Prospects for measles eradication

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Measles remains one of the 10 most important causes of death due to infectious diseases

Faroe Islands measles outbreak in 1846 was the first in >60 years

Peter Panum, a Danish physician observed:

The disease is contagious

There is a 14 day incubation period

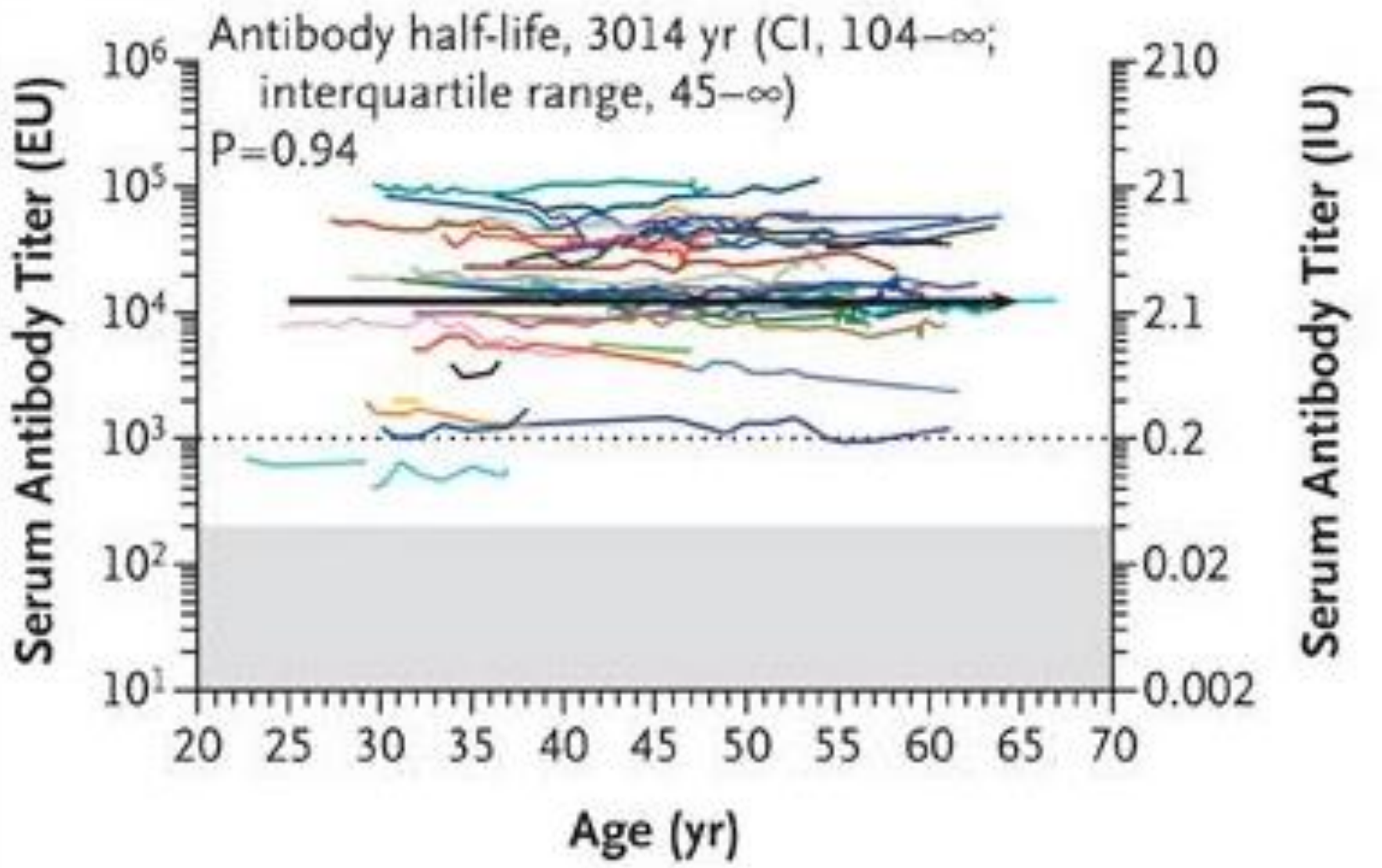
100% attack rate for susceptibles

Life long immunity

R_0 for some important human viruses

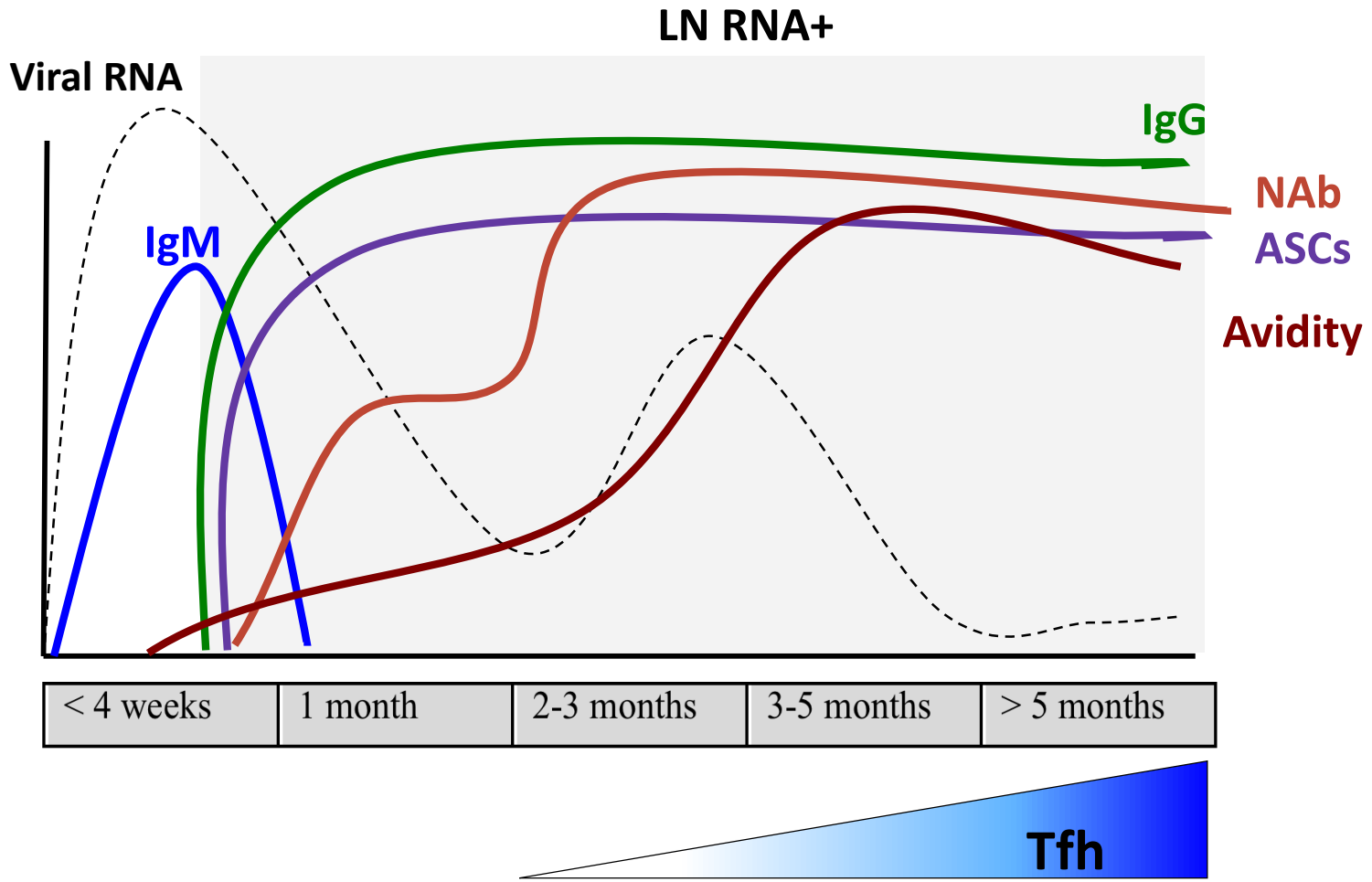
Virus	R_0
Measles	**12-18**
Mumps	10-12
Polio	10-15
Rubella	7-8
Smallpox	**5-7**
Influenza	3-4

