Immunization, vaccination programs and immunization schedule

History of vaccination I.

- Variolation: against smallpox 10th or 11th century in Central Asia (India)
- 1796: Jenner used cowpox inoculation to prevent smallpox (immunization)

Edward Jenner
(May 17, 1749 – January 26, 1823)

The Cow-Pock — or — the Wonderful Effects of the New Inoculation! — Vide the Publications of ye Anti-Vaccine Society.

History of vaccination II.

- Works with anthrax and chicken cholera, developing artificially weakened microorganisms
- He gave the name vaccination (Vacca - cow in Latin) to honour Jenner's work.
- July 6, 1885: First rabies vaccination on a nine-year old boy (with Emile Roux)

Louis Pasteur
(December 27, 1822 – September 28, 1895)

History of vaccination III.

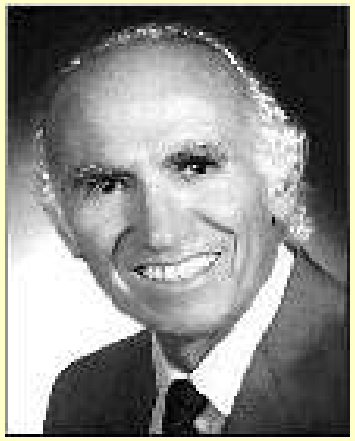
- Tetanus – first vaccine in 1890
- BCG (Bacillus Calmette-Guérin) – vaccine against tuberculosis. First used in humans in 1921, but widespreaded only after World War II.
- Diphtheria – first successful vaccine in 1923
- Pertussis – first successful vaccine in 1925 by Thorvald Madsen

Léon Charles Albert Calmette
(July 12, 1863 – October 29, 1933)

Jean-Marie Camille Guérin
(December 22, 1872 - June 9, 1961)

History of vaccination IV.

- DTP vaccine by Kendrick – 1942
- Polio vaccine by Salk – 1952
- Polio vaccine by Sabin – 1961
- Measles – 1963
- Mumps – 1967
- Rubella – 1970
- Hepatitis B – 1981
- Haemophilus influenzae B – 1985

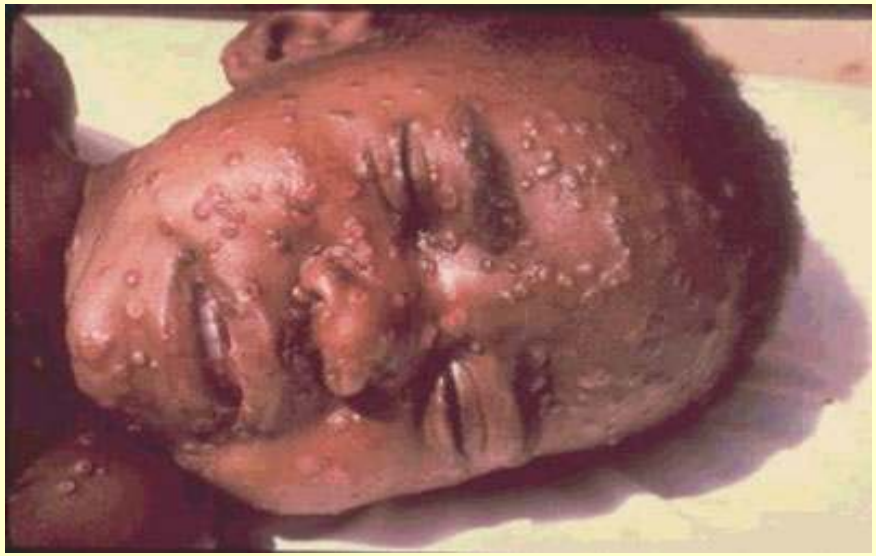


Jonas Edward Salk
(October 28, 1914 – June 23, 1995)

Albert Bruce Sabin
(August 26, 1906 - March 3, 1993)

The benefit of vaccination I. Smallpox eradication

- 1958: Soviet Union calls for eradication (2 million death / year)
- 1967: WHO team formed
- Quaranteene vaccination
- 1975: Last variola major case in Bangladesh
- 1977: Last variola minor case in Somalia
- 1979: The world is officially smallpox-free
- 2004: Bush vaccinates himself

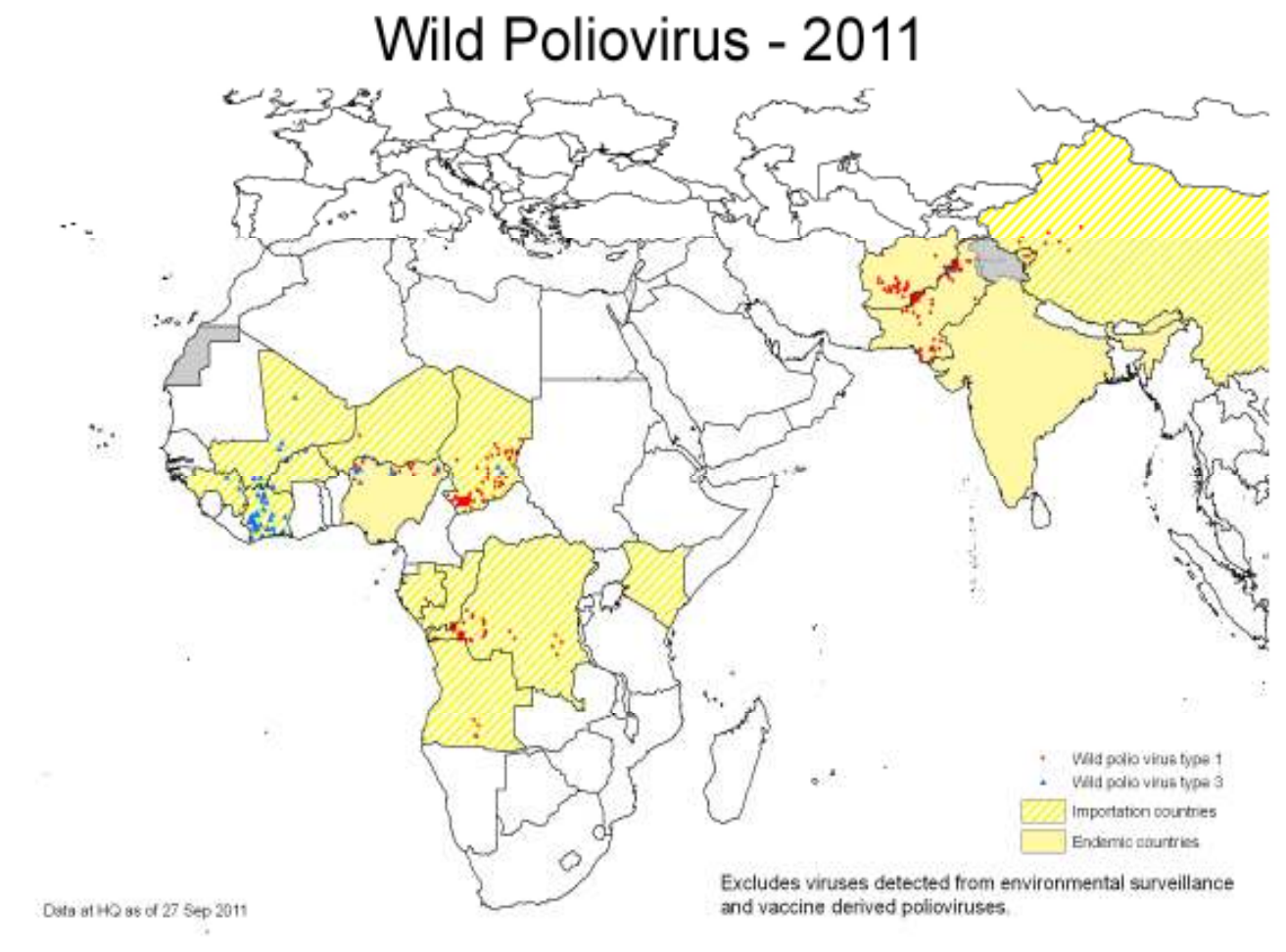


The benefit of vaccination II. Polio eradication in progress

- 1988: WHO, UNICEF and Rotary Foundation
- 1994: the Americas were certified as polio-free
- 2000: the Western Pacific Region (including China) was certified Polio-free
- 2002: Europe was certified as polio-free

