

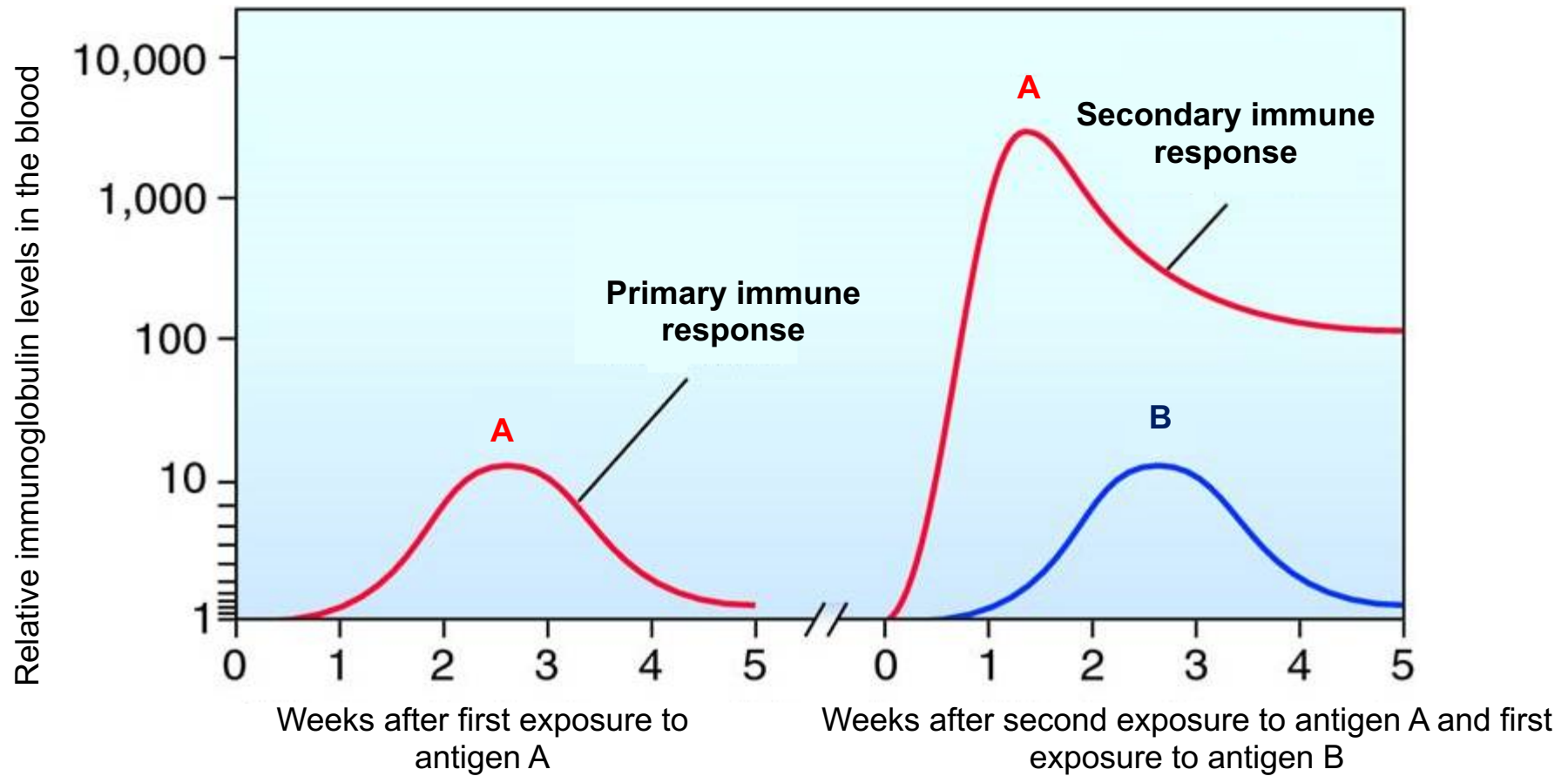
# Basic immunology

Lecture 14.

