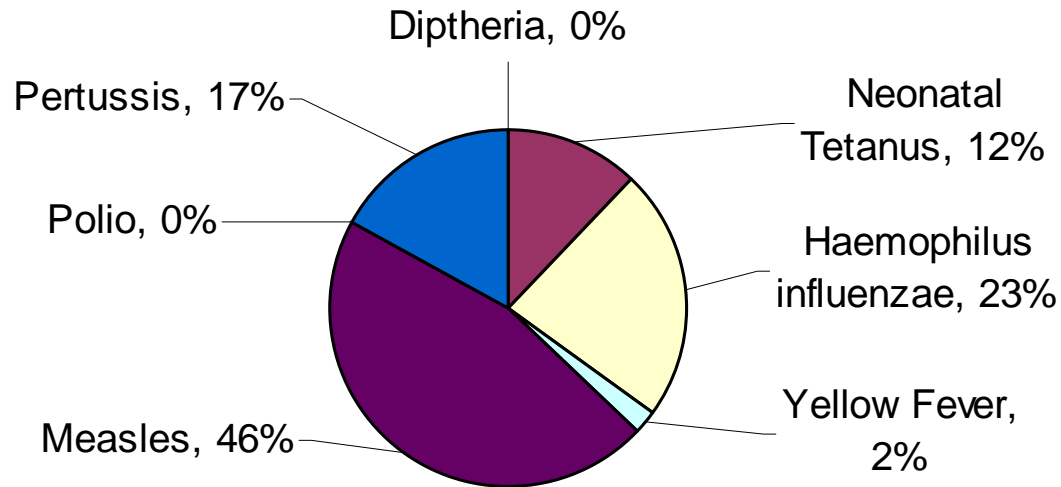
- Syphilis
- Gonorrhea
- E. coli*
- Lyme disease
- C. trachomatis*
- Group A streptococci
- Oral streptococci

Parasites

- Malaria
- Helminths
- Schistosomes

1.7 Million Childhood Deaths

- 1.7 million childhood deaths due to vaccine-preventable diseases in 2000 (not including influenza, pneumococcal, and meningococcal diseases)



Why Do We Still Have So Much Preventable Disease?

1. Failure of delivery systems
2. Incomplete protection from some vaccines
3. Financing

Why Aren't Some Vaccines More Effective?

- Influenza: rapid evolution of new strains
- Human variability: genetic differences
 - Hepatitis B, measles (1 dose): ~95–98%
- Incomplete immunity
 - Pertussis: 70–90% (June 2005—booster at 11–12 years for U.S.)
 - Varicella (1 dose): 70–90% (2 doses 2006)
- Errors in storage or administration
- Evasion of the immune system
 - HCV, HIV, parasites

Vaccine Shortages

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Los Angeles Times

October 6, 2004 Wednesday - Home Edition

Anticipated Supply of Flu Vaccine for U.S. Is Abruptly Cut in Half

BY: Denise Gellene and Melissa Healy, Times Staff Writers

U.S. public health officials warned Tuesday of serious flu vaccine shortages after the because of unspecified manufacturing problems. The plant makes Chiron's entire

L.A. Times

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The San Francisco Chronicle

OCTOBER 16, 2004, SATURDAY, FINAL EDITION

All of Chiron's flu vaccine deemed unsafe; FDA checks firm's plant, says no doses can be salvaged

BYLINE: Sabin Russell

British and American drug regulators have found additional contaminated lots of influenza vaccine at A team of FDA inspectors, dispatched to the Chiron plant after British regulators suspended its license Oct.

San Francisco Chronicle

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The Baltimore Sun

October 8, 2004 Friday FINAL Edition

Vaccine gap shows faults in supply system; \$85 vial may cost \$600 amid shortage in U.S.