The benefit of vaccination III.
Polio eradication in progress

International polio cases per year		
Év	Becsült	Regisztrált
1975	-	49,293
1980	400,000	52,552
1985	-	38,637
1988	350,000	35,251
1990	-	23,484
1993	100,000	10,487
1995	-	7,035
2000	-	2,971
2001	-	498
2002	-	1,922
2003	-	784
2004	-	1,258
2005	-	1,998
2006	-	1,985
2009	-	1,604



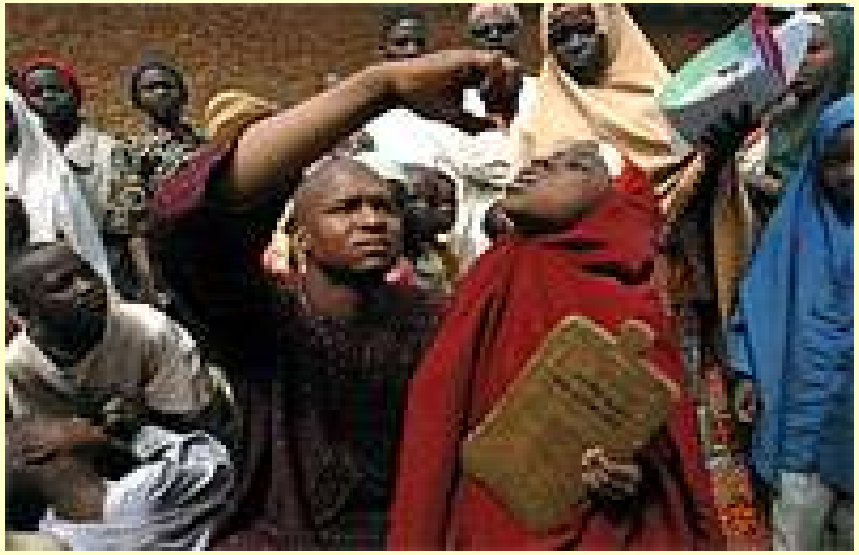
Reported wild poliovirus in 2009

Globally: 1604

India	741
Nigeria	388
Pakistan	89
Chad	64
Sudan	45
Guinea	42
Afghanistan	38
Angola	29
Côte d'Ivoire	26
Benin	20
Niger	15

From other countries 107

India



Nigeria

The benefit of vaccination IV.

- 1999-2003: Measles deaths dropped worldwide by almost 40% (still est. 345,000 deaths)
- 1999-2005: 9 countries of 57 eliminated MNT

- STILL: 2 million people die yearly from diseases preventable by vaccines (measles, pertussis, tetanus, Hib)

Global immunization coverage

- Diphteria-pertussis-tetanus

Global coverage of vaccinated infants: 78% (1985: 20%)

- Polio

Global coverage of vaccinated infants: 78% (1980: 22%)

- Measles

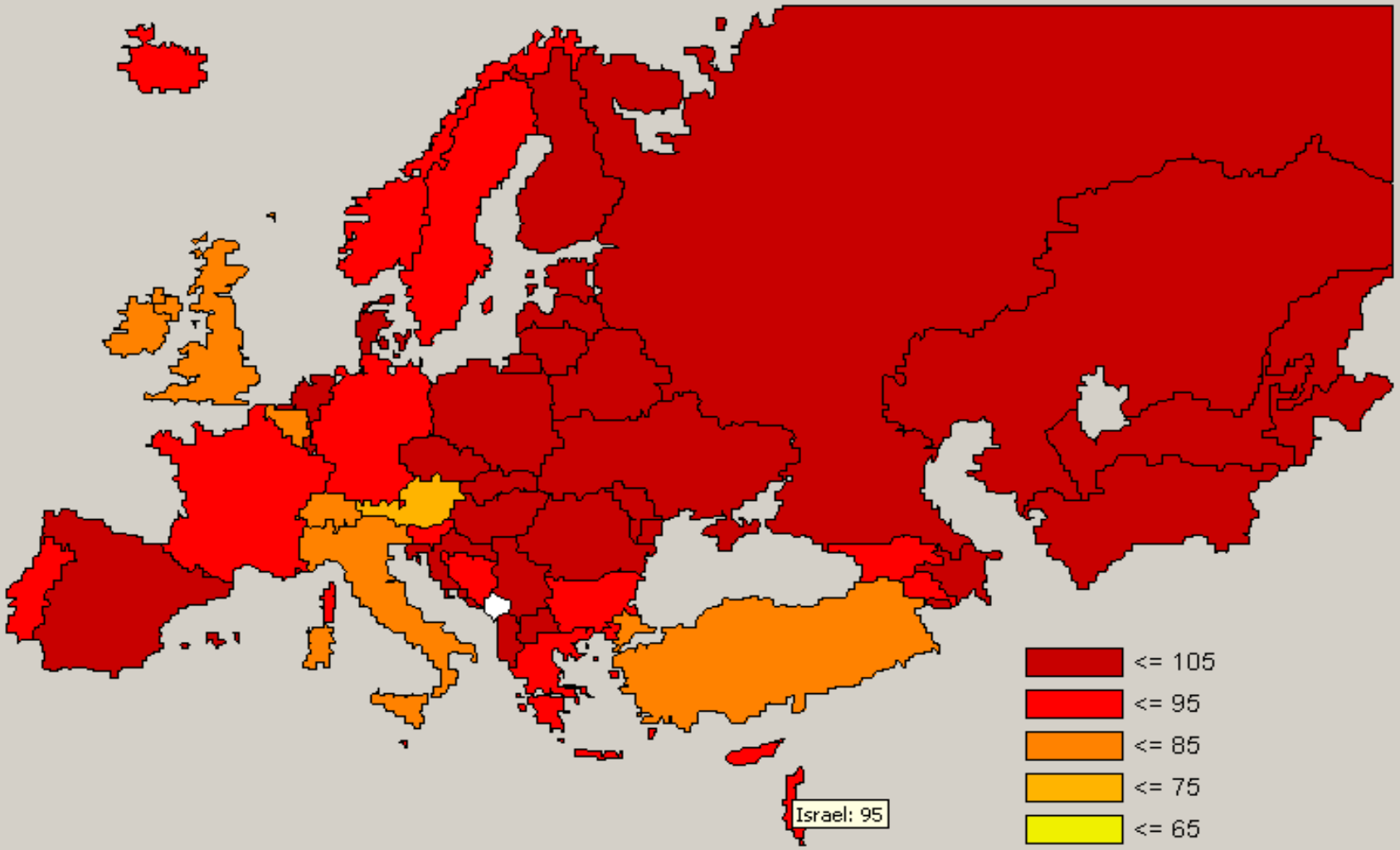
Global coverage of vaccinated infants: 77% (1980: 17%)

- Hepatitis B

Global coverage of vaccinated infants: 55% (1992: 3%)