## Vaccines

Péter Engelman

# Primary and secondary immune response



# Vaccines

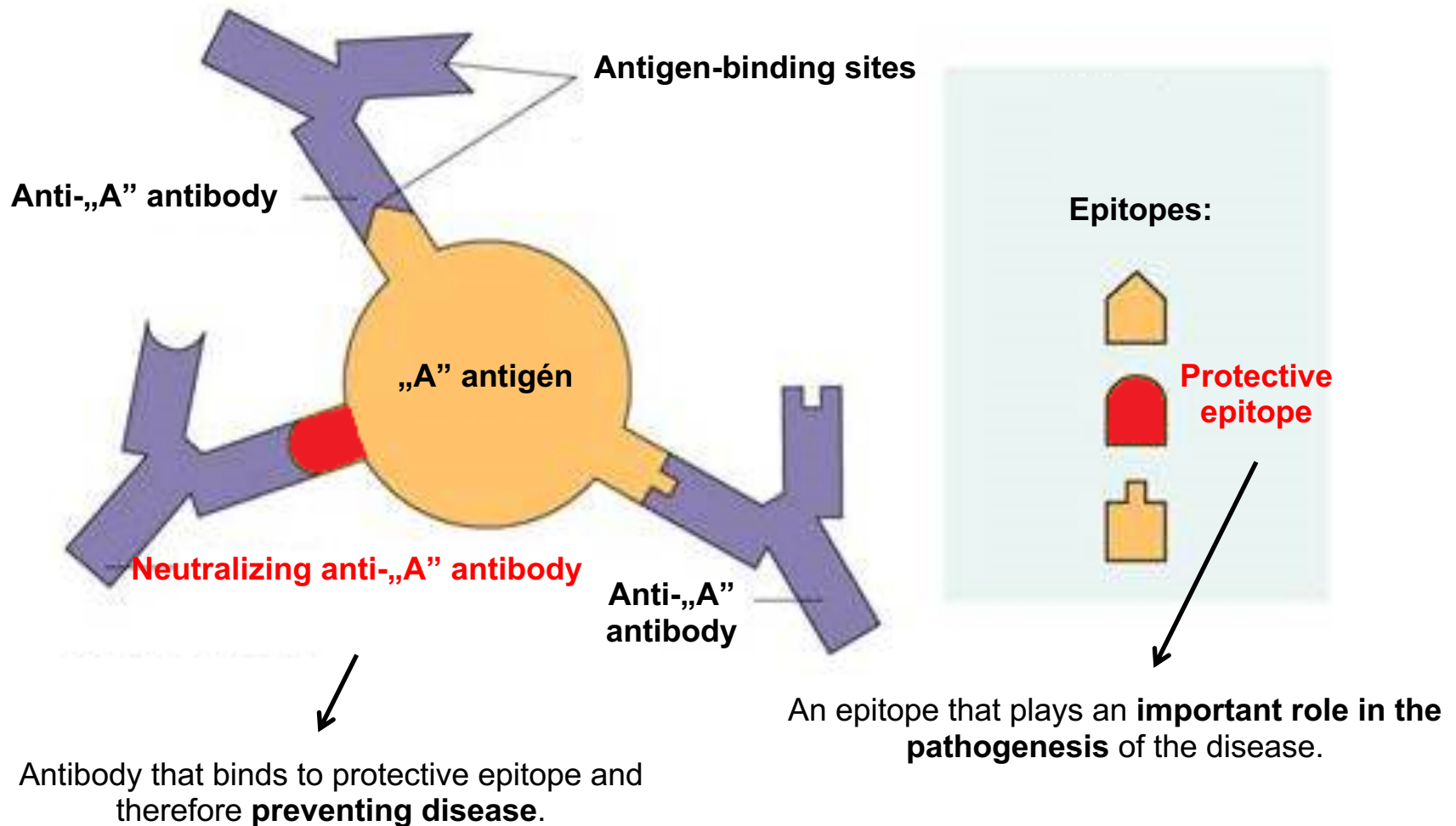
- Vacca, -ae (f): Cow
- Edward Jenner – 1796
- Variolation - Vaccination



Edward Jenner (1749-1823)