BY: M. William Salganik

To David Webster, an industry consultant, flu of a vaccine with a normal price tag of \$85. A

Baltimore Sun



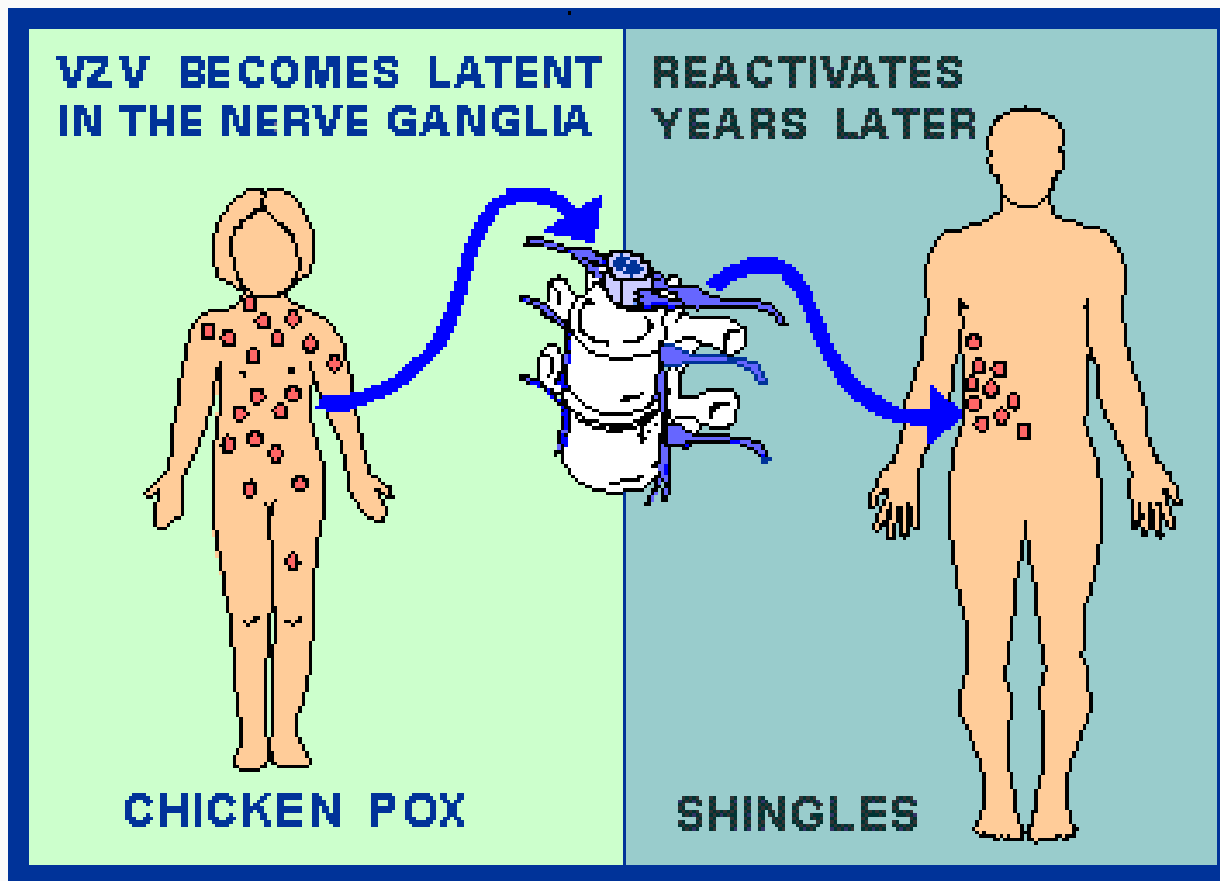
Photo courtesy of Lance McCord.
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Why Can't We Eradicate More Diseases?