Infection with wild type measles virus induces protective levels of antibody that are life-long

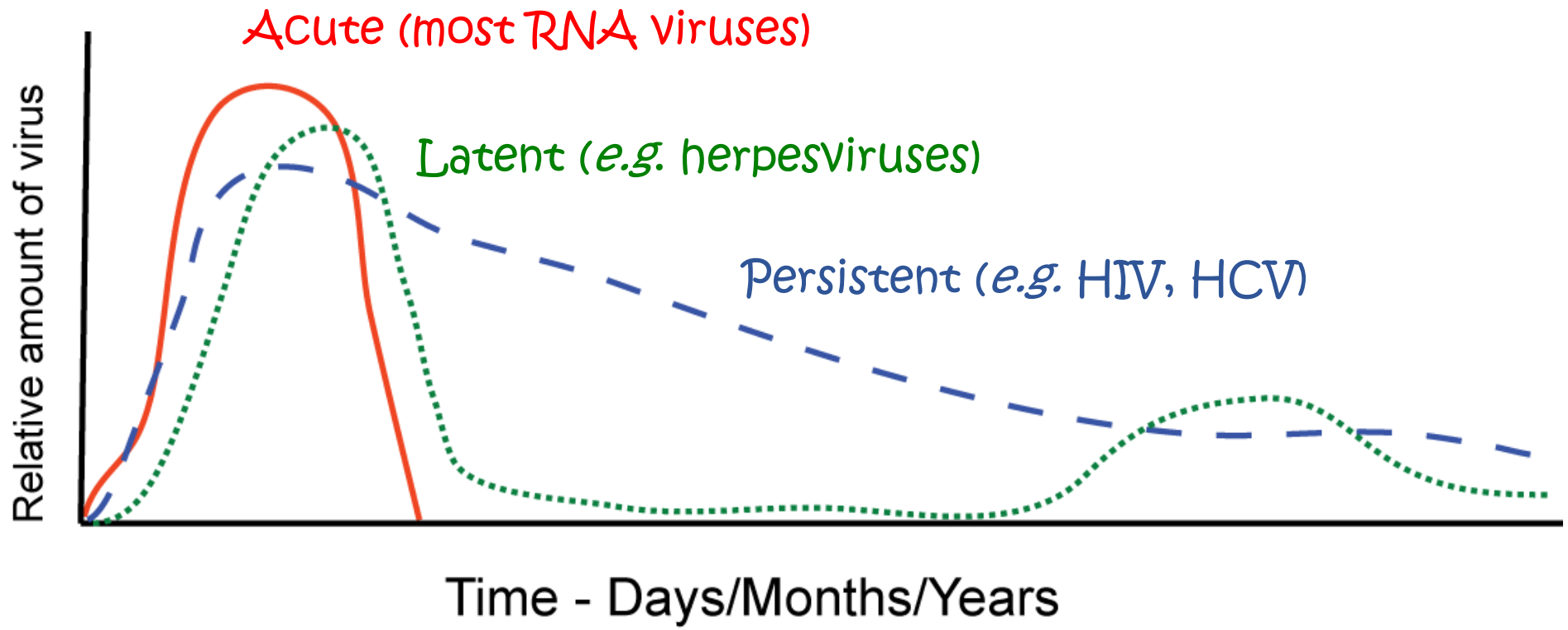


Amanna IJ et al. N Engl J Med 2007; 357:1903-1915.

Ongoing maturation of the measles virus-specific immune response over months after WT infection results in life-long immunity



Viral strategies for population-level persistence of human viruses



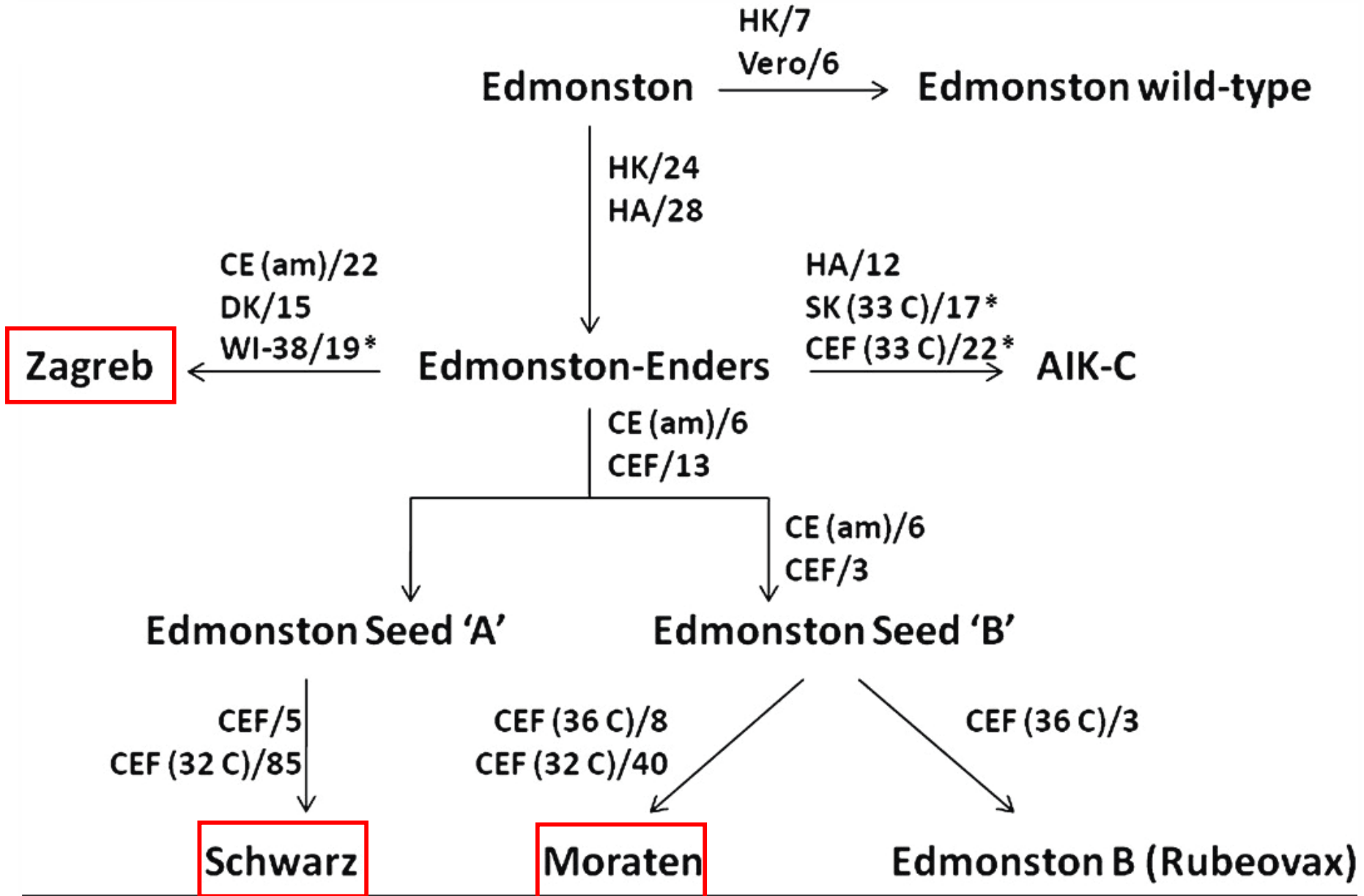
Characteristics of measles that affect eradication