# Neutralizing antibodies



# Passive and active immunity

## Natural active



Acquiring an **infection**



**Immunological memory**

## Natural passive



**Breastfeeding:**  
maternal antibodies  
**temporarily** protect  
the baby

## Artificial active



**Vaccine** (active immunization with  
an antigen)



**Immunological memory**

## Artificial passive

**Antiserums** (passive immunization  
with antibodies)

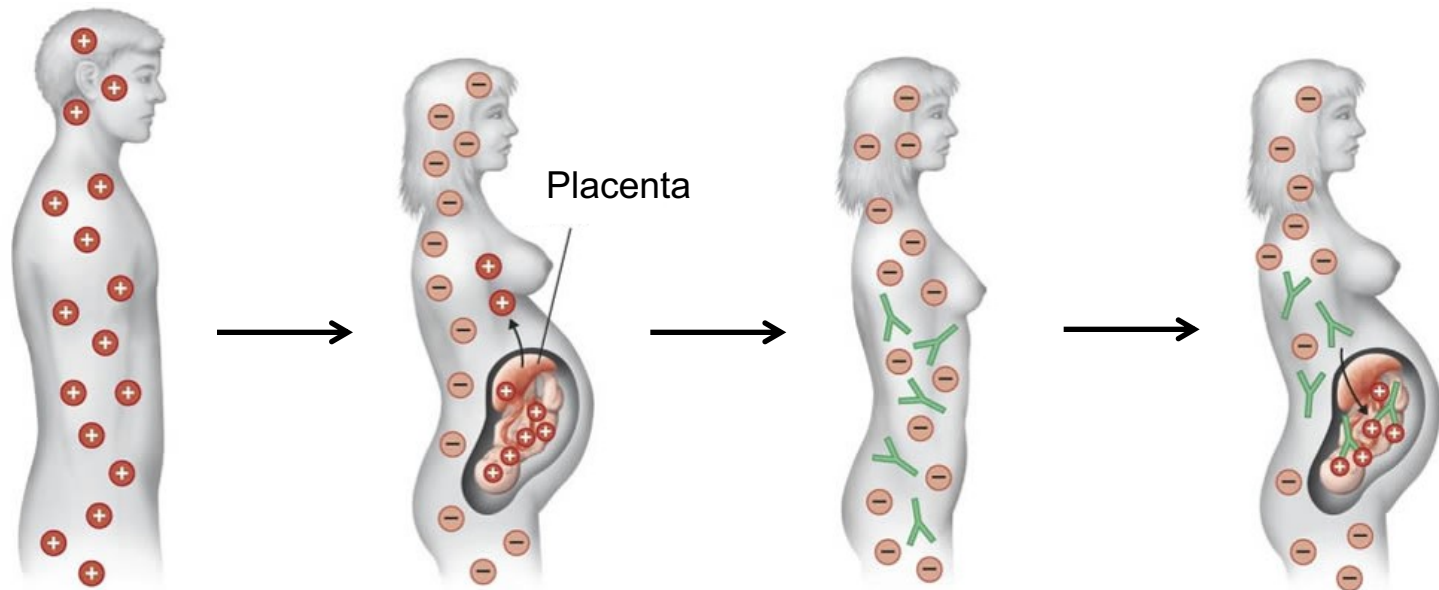


**Quick but only temporary  
protection**

# Passive Immunisation

- Anti-Rh(D) Antibody
- Tetanus Antitoxin
- Anti-HBsAg

# Rh alloimmunization



Rh+ father

First Rh+ pregnancy of  
Rh- mother

Immunization of mother

Second Rh-  
pregnancy

The blood of the mother and the fetus **do not mix** during pregnancy!

**During delivery** some of **newborn's blood** will inevitably **enter the mother**.

**Anti-Rh antibody**

**Anti-Rh IgG crosses the placenta**  
and causes hemolysis!

# Prevention of Rh alloimmunization



Human anti-Rh(D)  
immunoglobulin

The Rh- mother is treated with **anti-Rh(D) antibodies** (RhIG) after delivery.



The antibody is thought to **eliminate all the Rh+ erythrocytes** that have entered the mother.



**It prevents the recognition of Rh+ erythrocytes by the mother's immune system.**



If the Rh- mother has another Rh+ fetus, there won't be any anti-Rh antibodies that cross the placenta and do harm to the baby.