- Tetanus: animal reservoirs
- Pneumococcal disease: too many types
- Varicella and hepatitis B: viral persistent infections and transmissions

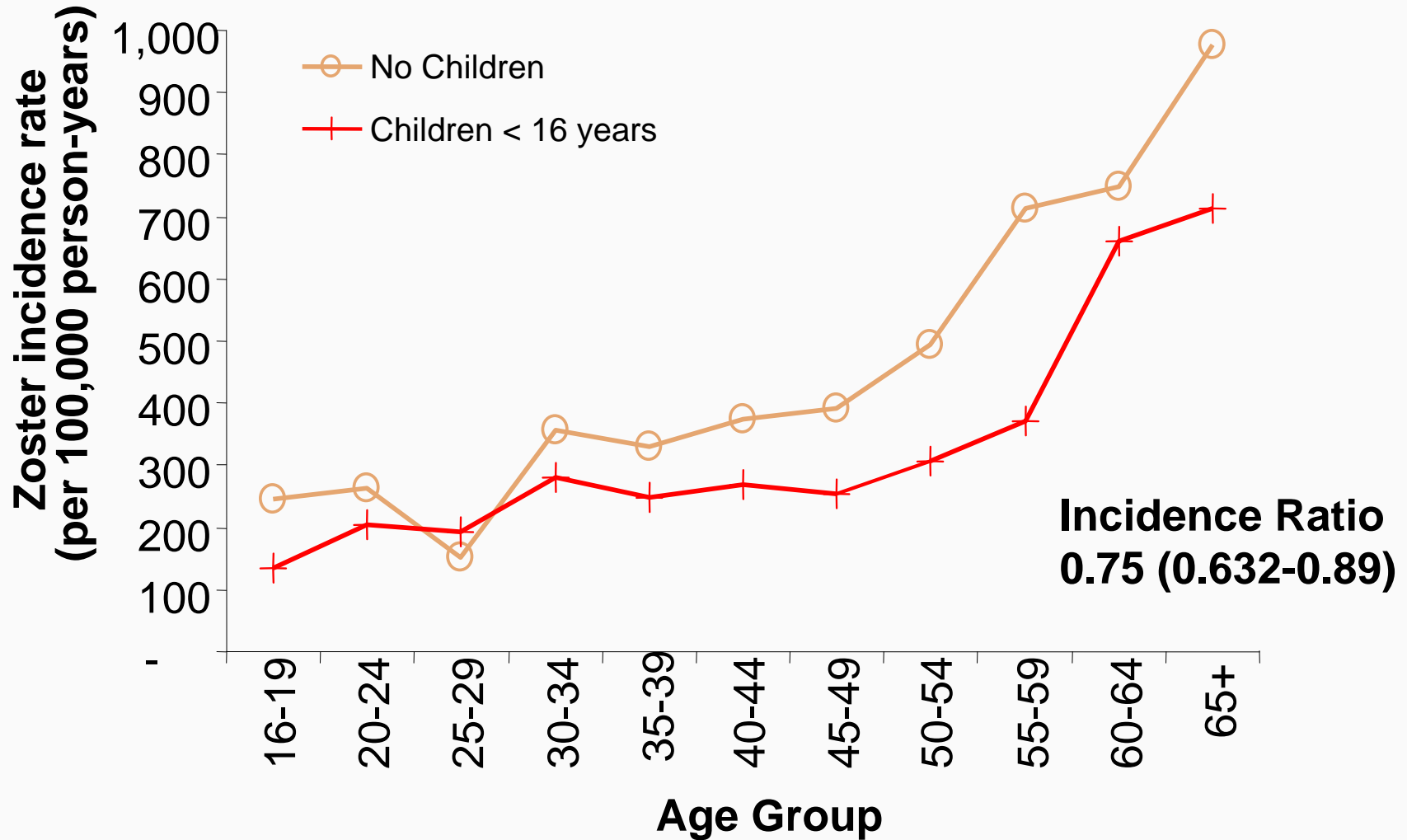
Varicella Zoster Virus Persists in Dorsal Root Ganglia