- Man - the only host
- Virus spread begins prior to onset of rash
- Permanent immunity after recovery
- Spread of virus by the respiratory route
- Transmission stops spontaneously in remote areas
- Vaccine provides long-term protection

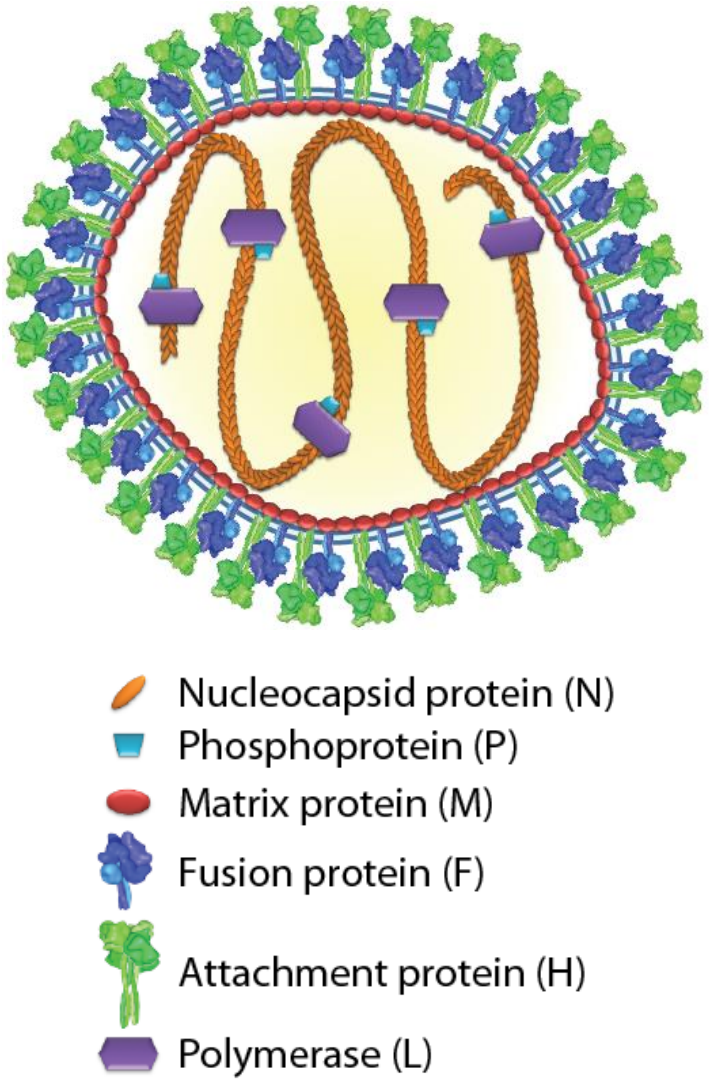
Isolation of measles virus in culture paved the way for vaccine development