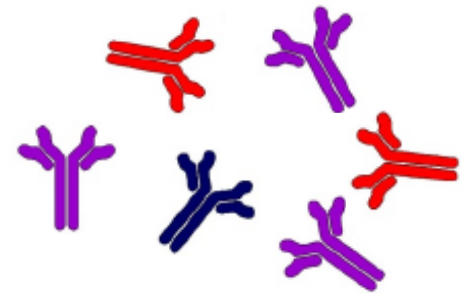
# Antivenoms



Milking the snake, gathering toxin A



Administering toxin A to a rabbit (**active immunization of the rabbit**)



**Neutralization** of toxin A ←



Administering anti-A antibodies after snakebite (**passive immunization of the human**)

Polyclonal rabbit anti-A antibodies

# Active immunization

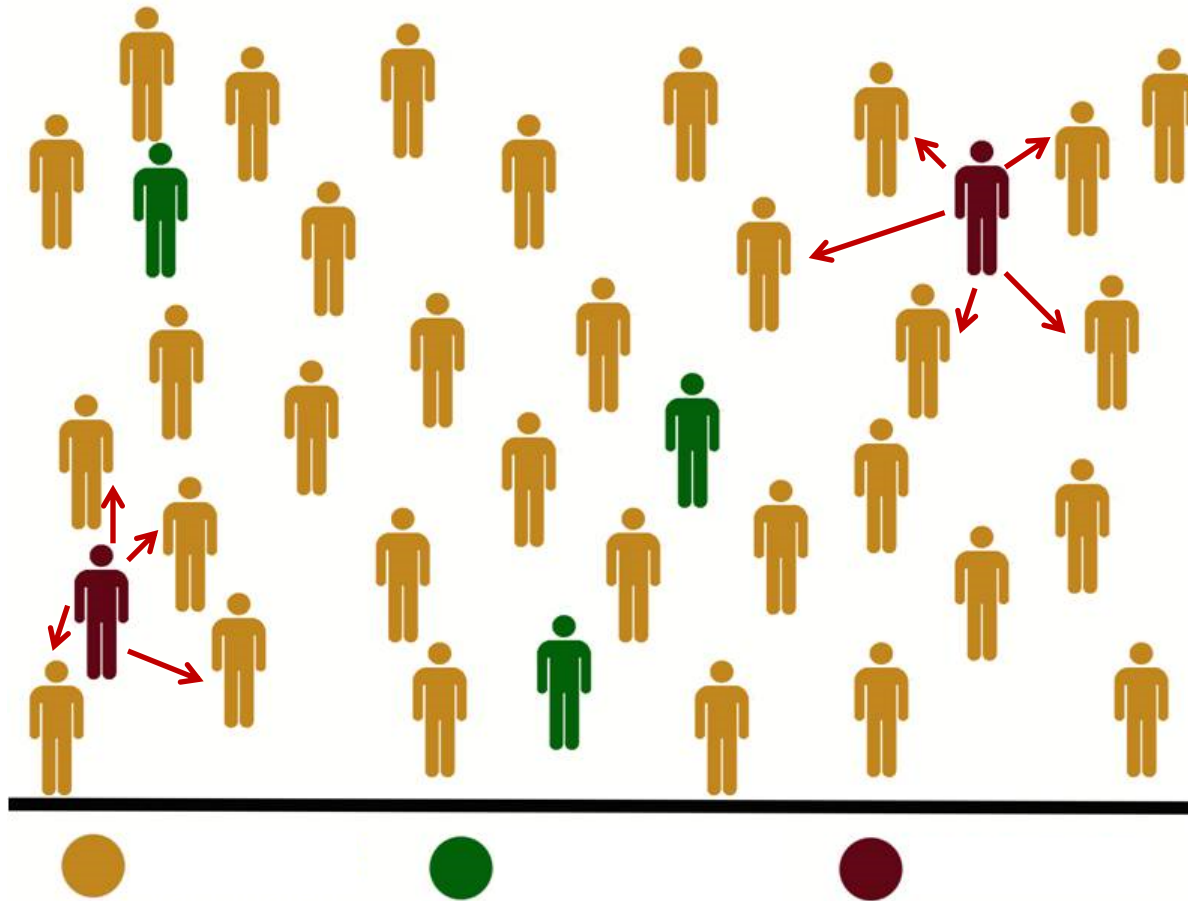
- **Administration of an antigen** in order to **provoke an immune response** against the antigen.
- In case of research animals:
  - **Production of antibodies** (e.g. hybridoma technique, antivenoms)
  - **Triggering autoimmunity** (e.g. human cartilage proteoglycan-induced arthritis in mice) for the **modelling** of human autoimmune disorders
- In case of people:
  - To develop a **long-lasting immunological memory** against a pathogen or a toxin
- **Adjuvants** → Immune response ↑<sup>[9.]</sup> (see 3rd practice)
- **Herd immunity**: Non-immunized are also protected.<sup>[10.]</sup>
- First vaccine: **Edward Jenner** vaccinated people with cowpox to prevent smallpox. vacca = cow in Latin