Scale Years Indicators Type of map Print Quit

% of children vaccinated against measles



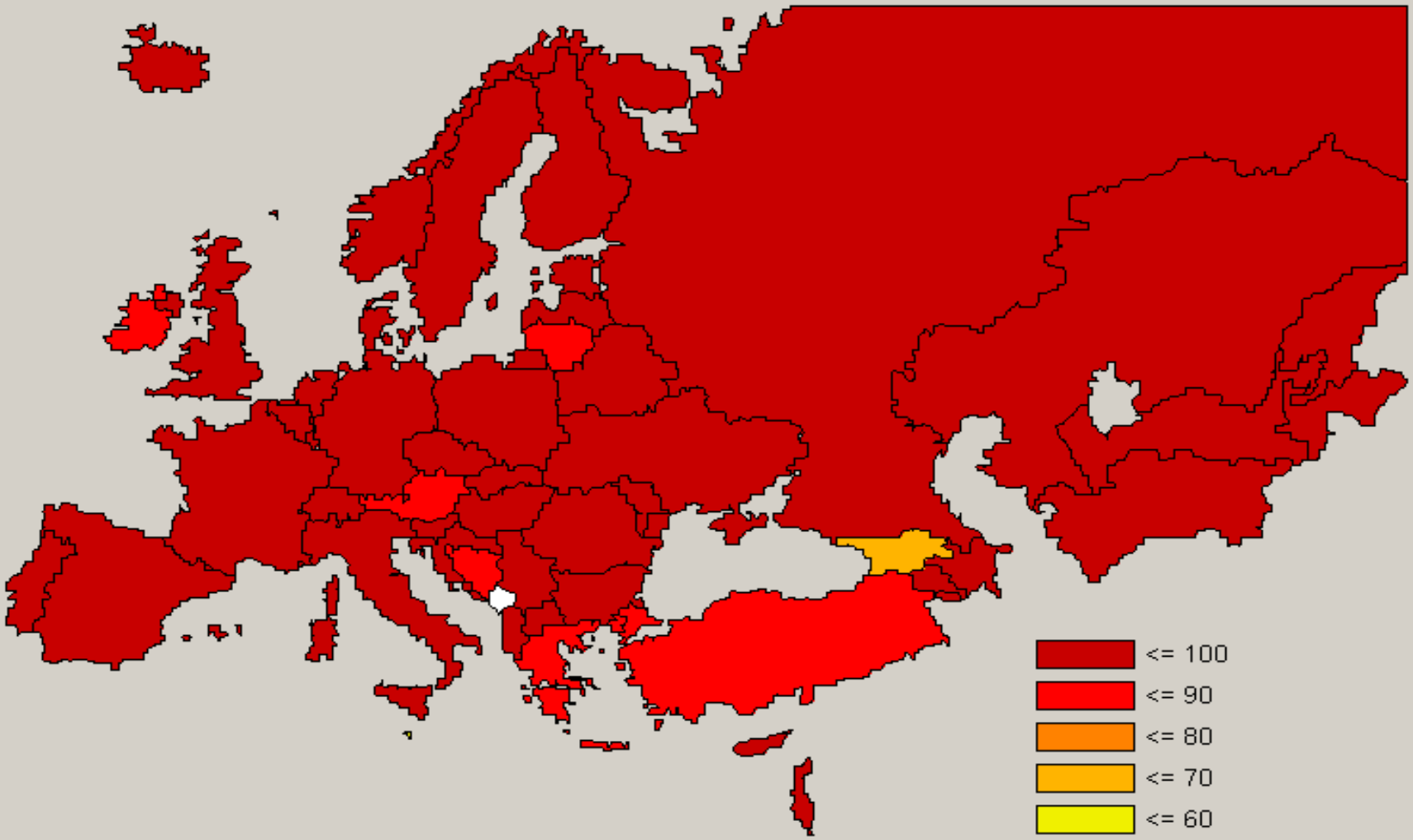
European Region
93.06

2004

Source: WHO/Europe, European HFA Database, January 2007

Scale Years Indicators Type of map Print Quit

% of infants vaccinated against poliomyelitis



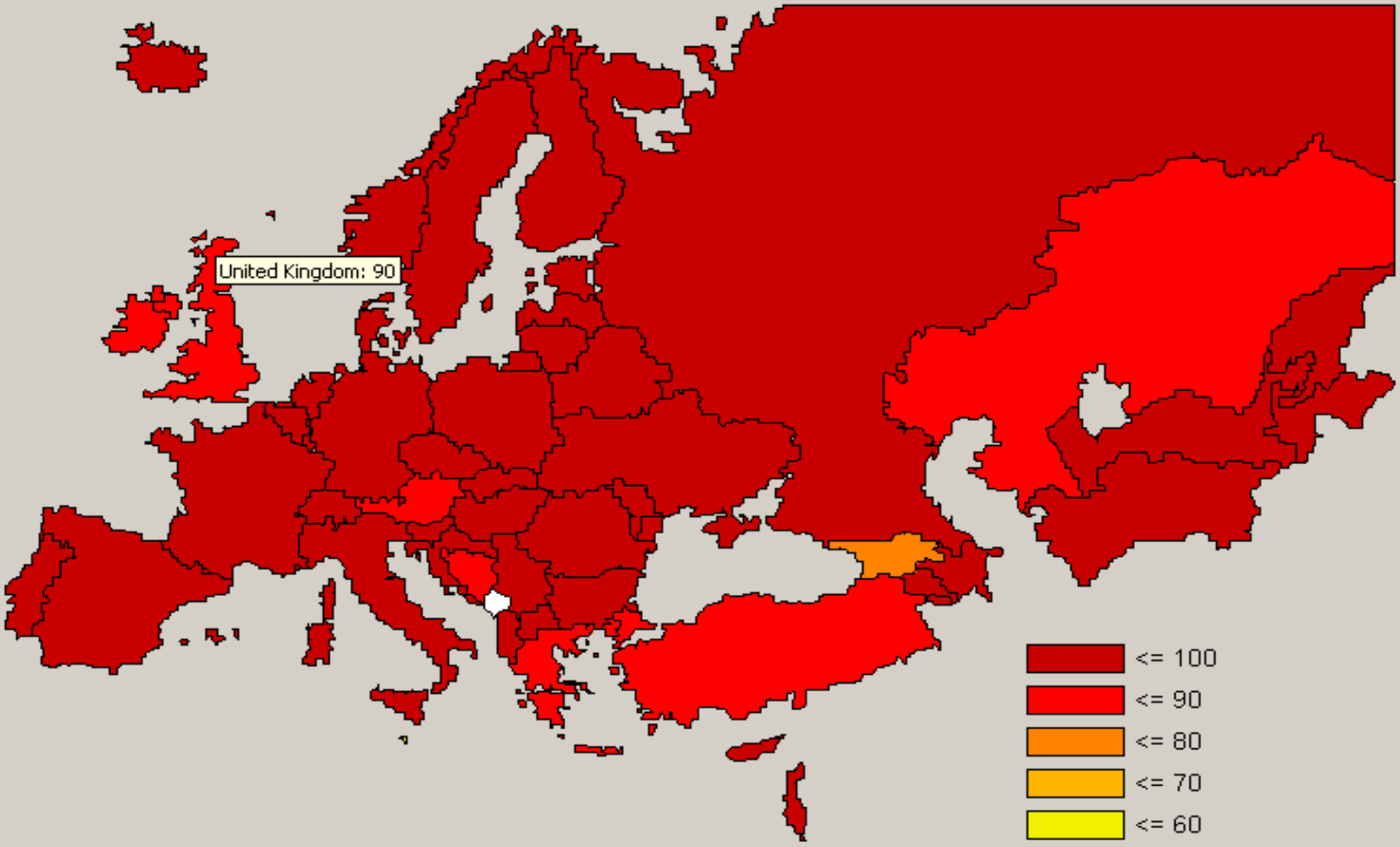
European Region
96.02

2004

Source: WHO/Europe, European HFA Database, January 2007

Scale Years Indicators Type of map Print Quit

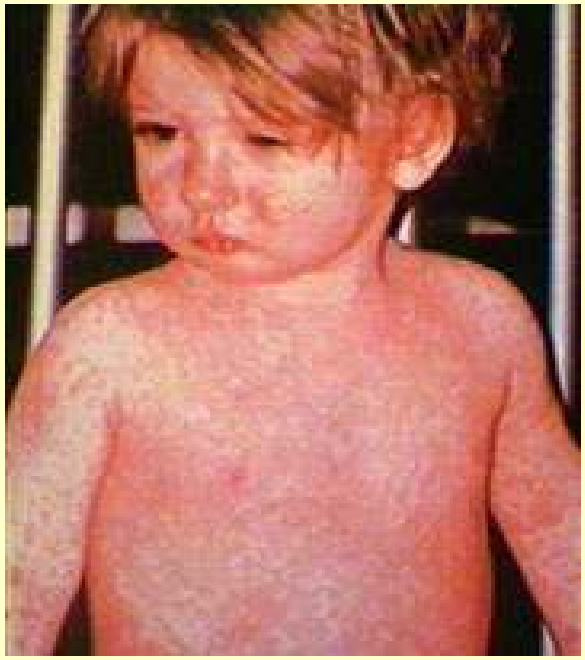
% of infants vaccinated against tetanus