John Franklin Enders
1897–1985

Measles vaccine passage history

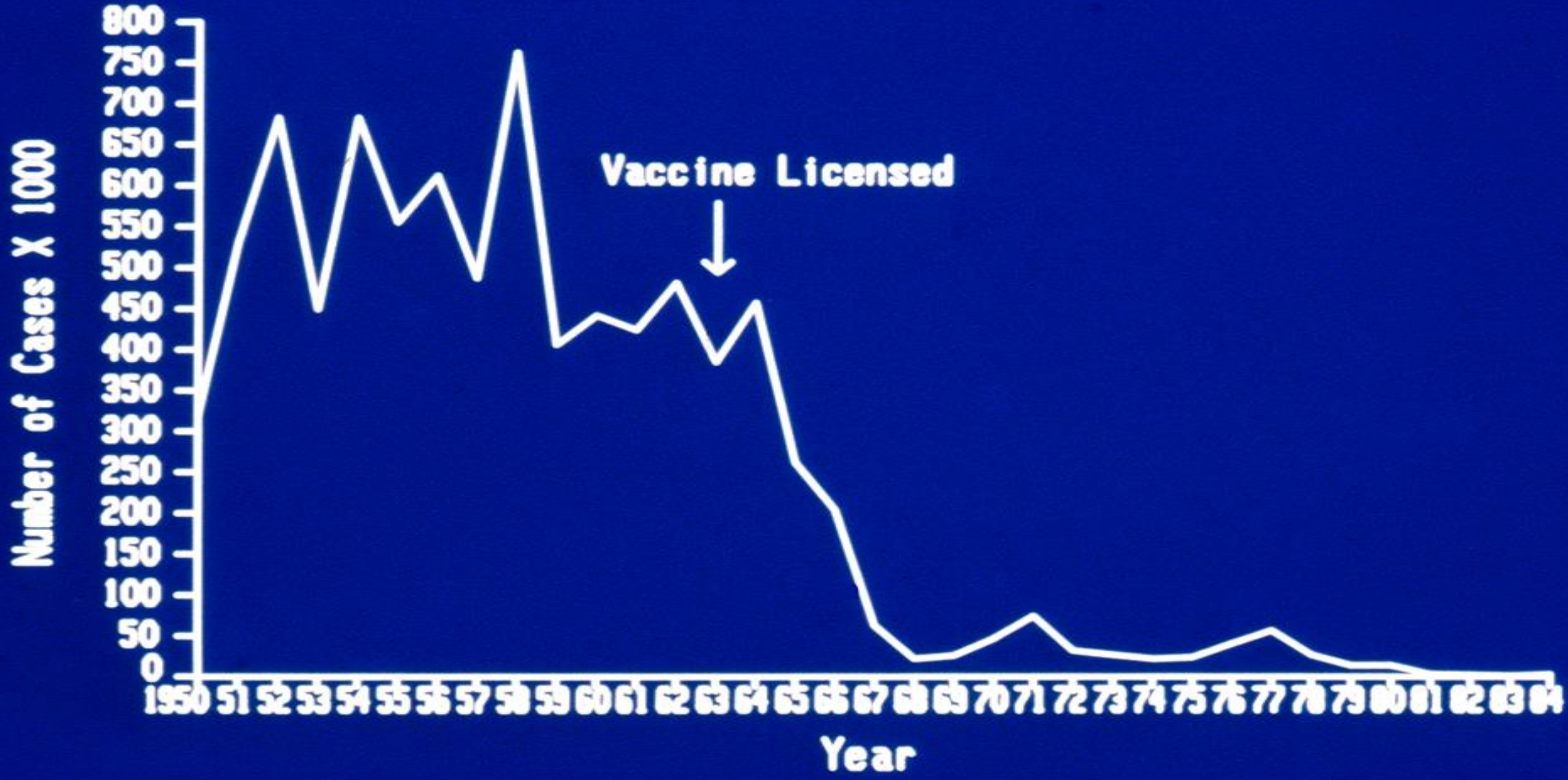


Amino acid differences from Edmonston "WT" shared by all vaccine s



Prot	aa	Mor	EZ	WT
N	148	G	E	E
	479	T/A	S	S
P/V	**225**	**G**	**G**	**E**
C	**73**	**V**	**V**	**A**
	104	T	M	M
M	4	T	I	I
	17	S	L	S
	61	**D**	**D**	**G**
	64	S	P	P
	75	F	S	S
	82	R	K	R
	89	**K**	**K**	**E**
	142	N	S	N
	285	M	I	M

F	163	T	A	A
	263	G	R	R
	362	Y/A	S	S
H	117	L	F	F
	211	**G**	**G**	**S**
	280	V	A	V
	481	**Y**	**Y**	**N**
	484	T	N	T
	546	S	G	G
L	331	T	I	I
	1409	A	T	A
	1649	M	R	R
	1887	D	N	N



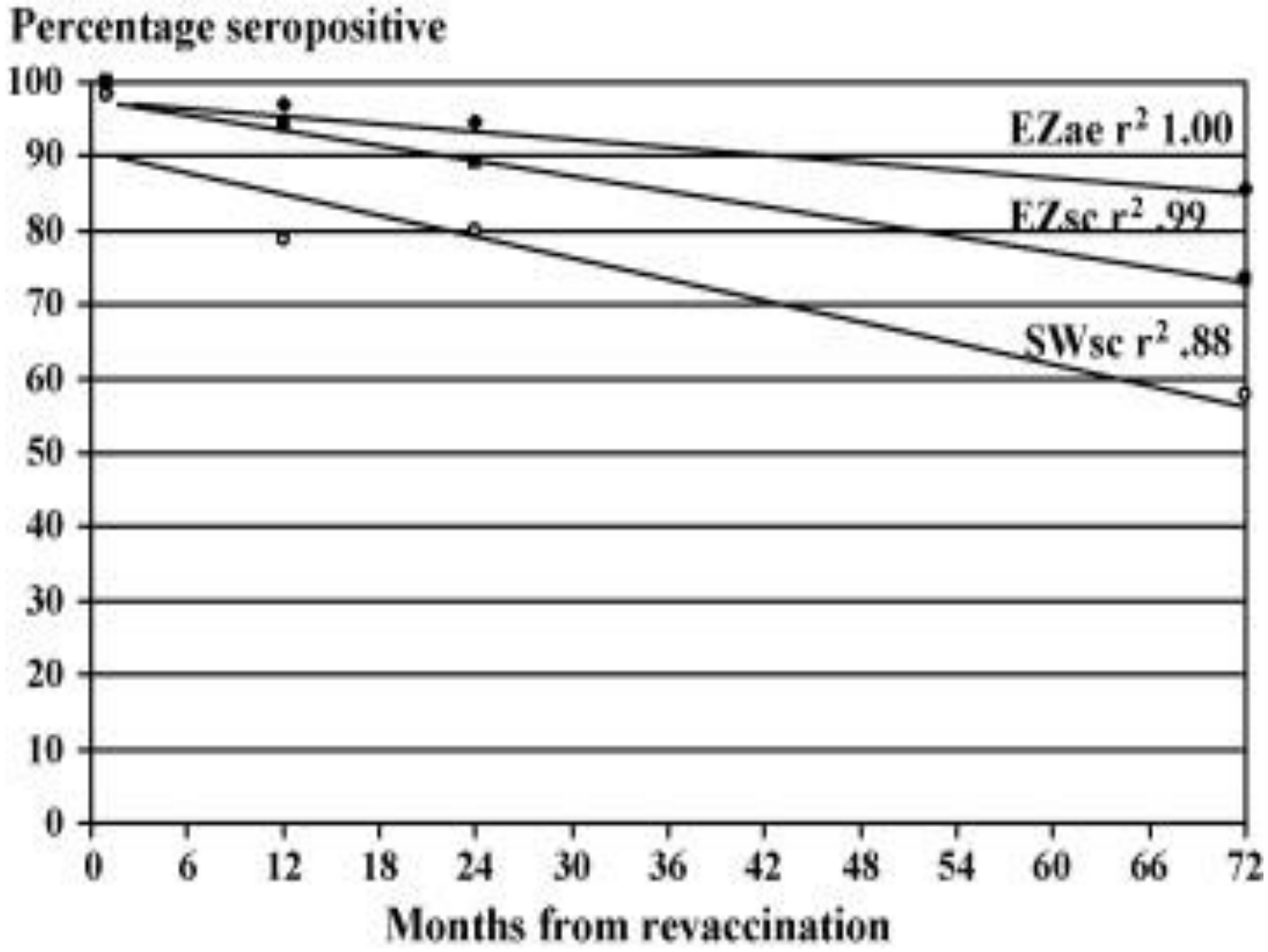
Reported measles cases, United States, 1950–1984.*

*1984 provisional data.

Current measles vaccine

- Live attenuated virus derived from the Edmonston strain of MeV
- Requires cold chain
- Given s.c. or i.m. at 12-15 months of age
- Requires 2nd dose to assure high levels of population immunity
- Safe and efficacious

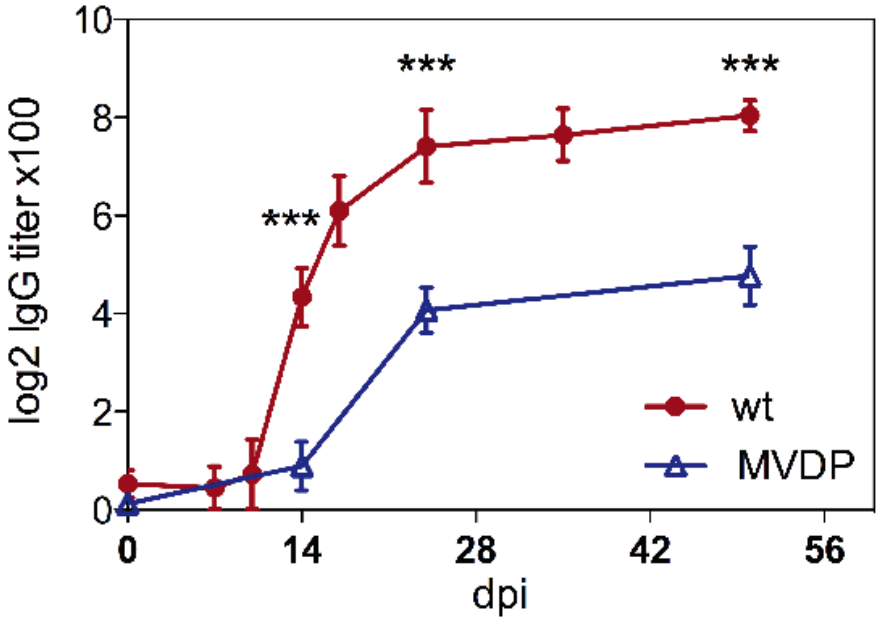
Vaccine-induced immunity is not as durable as natural immunity