- Varicella zoster virus persists in dorsal root ganglia of sensory nerves



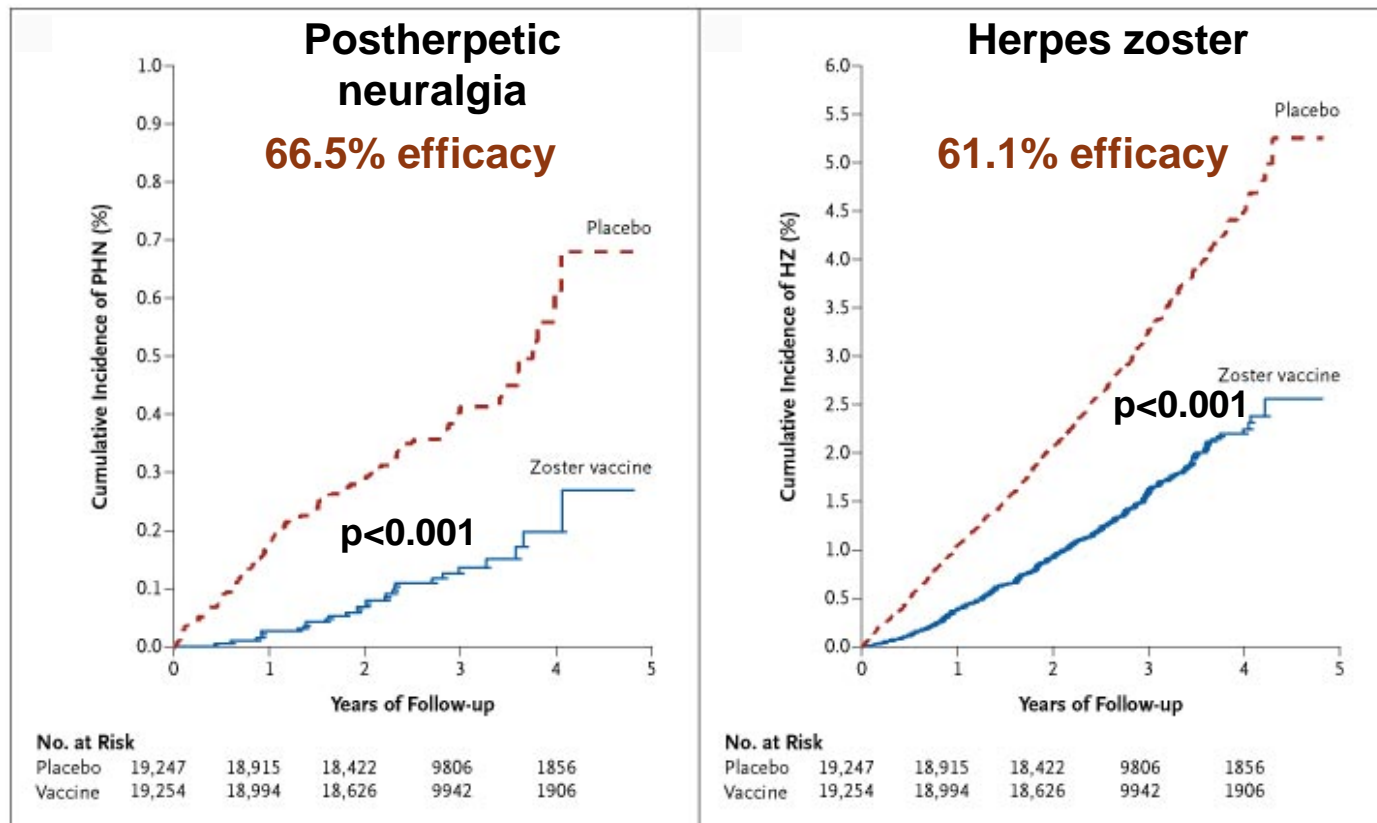
Herpes Zoster and Presence of Children in Household