↓  
Vaccination



Edward Jenner (1749-1823)

# Herd immunity I.

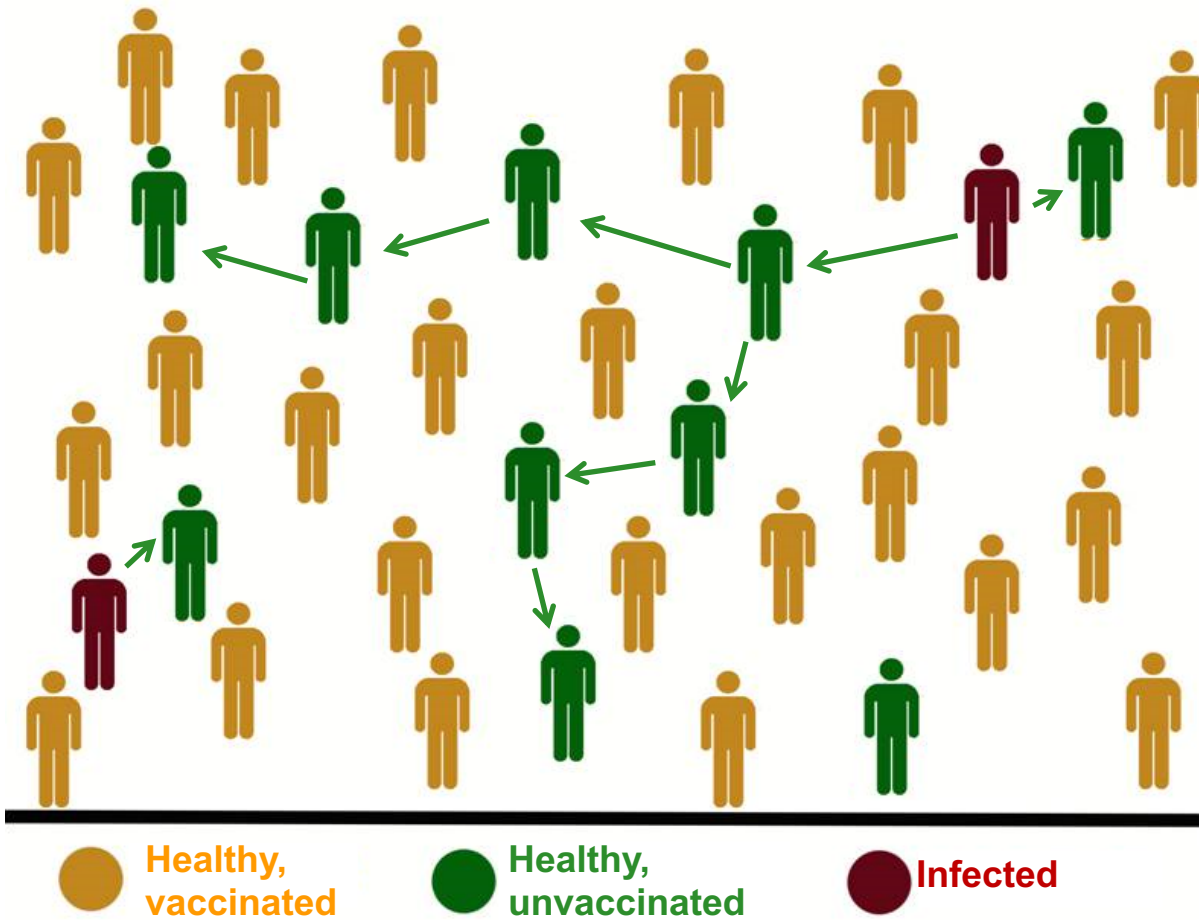


A large percentage of the population is vaccinated.