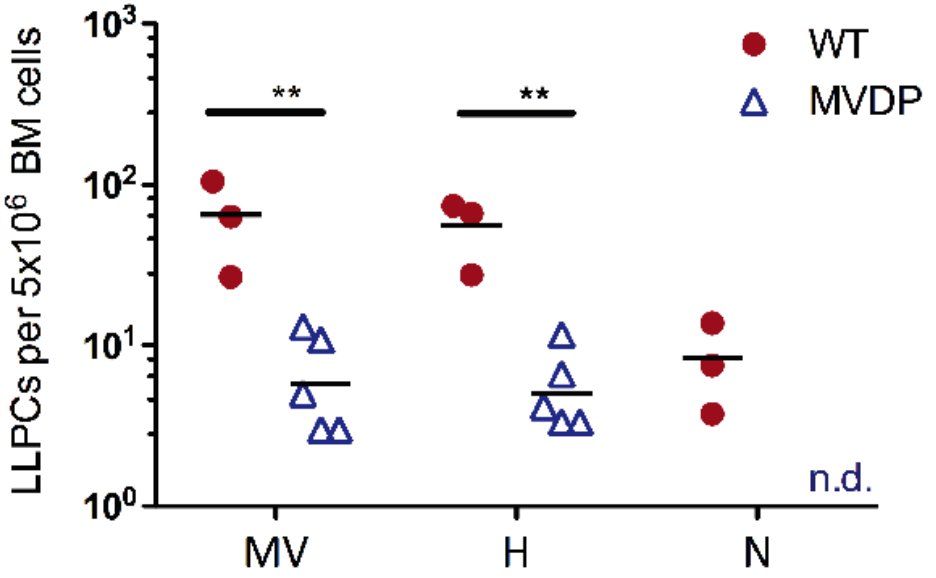
Dilraj et al, Vaccine 25:4170, 2007

Antibody responses are better after wild type MeV than vaccine MeV lung infection

H-specific IgG



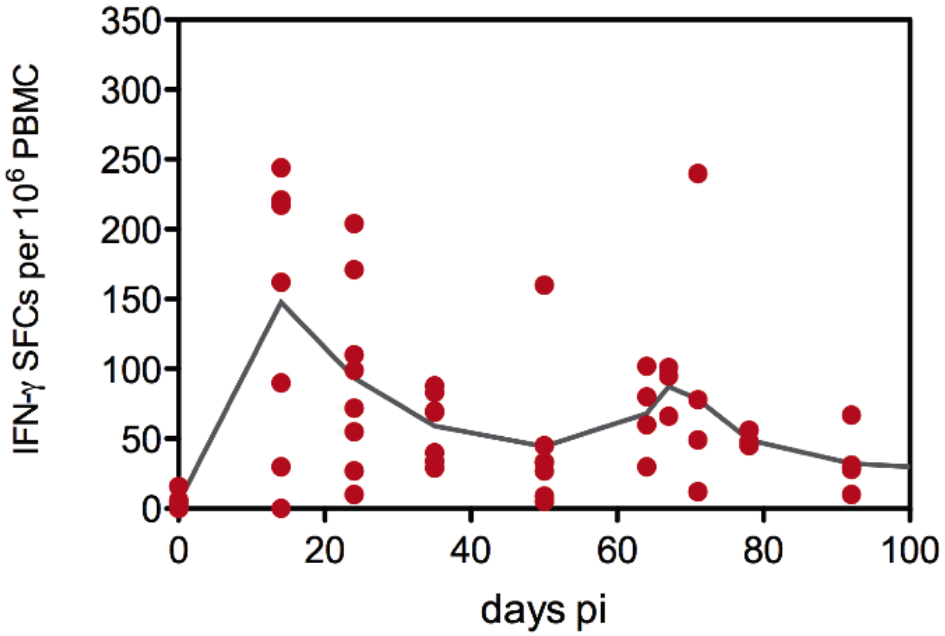
Plasma cells in bone marrow



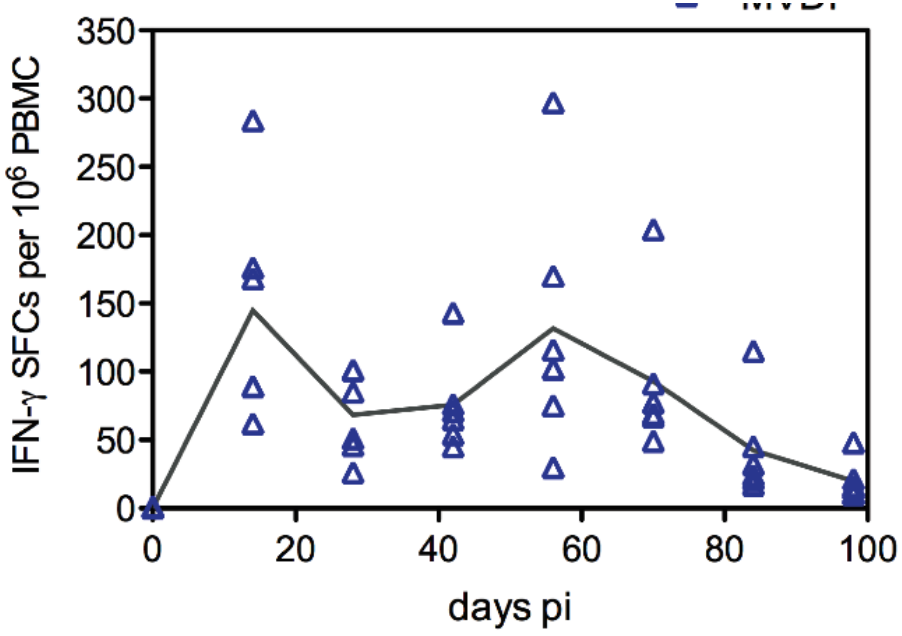
Lin et al, unpublished

Similar biphasic induction of MeV-specific IFN-γ-producing T cells after infection with wild type and vaccine MeV