- Rate of herpes zoster by presence of children in household



Postherpetic Neuralgia, Herpes Zoster after Zoster Vaccine

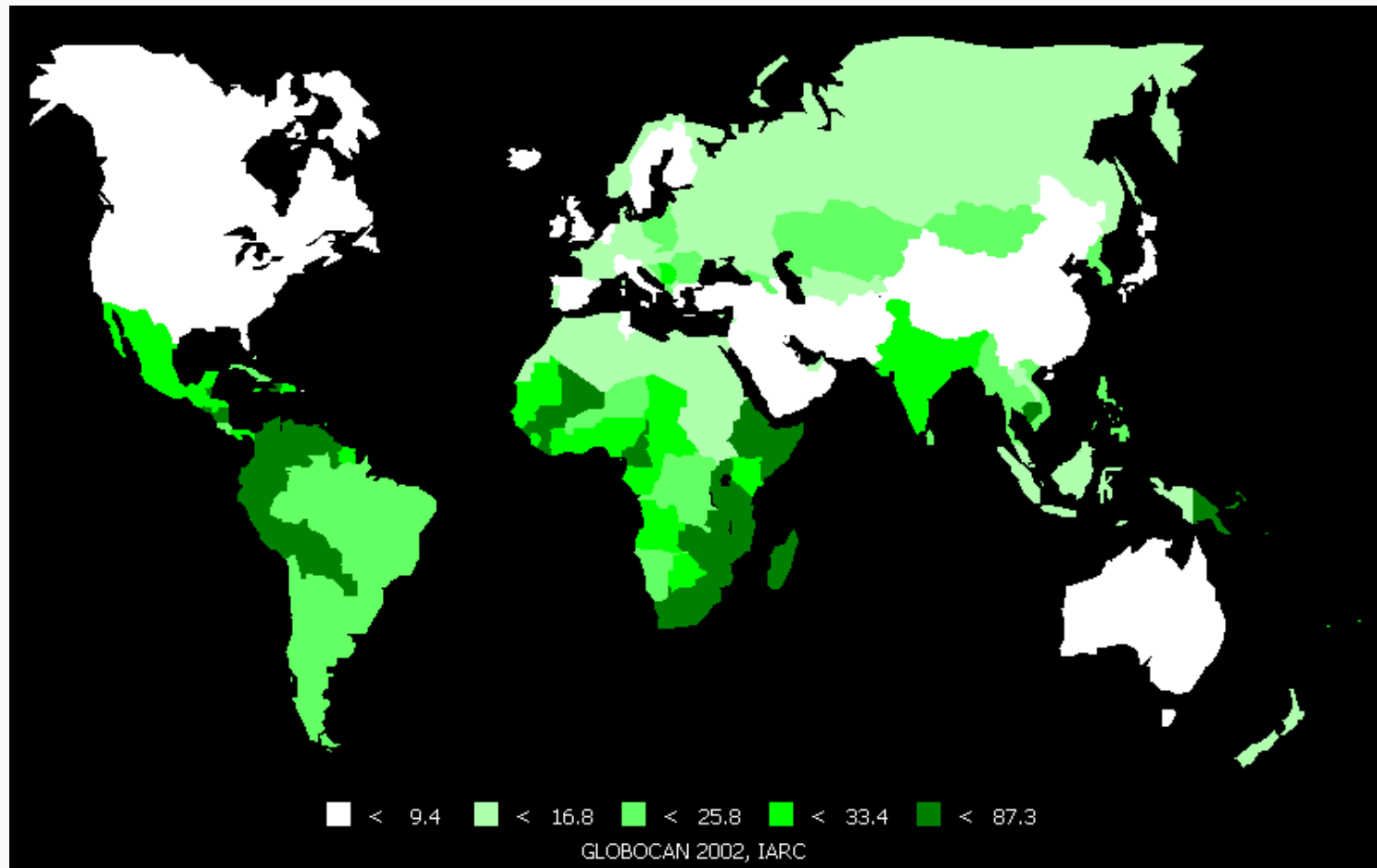
- Incidence of Postherpetic Neuralgia and Herpes Zoster following Zoster Vaccine (5-6 X Potency of Varicella Vaccine)