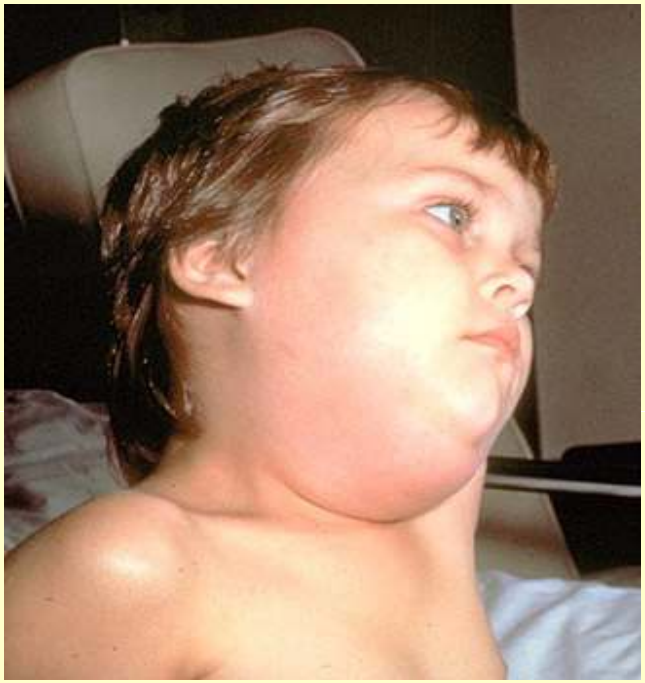


European Region
95.86

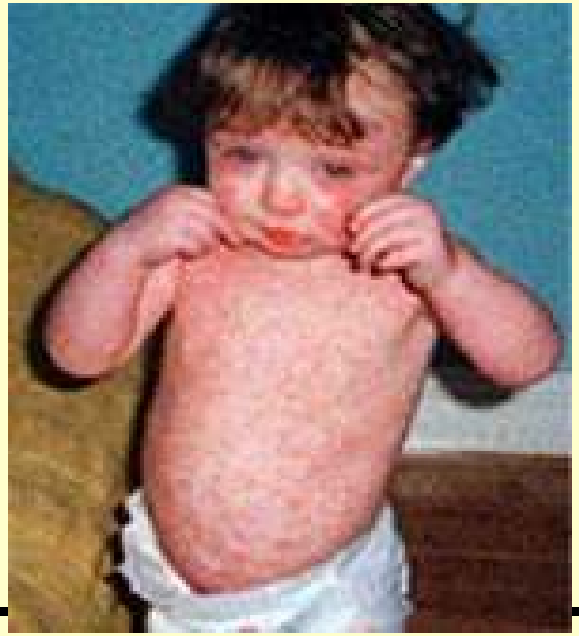
2004

Source: WHO/Europe, European HFA Database, January 2007





Measles (Morbilli)



Mumps (Infectious parotitis)

Rubella

(German measles)

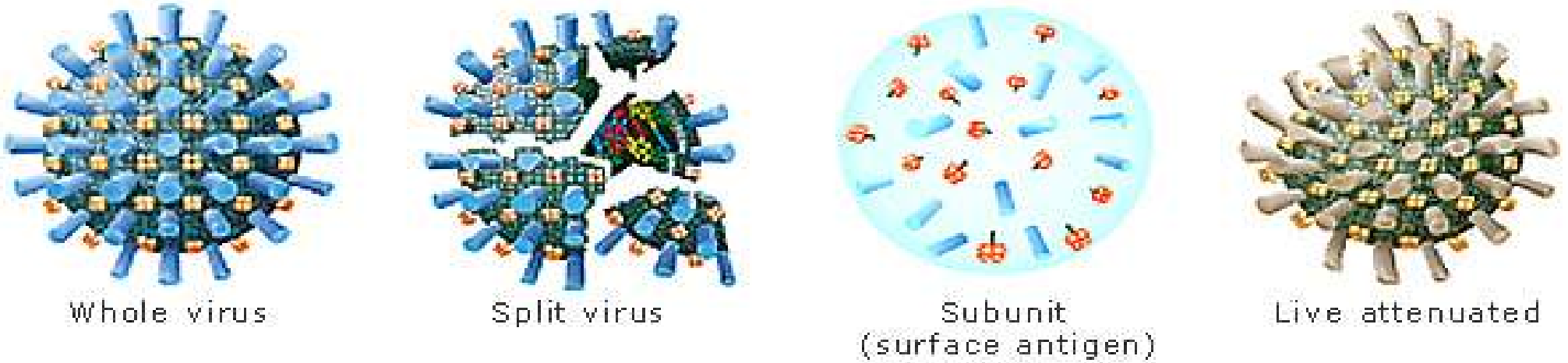
SC Dept. of Public Health

The cost of vaccination

- 2002, Kenya: One week measles vaccination = 12 million USD saved for ten years
- US: 1 USD for vaccine = 2-27 USD saved in healthcare
- Complete immunization of a child = 20-40 USD

Types of vaccines I.