Wild type

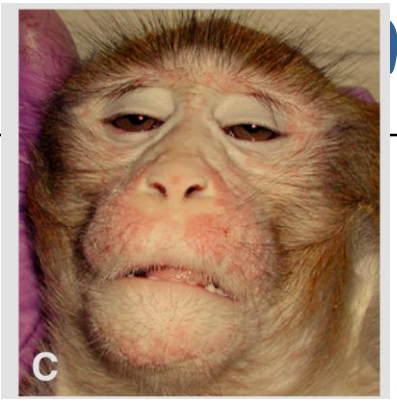


Vaccine

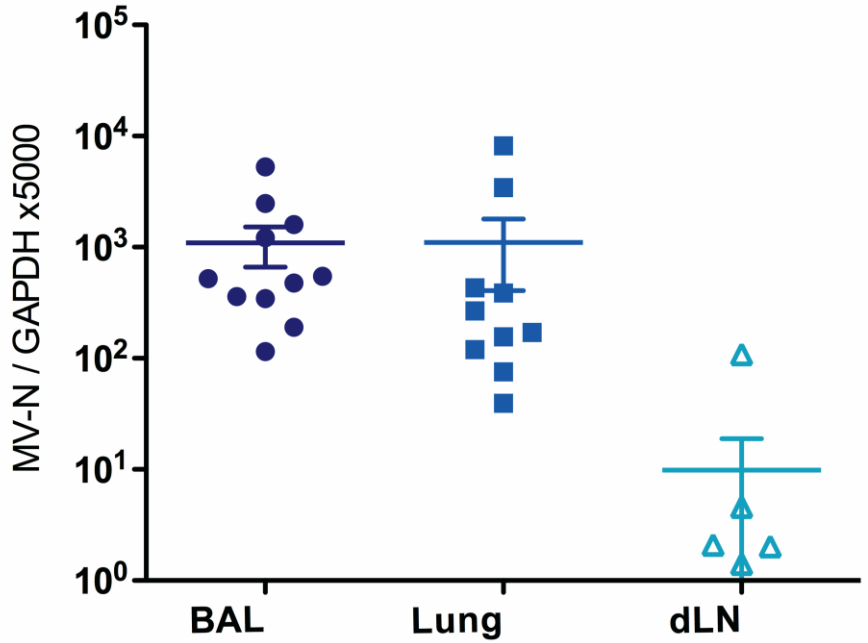


Lin et al, unpublished

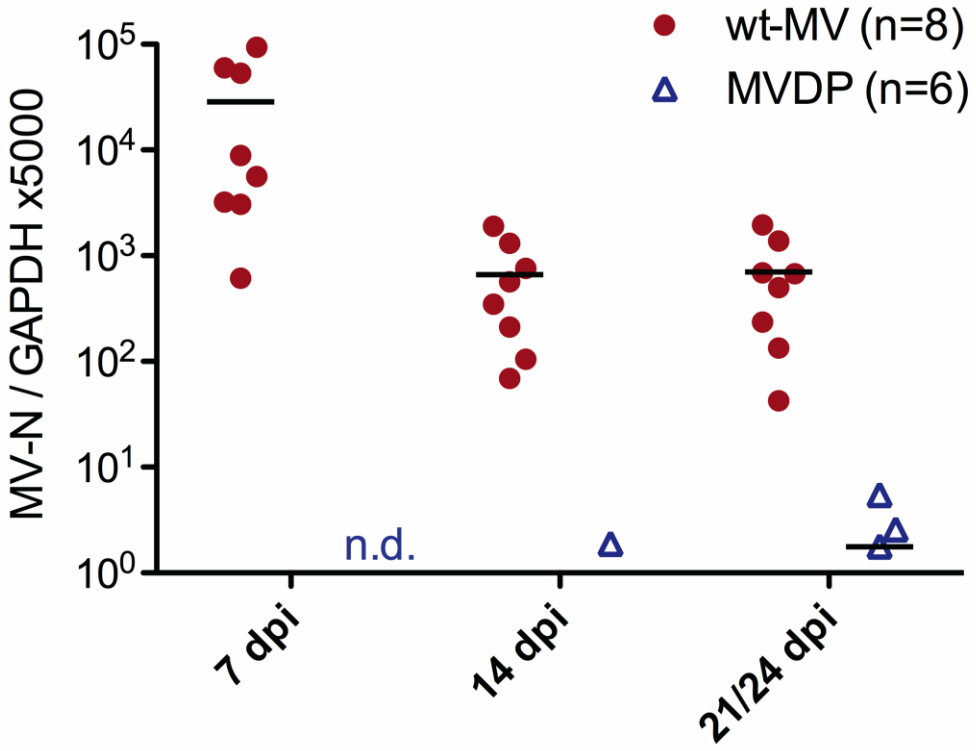
In macaques vaccine MeV replication in lymphoid tissue and PBMCs is restricted compared to WT