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Cervical Cancer

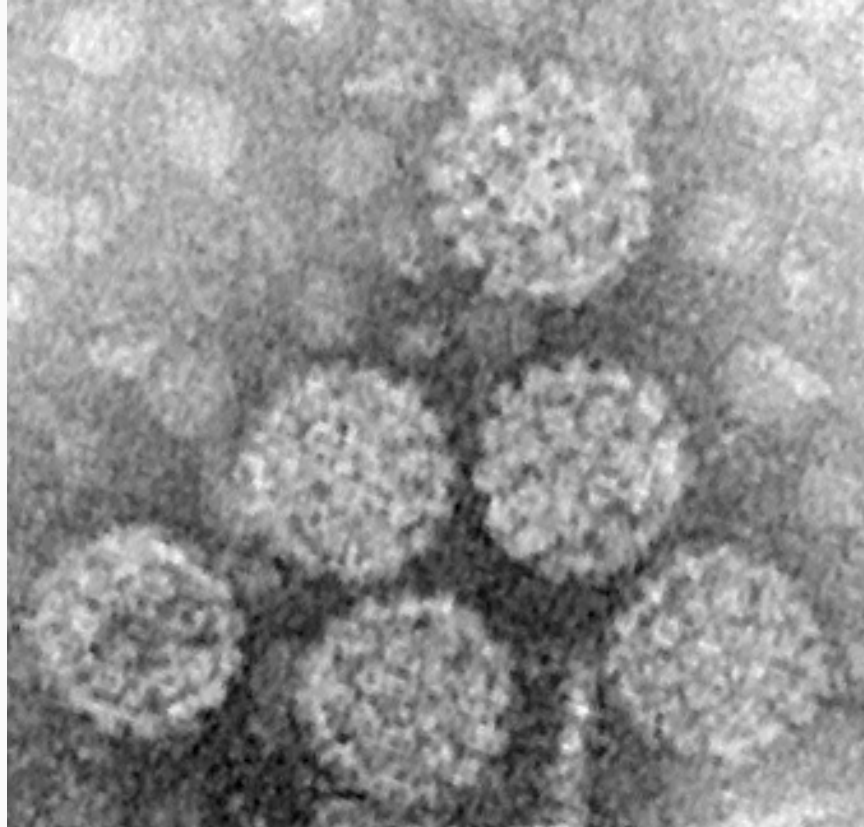
- Age-standardized incidence rate per 100,000