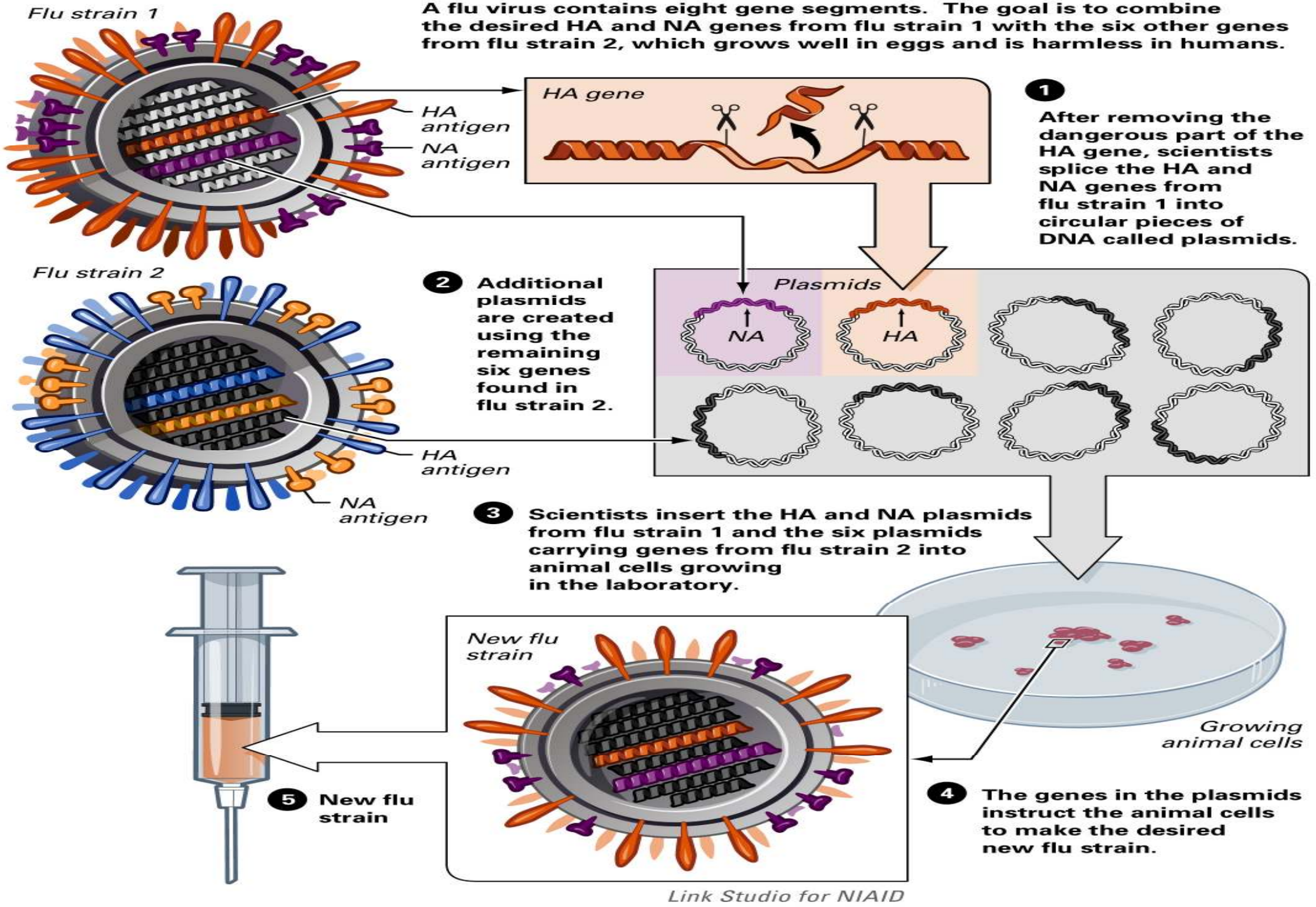
- **Inactivated** - these are previously virulent micro-organisms that have been killed with chemicals or heat. Examples: cholera, hepatitis A.
- **Live, attenuated** - these are live micro-organisms that have been cultivated under conditions that disable their virulent properties. Examples: yellow fever, measles, rubella and mumps.
- **Toxoids** - these are inactivated toxic compounds from micro-organisms. Examples: tetanus and diphtheria.
- **Subunit** - rather than introducing a whole inactivated or attenuated micro-organism to an immune system, a fragment of it can create an immune response. Example: HBV



1. **Whole virus vaccines** consisting of **inactivated viruses**.
2. **Split virus vaccines** consisting of **inactivated virus particles** disrupted by detergent treatment.
3. **Subunit or surface antigen vaccines** consisting essentially of **purified hemagglutinin and neuraminidase** from which other virus components have been removed.
4. **Live attenuated** (cold-adapted) virus vaccines consisting of weakened (non-pathogenic) whole virus.

Types of vaccines II.

- **Conjugate** - certain bacteria have polysaccharide outer coats that are poorly immunogenic. By linking these outer coats to proteins (e.g. toxins), the immune system can be led to recognize the polysaccharide as if it were a protein antigen. Example: *Haemophilus influenzae* type B.
- **Recombinant vector** - by combining the physiology of one micro-organism and the DNA of the other, immunity can be created against diseases that have complex infection processes. Example: HPV
- **DNA vaccination** - in recent years a new type of vaccine, created from an infectious agent's DNA called *DNA vaccination*, has been developed. It works by insertion (and expression, triggering immune system recognition) into human or animal cells, of viral or bacterial DNA. Some cells of the immune system that recognize the proteins expressed will mount an attack against these proteins and cells expressing them.


Flu strain 1
A flu virus contains eight gene segments. The goal is to combine the desired HA and NA genes from flu strain 1 with the six other genes from flu strain 2, which grows well in eggs and is harmless in humans.
HA antigen
NA antigen
HA gene
1
After removing the dangerous part of the HA gene, scientists splice the HA and NA genes from flu strain 1 into circular pieces of DNA called plasmids.
Flu strain 2
2
Additional plasmids are created using the remaining six genes found in flu strain 2.
Plasmids
NA
HA
HA antigen
NA antigen
3
Scientists insert the HA and NA plasmids from flu strain 1 and the six plasmids carrying genes from flu strain 2 into animal cells growing in the laboratory.
New flu strain
Growing animal cells
5
New flu strain
4
The genes in the plasmids instruct the animal cells to make the desired new flu strain.
Link Studio for NIAID