Vaccine at 7 days



PBMCs WT and vaccine



Lin et al unpublished

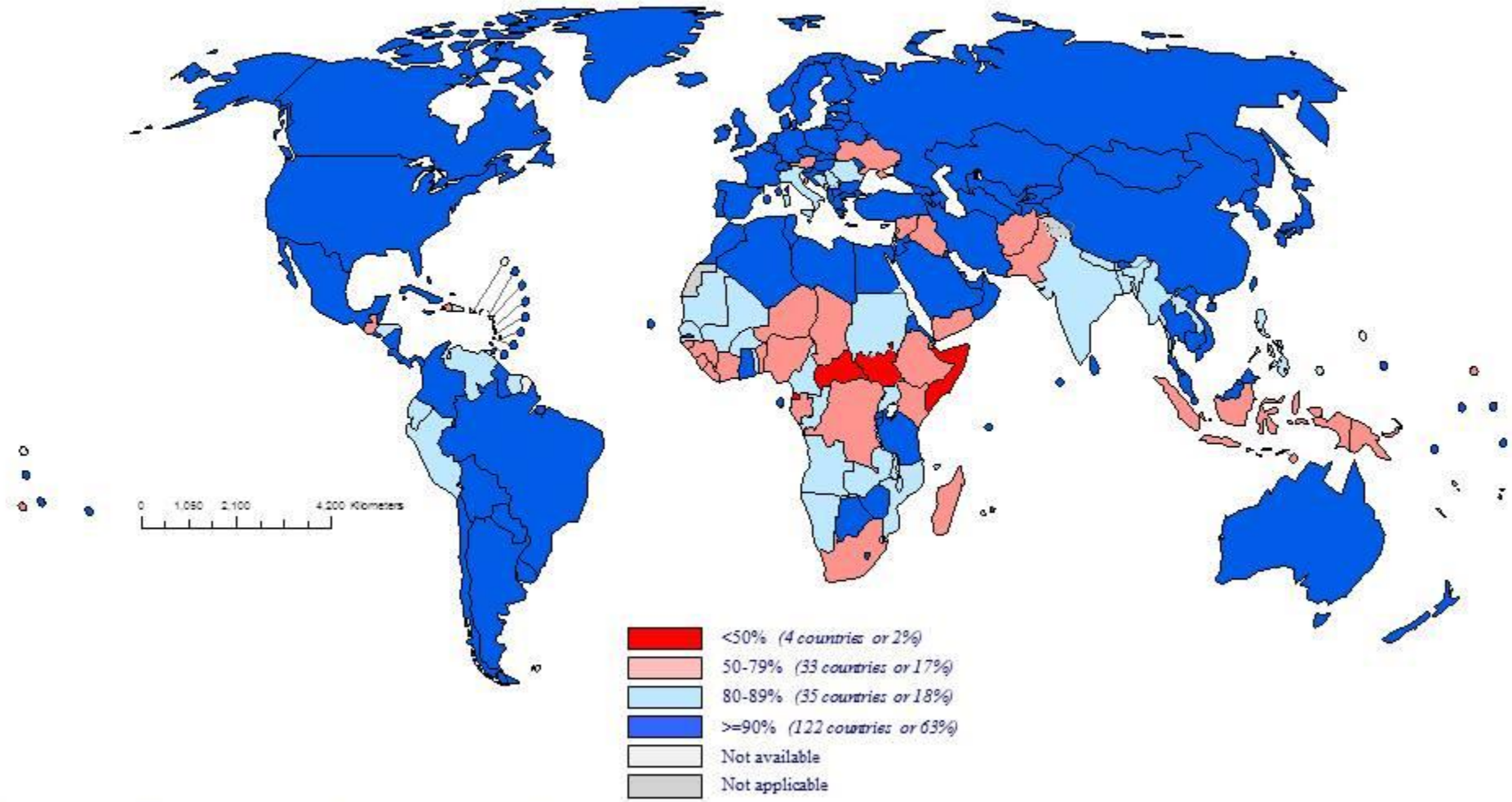
Measles Eradication

"Participants agreed that measles eradication is technically feasible with available vaccines and recommended the adoption of the goal of global eradication with a target date during 2005-2010."

WHO, Pan American Health Organization and CDC

MMWR June 1997

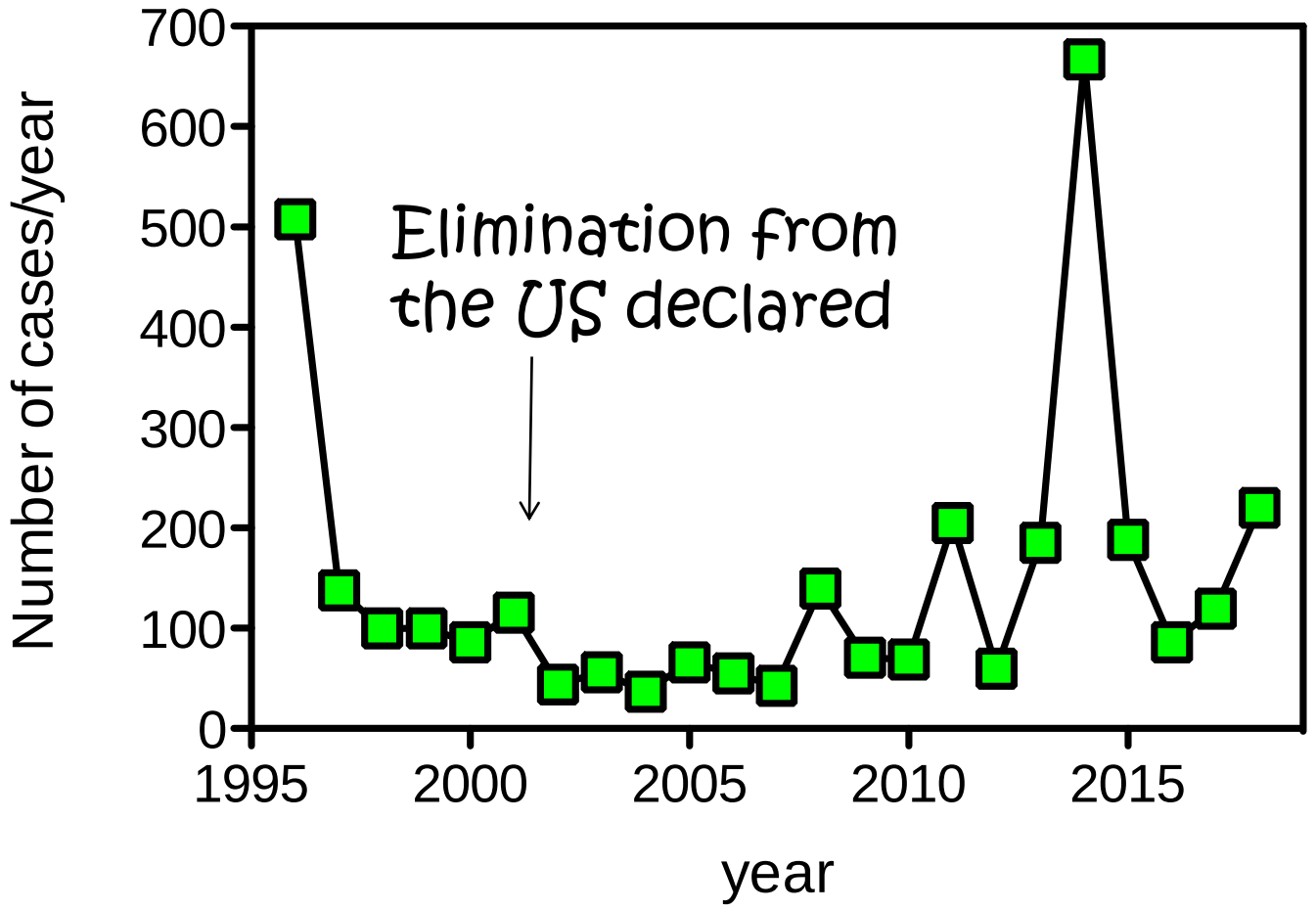
Immunization coverage with 1st dose of measles containing vaccines in infants, 2014



Source: WHO/UNICEF coverage estimates 2014 revision. July 2015. Map production: Immunization Vaccines and Biologicals, (IVB). World Health Organization
Date of slide: 16 July 2015