Burden of Cervical Cancer

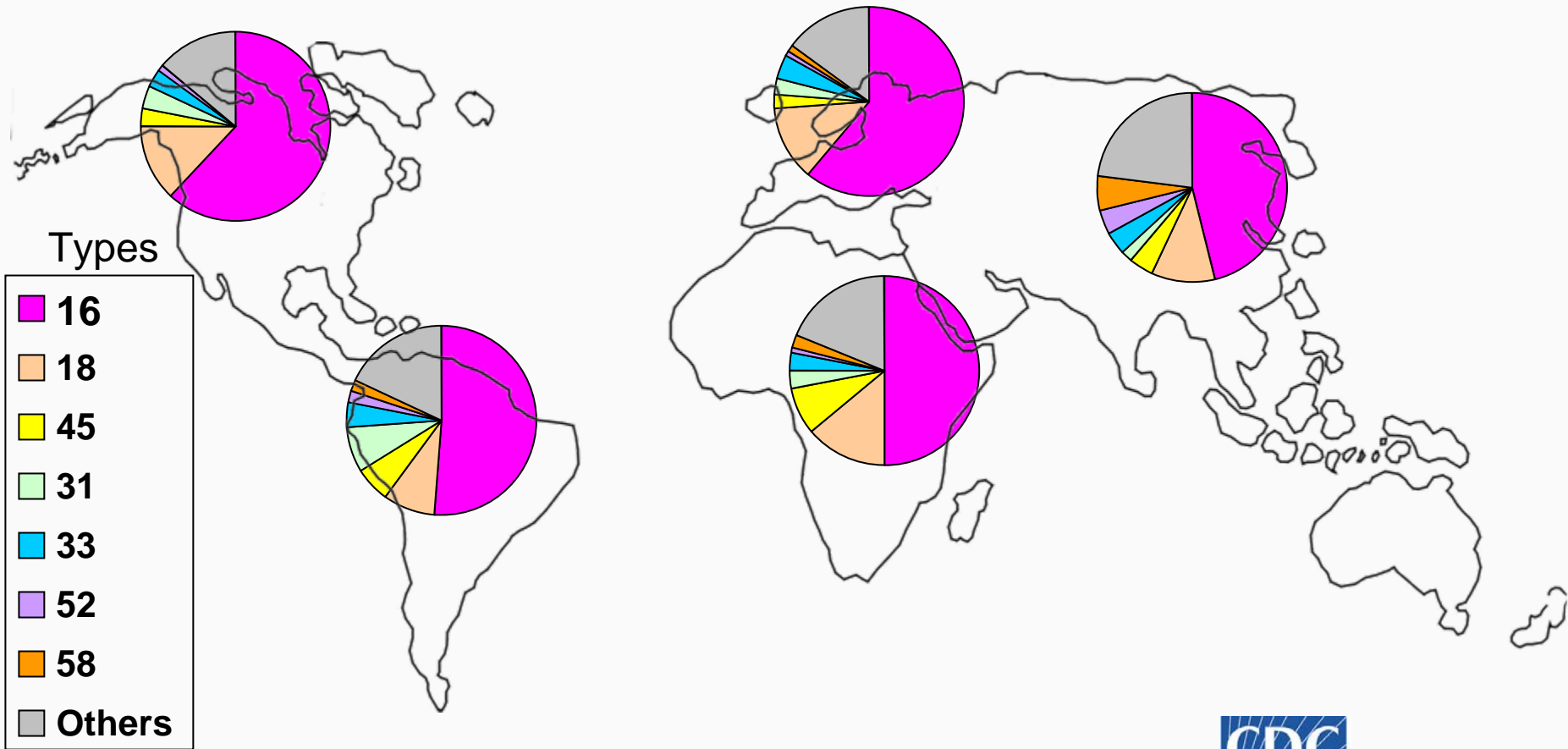
- 400,000–500,000 cases and 230,000 deaths from cervical cancer each year
- Second leading cause of cancer-related deaths among women worldwide