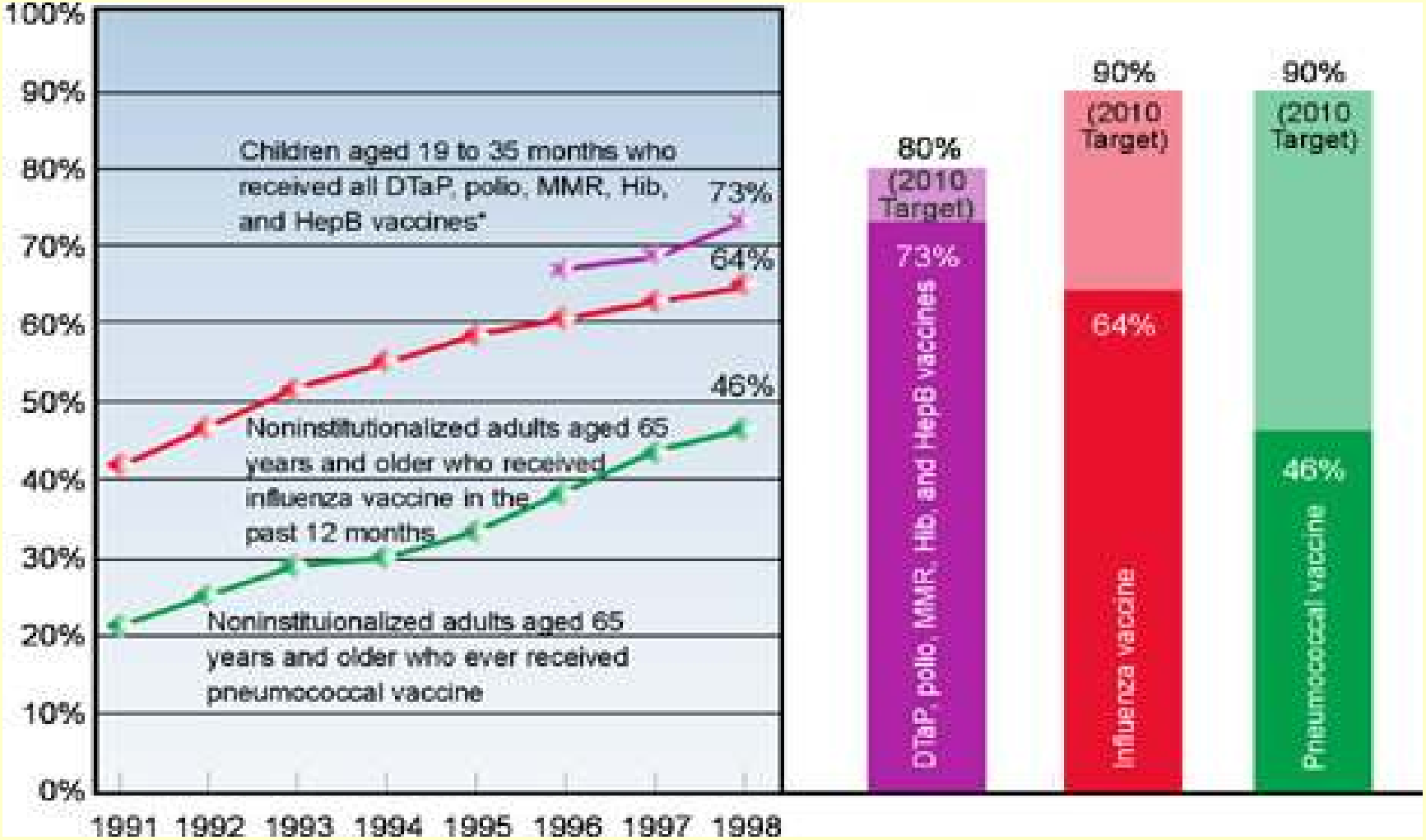
Vaccines of the present / future

- Rotavirus – 3-600.000 death / year worldwide
- HPV – cervical cancer
- Pneumococcus – 2 million death / year
- Conjugated meningococcus
- Malaria
- HIV / AIDS
- S. mutans (caries)
- Cancer
- Nicotine
- Allergy

AIMS of immunization/vaccination

- **Individual**: reducing susceptibility to infectious diseases
- **Community**: breaking route of infection
  herd immunity, community immunity

Immunization coverage, USA 1991-1998



Classification of immunization

- Active vs. passive
- Pre-exposure vs. post-exposure
- Parenterally vs. orally vs. intranasally administered
- Live (attenuated), inactivated & toxoid/anatoxin
- Compulsory vs. recommended
    1. Age-related (continuous or campaign-like)
    2. Exposure-related

Tasks of the vaccinating physician I.

- Examination of the subject
  - Any illness in past four weeks
  - Chronic diseases (immune-suppression)
  - Blood transfusion or immunoglobulin received within the past 3 months
  - Vaccination history including possible adverse reactions
  - Time of last vaccination
  - Possibility of pregnancy
  - Medical history plus physical examination
- Informing the subject
  - Purpose
  - Risk of adverse reactions
  - Information about the immune-status and the time course of vaccination
  - Information about the vaccine injury compensation $
  - In case of refusal: dangers to self and surroundings, possible sanctions §

Tasks of the vaccinating physician II.

- Vaccine
  - Is it the right vaccine? Read brochure before vaccination! 🕮
  - Was it stored properly (e.g. cold chain)?
  - Expiry date? (except: influenza vaccines can only be used in a single influenza season regardless of a later expiry date)
  - Does anything about the vaccine's appearance (cloudy, discolored) indicate quality loss

- Documentation
  - Informed consent of the vaccinated person or their legal representative (legal representative in case of children)
  - Refusal of vaccination only with written statement by the subject ✎
  - Refusal cases should be reported to the public health authorities ✉
  - Registering vaccinations into vaccination booklet/international certification

Most common contraindications of vaccination

- Conditions accompanied by fever 🌡
- Severe previous complication related to the given vaccine
- Childhood neurological conditions
- Pregnancy (no live vaccines, except vital indication, limited number of others)
- Hypersensitive / anaphylactic reaction to egg-proteins or antibiotics (skin test when applicable)

Vaccination of special groups

- Any form of immunosuppression
  (generally no BCG & live vaccines)

- Symptomatic AIDS patients, children of HIV-positive mothers
  (no BCG, yellow fever, live S. Typhi, MMR individually)

- Splenectomized persons
  (diminished reaction to capsular bacteria)

Required intervals between various types of immunizations

	Inactivated / toxoid	***Live viral***	**BCG**	***IgG***
Inactivated / toxoid	**0**	**0**	**0**	**0**
Live viral	**0**	**0/4** weeks	**4** weeks	**2** weeks
BCG	**0**	**4** weeks	**.**	**0**
IgG	**0**	**3** months	**0**	**3** months

Required intervals between certain types of immunization and blood/blood products (6-11 months)

Incorrect reasons for delaying or avoiding a vaccine

You <u>DO NOT</u> have to avoid or delay immunization due to:

- *a minor infection without a fever such as a cough or cold*
- *a family history of adverse reactions following immunizations*
- *a previous history of diseases such as whooping cough, measles, rubella or mumps infection*
- *premature birth*
- *stable neurological conditions such as cerebral palsy*
- *contact with infectious disease*
- *asthma, hay fever, eczema or 'snuffles'*
- *treatment with antibiotics or locally acting steroids*
- *the child's mother is pregnant*
- *the child is being breastfed*
- *history of jaundice after birth*
- *the child is under a certain weight*
- *the child is over the immunisation age recommended in schedule*
- *'replacement' corticosteroids*
- *a history of allergy*
- *a personal or family history of inflammatory bowel disease (Crohn's disease or ulcerative colitis)*
- *a personal or family history of autistic spectrum disorders*
- *recent or imminent surgery.*

Possible responses to vaccination

- Immunization-related ***reactions*** (normal-mild symptoms)
- Immunization-related ***complications*** (stronger reaction by the individual - hypersensitivity)
- Immunization-related ***accidents*** (problems with vaccine quality or administration)
- Immunization related complications and accidents always have to be reported to the local public health authorities ☎ 🖷 💻

Hungarian schedule of compulsory, age-related vaccination 2009

Age	Immunization
0-6 weeks:	BCG
2 months:	DPaT + IPV + Hib I
3 months:	DPaT + IPV + Hib II
4 months:	DPaT + IPV + Hib III
15 months:	MMR
18 months:	DPaT + IPV + Hib IV
6 years:	DPaT + IPV
11 years:	diphtheria - tetanus (September)
11 years:	MMR (October)
13 or 14 years:	Hepatitis B

Recommended vaccine: PCV-7 (7 component pneumococcus vaccine at age 2,4 and 15 month)

BCG: Bacille Calmette-Guerin, DPaT: Diphtheria-Pertussis-Tetanus, IPV: Inactivated Polio Vaccine, MMR: Measles-Mumps-Rubella

DEPARTMENT OF HEALTH AND HUMAN SERVICES • CENTERS FOR DISEASE CONTROL AND PREVENTION

Recommended Immunization Schedule for Persons Aged 0–6 Years—UNITED STATES • 2007

Vaccine ▼ Age ►	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
Hepatitis B[1]	HepB	HepB		see footnote 1	HepB				HepB Series		
Rotavirus[2]			Rota	Rota	Rota						
Diphtheria, Tetanus, Pertussis[3]			DTaP	DTaP	DTaP		DTaP				DTaP
Haemophilus influenzae type b[4]			Hib	Hib	*Hib*[4]	Hib		Hib			
Pneumococcal[5]			PCV	PCV	PCV	PCV				PCV PPV	
Inactivated Poliovirus			IPV	IPV	IPV						IPV
Influenza[6]					Influenza (Yearly)						
Measles, Mumps, Rubella[7]						MMR					MMR
Varicella[8]						Varicella					Varicella
Hepatitis A[9]						HepA (2 doses)				HepA Series	
Meningococcal[10]										MPSV4	

Range of recommended ages

Catch-up immunization

Certain high-risk groups

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2006, for children aged 0–6 years. Additional information is available at http://www.cdc.gov/nip/recs/child-schedule.htm. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at http://www.vaers, hhs.gov or by telephone, 800-822-7967.