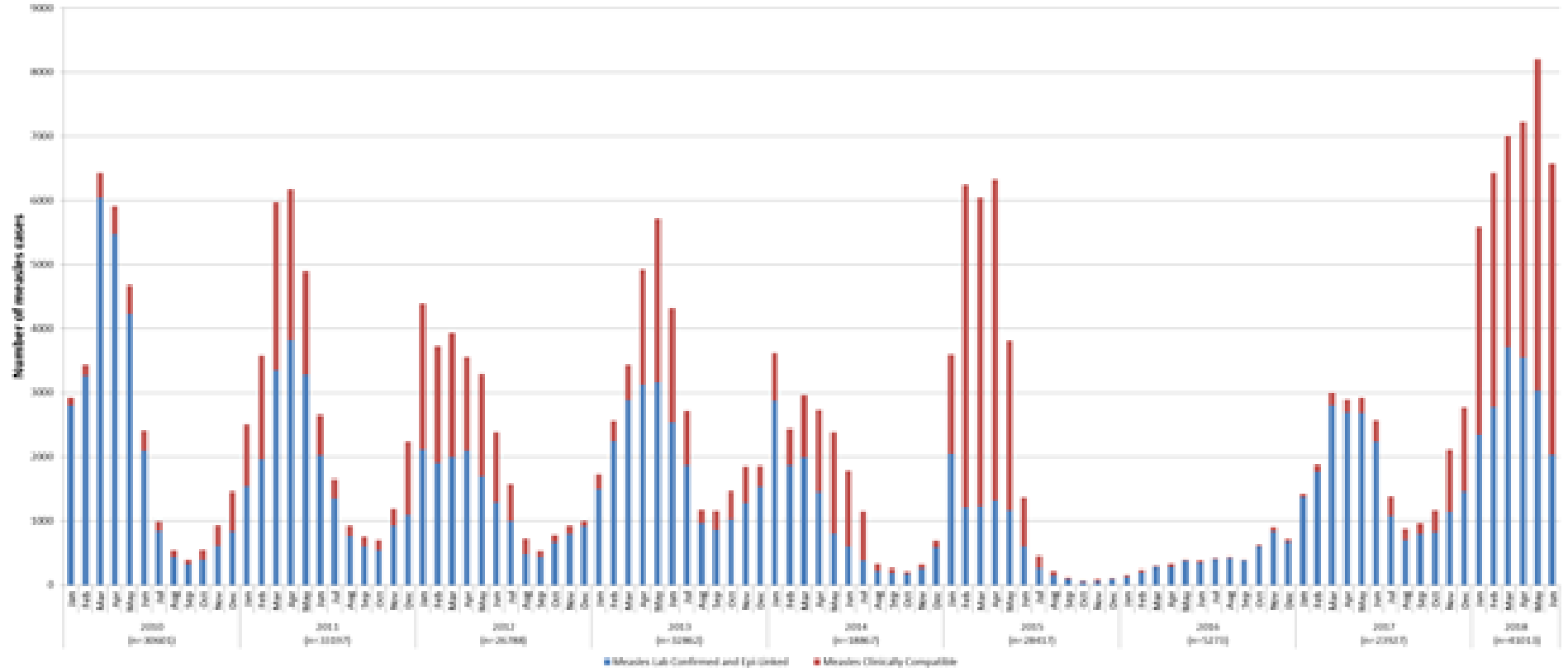
WHO

Measles cases in the United States



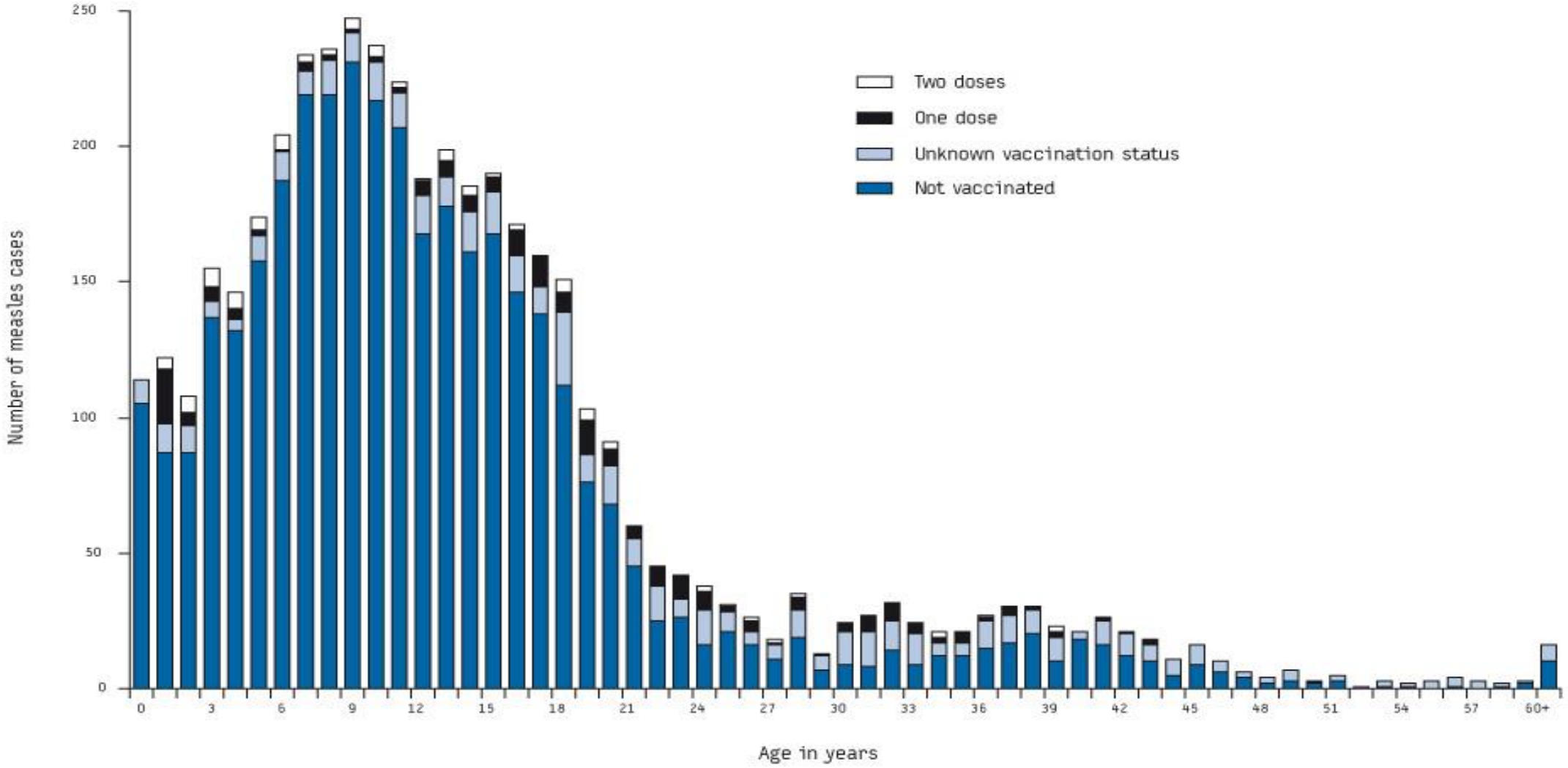
Centers for Disease Control

Measles: WHO European region 2010-2018



Swiss measles cases were primarily in unvaccinated person

Vaccination status by age for notified cases of measles, Switzerland, 15 November 2006 to 17 September 2009 (n=4,391)



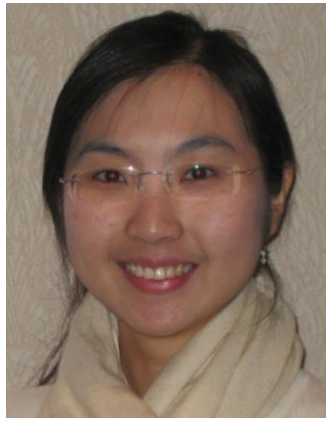
Richard et al, Euro Surveill 14:19443, 2009

Failure of measles control

- Need for very high coverage to interrupt transmission (≥95%)
- Problems with vaccine delivery in developing countries
  - Health infrastructure for routine infant immunization
  - Second dose/need for mass vaccination campaigns
  - Cold chain
  - Needles and syringes/need for skilled health workers
- Problems with vaccine acceptance in developed countries
  - Safety worries/sins of omission vs commission
  - Individual rights vs public health
- Secondary vaccine failure?

Acknowledgments

- Wen-Hsuan Lin
- Ashley Nelson
- Nicole Putnam
- Robert Adams
- Kelly Pate



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