Papillomaviruses



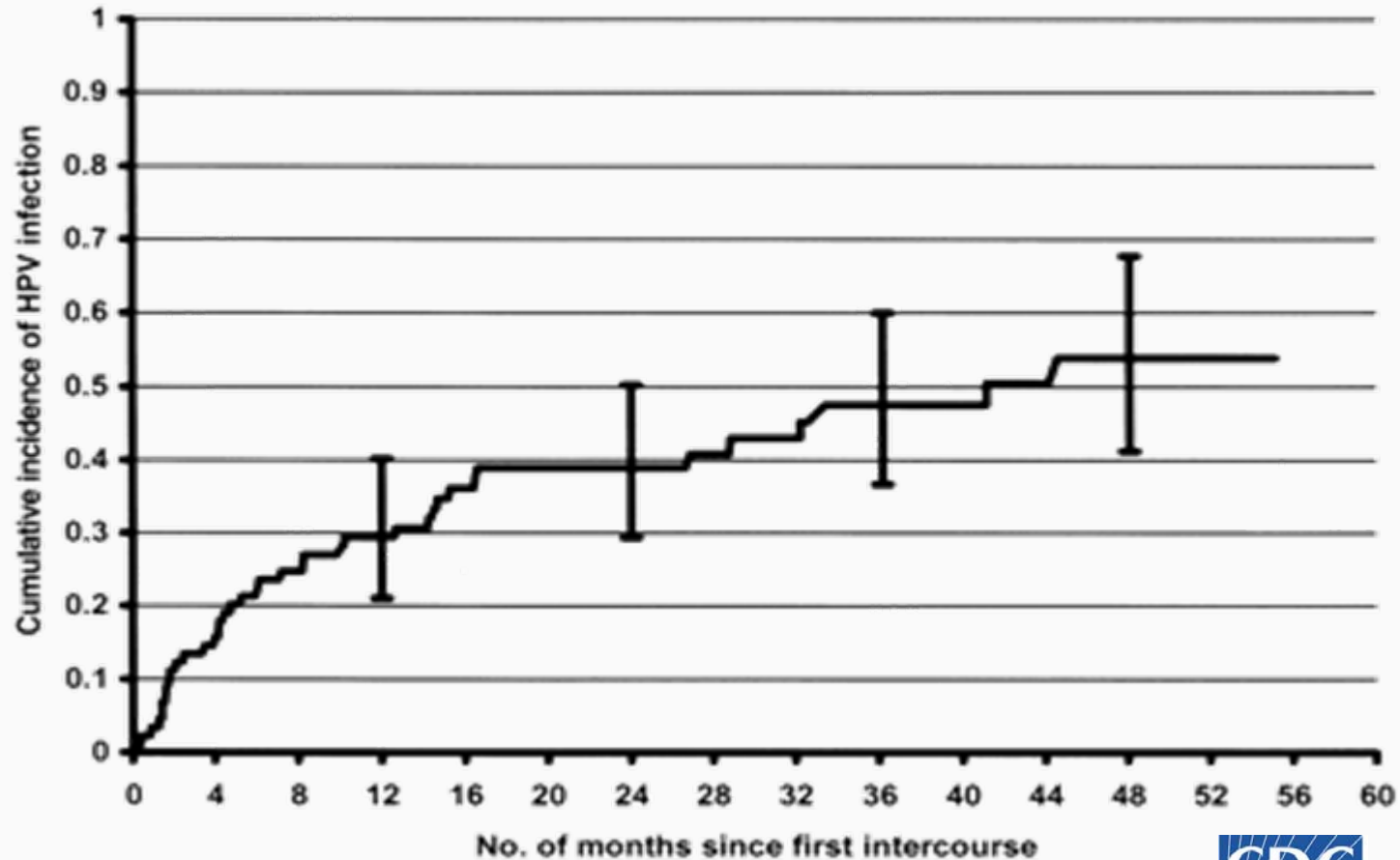
HPV Types and Cervical Cancer Worldwide

- HPV types in cases of cervical cancer from different regions of the world



Cumulative Incidence of HPV Infection

- Cumulative incidence of HPV infection from time of first sexual intercourse, female college students, U.S.



Vaccines That Prevent Cervical Cancer

- Types 16 and 18 cause ~70% of cancer
- Types 6 and 11 cause 90% of genital warts

	HPV types
GARDASIL™ (Merck)	6, 11, 16, 18
Cervarix (GSK)	16, 18

Infectious Causes of Cancer

1. Hepatitis B	Liver cancer
2. HPV	Cervical, penile, anal
3. EBV	Lymphoma
4. HTLV-I	Lymphoma
5. HHV-8	Kaposi's sarcoma
6. <i>H. pylori</i>	Gastric carcinoma
?	

All Vaccines Cause Adverse Events

1. Pain
2. Local reactions
3. Fever
4. Allergic reactions
5. Unchecked replication (immune deficient)
6. Adverse immune responses

Vaccine-Associated Paralytic Poliomyelitis

- Oral polio vaccine can cause vaccine-associated paralytic poliomyelitis
 1. Similar to wild type paralysis
 2. Risk ~ 1 per 760,000 children vaccinated

Diseases Once Common in the U.S.



Measles



Mumps



Congenital rubella



Diphtheria



Tetanus



Smallpox

Current Vaccine Dilemmas

1. How do we maintain high acceptance in absence of disease?
2. Causal assessment: science vs. legal?
3. Vaccines to treat chronic infections (hep B)
4. Criteria to stop vaccinating (polio)?
5. Who should receive vaccines for bioterrorism agents?
6. How do we get new expensive vaccines introduced and sustained in developing countries?