DEPARTMENT OF HEALTH AND HUMAN SERVICES • CENTERS FOR DISEASE CONTROL AND PREVENTION

Recommended Immunization Schedule for Persons Aged 7–18 Years—UNITED STATES • 2007

Vaccine ▼ / Age ▶	7–10 years	11–12 YEARS	13–14 years	15 years	16–18 years
Tetanus, Diphtheria, Pertussis[1]	*see footnote 1*	Tdap	Tdap		
Human Papillomavirus[2]	*see footnote 2*	HPV (3 doses)	HPV Series		
Meningococcal[3]	MPSV4	MCV4	MCV4	MCV4[3]	
Pneumococcal[4]	PPV				
Influenza[5]	Influenza (Yearly)				
Hepatitis A[6]	HepA Series				
Hepatitis B[7]	HepB Series				
Inactivated Poliovirus[8]	IPV Series				
Measles, Mumps, Rubella[9]	MMR Series				
Varicella[10]	Varicella Series				

Range of recommended ages

Catch-up immunization

Certain high-risk groups

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2006, for children aged 7–18 years. Additional information is available at http://www.cdc.gov/nip/recs/child-schedule.htm. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at http://www.vaers.hhs.gov or by telephone, 800-822-7967.

Comparison of oral (Sabin) and parenteral (Salk) Polio vaccines

SALK (IPV, inactivated)	SABIN (OPV, live, attenuated)
Confers humoral immunity	Confers humoral and mucosal immunity
Highly effective	Highly effective
No reactivation of virus	Virus reactivation theoretically possible
No danger of vaccination poliomyelitis	Very rare vaccination poliomyelitis
Suitable in immunosuppression	Not recommended in immunosuppression
Parenteral administration	Oral administration
Relatively expensive	Relatively inexpensive

WHO recommendation: eradication of both wild type and mutant polioviruses.
From 2010 no OPV will be used worldwide

Compulsory vaccination in case of exposure

Active immunization
(for contacts)

- **Abdominal typhoid**
- **Diphtheria**
- **Pertussis**
- **Measles**
- **Rubella**
- **Mumps**
- **Tetanus** (exposed patient)
- **Lyssa/Rabies** (exposed patient)

Passive immunization
with gamma globulin

- **Hepatitis A** contacts (within 14 days of exposure)
- **Measles** contacts (ages 15 months or younger, or if active immunization is contraindicated and within 6 days of exposure)

Mixed (active - passive): tetanus, HbsAg positive mother's newborn

Recommended Adult Immunization Schedule, by Vaccine and Age Group

UNITED STATES • OCTOBER 2006–SEPTEMBER 2007

Vaccine ▼ / Age group ▶	19–49 years	50–64 years	≥65 years
Tetanus, diphtheria, pertussis (Td/Tdap)[1,*]	1-dose Td booster every 10 yrs; Substitute 1 dose of Tdap for Td		
Human papillomavirus (HPV)[2]	3 doses (females)		
Measles, mumps, rubella (MMR)[3,*]	1 or 2 doses	1 dose	
Varicella[4,*]	2 doses (0, 4–8 wks)	2 doses (0, 4–8 wks)	
Influenza[5,*]	1 dose annually	1 dose annually	
Pneumococcal (polysaccharide)[6,7]	1–2 doses		1 dose
Hepatitis A[8,*]	2 doses (0, 6–12 mos, or 0, 6–18 mos)		
Hepatitis B[9,*]	3 doses (0, 1–2, 4–6 mos)		
Meningococcal[10]	1 or more doses		

*Covered by the Vaccine Injury Compensation Program. NOTE: These recommendations must be read with the footnotes (see reverse).

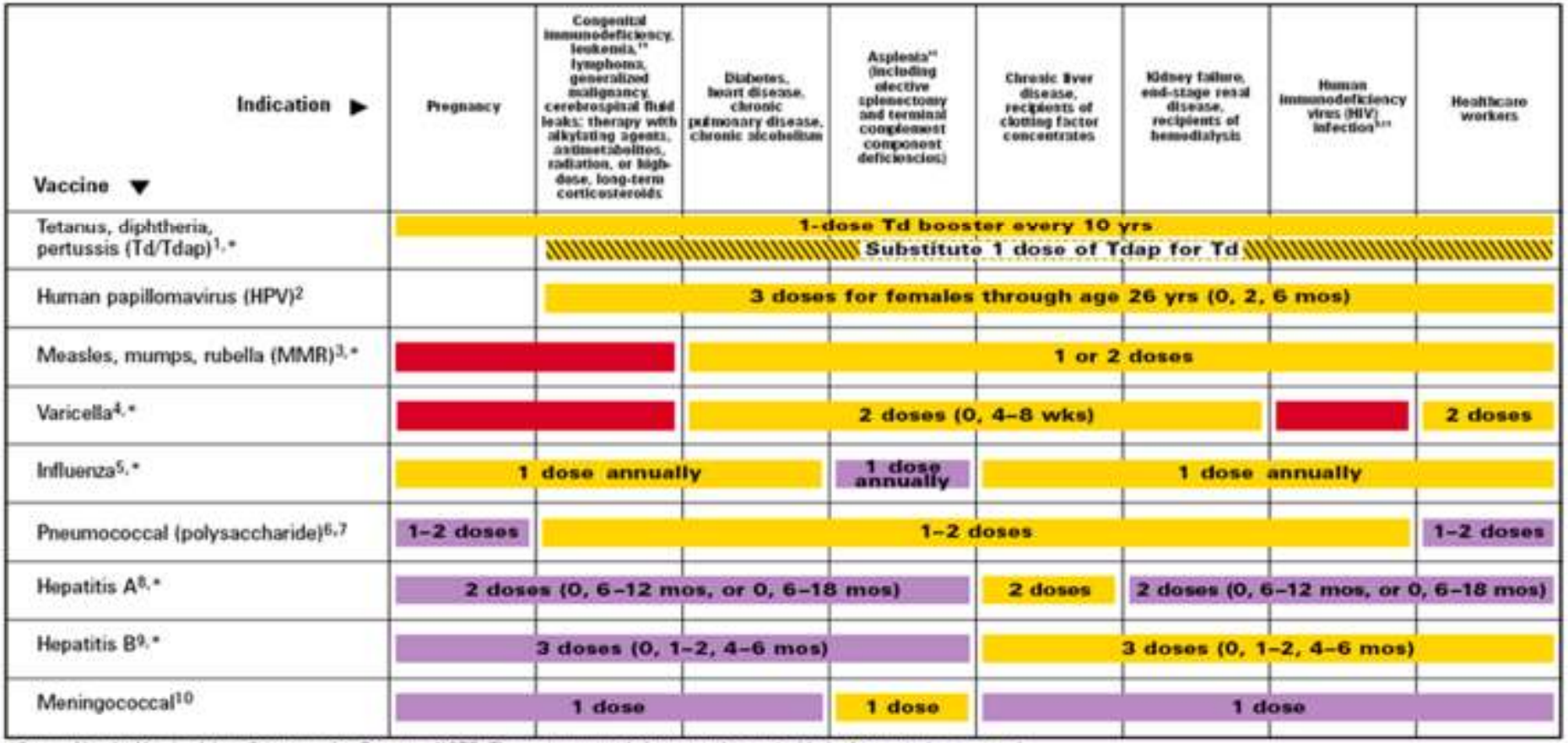
For all persons in this category who meet the age requirements and who lack evidence of immunity (e.g., lack documentation of vaccination or have no evidence of prior infection)

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

Source: US National Immunization Program, URL: http://www.cdc.gov/nip

Recommended Adult Immunization Schedule, by Vaccine and Medical and Other Indications

UNITED STATES • OCTOBER 2006–SEPTEMBER 2007



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Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

Contraindicated

Approved by
the Advisory Committee on Immunization Practices,
the American College of Obstetricians and Gynecologists,
the American Academy of Family Physicians,
and the American College of Physicians

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

CDC

Source: US National Immunization Program, URL: http://www.cdc.gov/nip

Tetanus Wound Management

Vaccination History	Clean, minor Wounds		All other wounds	
	Td	TIG	Td	TIG
Unknown or <3 doses	Yes	No	Yes	Yes
3+ doses	No*	No	No**	No***

* Yes, if >10 years since last dose

** Yes, if >5 years since last dose

*** Yes, if >10 years since last dose and serious damage [in Hungary]

Source: Heymann DL. Control of Communicable Diseases Manual, APHA 2004.; National Center for Epidemiology, Methodological guidence on vaccination, 2007.

Vaccination protocol in case of potential rabies exposure in Hungary

Animal causing exposure[2]		Action to be taken
Species	Health status	
Cat, dog	Healthy, observable for 14 days[3]	No vaccination
	No observation possible	Consultation with health authority, vaccination if rabies cannot be excluded[4]
	Suspicion of rabies[1,3]	Vaccination
Fox	Assumed to be rabid	Vaccination
Other	Consultation with health authority/ animal health authority	

1. Any animal showing atypical behavior in an endemic area should raise suspicion of rabies.
2. Exposures include contamination with saliva on skin or mucous membranes, abrasions, scratches, bites.
3. If the observed animal shows signs of rabies during the observation period, vaccination is to be initiated without delay. If rabies infection can be excluded in a previously suspicious animal, vaccination should be discontinued.
4. If the animal becomes observable, vaccination should provisionally be discontinued.

*Vaccination = 5 shots of inactivated Lyssa virus on days 0., 3., 7., 14., 28.

She survived rabies without vaccination.

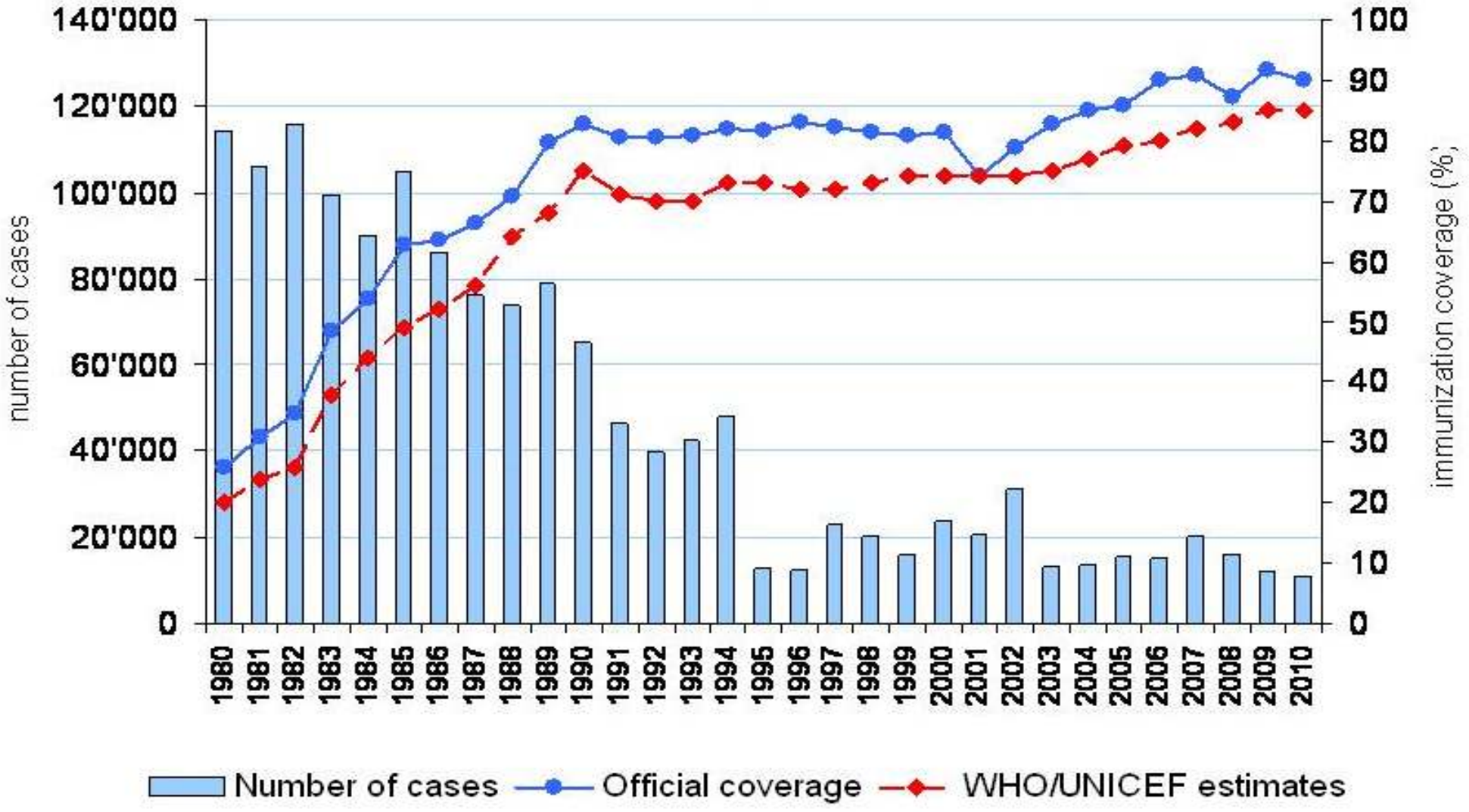
A medical marvel - Jeanna Giese

Rabies, a viral disease spread by the bite of an infected animal, attacks the nervous system and is usually fatal once symptoms develop. The other five people known to have survived it after symptoms appeared either were vaccinated in advance or received vaccine soon afterward. All but one ended up with persistent movement difficulties.

She was bitten by a bat she picked up in church.

SU Dept. of Public Health

Total tetanus global annual reported cases and DTP3 coverage, 1980-2010



WHO/IVB database, 2011

Vaccinations for occupational infections

- **Abdominal typhoid** – sewage workers, underground construction workers, laboratory staff, hospital infectious ward staff
- **Tick-borne encephalitis** – forestry workers
- **Hepatitis B** – health care workers, who regularly come into contact with blood and various body fluids
- **Hepatitis A** – health care workers (although hygienic precautions are usually sufficient to prevent infection)
- **Rabies** – laboratory staff who work with the Lyssa virus, veterinarians, flayers, pet shop staff, zoo staff
- **Diphtheria** – infectious ward staff, laboratory staff, medical students, booster immunization >10 years
- **Tetanus** – underground construction workers, agricultural workers, those involved in animal care, booster immunization >10 years
- **Meningococcus** - infectious ward staff, laboratory staff

An oral inactivated cholera vaccine. Large phase three trial initiated in 1985 showed that the vaccine provided **about 85% short term protection and about 60% protection over three years** (protection among children under five lasted only about one year, suggesting booster doses may be needed for these children).

Travel-related vaccinations

Compulsory

- **Yellow fever vaccine** when traveling to an endemic area
- **Meningococcal vaccination** during the Hajj (Saudi Arabia)
- **Any vaccine the country of destination requires**

May be recommended

- **Cholera**
- **Diphtheria** (former Soviet Union)
- **Hepatitis B, A**
- **Abdominal typhoid**
- **Tick-borne encephalitis**
- **Poliomyelitis**
- **Others**

The WHO annually publishes which vaccines are required in which countries. Up-to-date information can be obtained at the WHO's International Travel Health website at http://www.who.int/ith.

Summary

- **Vaccination is one of the most powerfool tool in the hand of medicine**
- **Administratration of vaccines are safe**
- **No lifestyle change is needed from patients**
- **Vaccination is cost-effective**

Recommended literature

- The CDC's **Pink Book** on Immunization (http://www.cdc.gov/nip/publications/pink/def_pink_full.htm)

- http://www.who.int
- http://www.cdc.gov
- http://www.immunisation.nhs.uk