The **infection cannot spread** in the population and even the unvaccinated people are protected.

# Herd immunity II.



A relatively large percentage of the population is unvaccinated.

**The infection can spread in the population.**

# The MMR scandal

- February of 1998: Andrew Wakefield and his colleagues publish an article in the Lancet (one of the leading journals in medicine) about the possibility of **MMR to cause autism**.<sup>[22.]</sup>
- MMR vaccination at that time was **compulsory in many countries** (including Hungary).



## SCANDAL

- Between 2002 and 2003 more and more studies denied Wakefield's claim as they did not find a correlation between autism and the MMR vaccine<sup>[23.]</sup>, many regulators and organizations (including the American CDC) declared that **there was no correlation**.
- 2004: A reporter at the Sunday Times identified undisclosed **financial conflict of interest** on Wakefield's part and it was found out that Wakefield also **falsified data** in his research.<sup>[24,25,26.]</sup>
- Ten of the twelve co-authors retracted the article in 2004, and the **article was fully retracted** by Lancet in 2010.<sup>[27.]</sup>
- Wakefield was **struck off the UK medical register** by the GMC in 2010.<sup>[28.]</sup>



Dr. Andrew Wakefield in front of the GMC headquarters shortly after losing his medical registration in 2010.

„Possibly the most damaging medical hoax of the last 100 years<sup>[29.]</sup>”



**EFFECT: A GENERAL DISTRUST IN WESTERN MEDICINE, RISE OF ANTI-VACCINATION MOVEMENTS**



# Active vaccines

## 1. live, attenuated vaccines

Contain living pathogens with a limited potential to replicate in the host

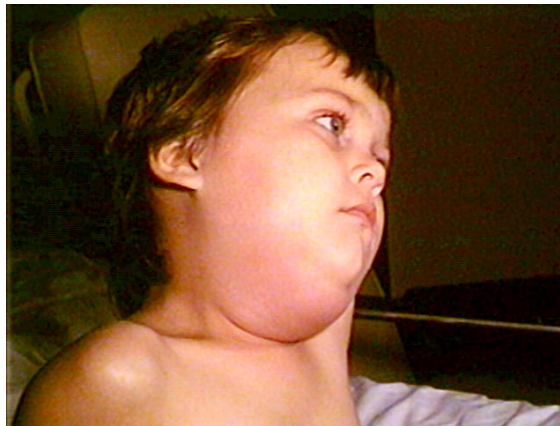
Advantages: mimics the course of natural infections the best, it triggers both the humoral and cellular immune response and leads to long-lasting protection

Disadvantages: The pathogen might regain its virulence after vaccination.

Examples: MMR, BCG, oral poliovaccine



*Measles*



*Mumps*



*Rubella*

# BCG



Scar at the site of BCG vaccination.

- Contains attenuated *Mycobacterium bovis* bacteria.
    - Used for the **prevention of severe tuberculosis** and the **complications of TB**.
    - Also used to treat **bladder cancer** (injected into the lumen of the bladder).<sup>[32.]</sup>
  - Administered intradermally, **leaves a scar**.
  - **Efficacy is variable** and somewhat controversial.<sup>[33,34,35.]</sup>
- 
- Not compulsory in many countries. (had been in the UK till 2005, but the USA never introduced it) In Hungary it is compulsory.
  - **WHO recommendation:** Every infant should be vaccinated in **places where TB is endemic** to prevent **miliary tuberculosis** and **TB meningitis**.<sup>[36.]</sup>
  - Provides some protection against **Leprosy** as well.<sup>[37.]</sup>



# Active vaccines

## 2. Inactivated vaccines

contain dead Pathogens

Advantage: safe

Disadvantage: trigger a weaker immune response

Examples: inactive polio vaccine, seasonal flu vaccines



# Active immunization

## 3. Subunit-vaccines

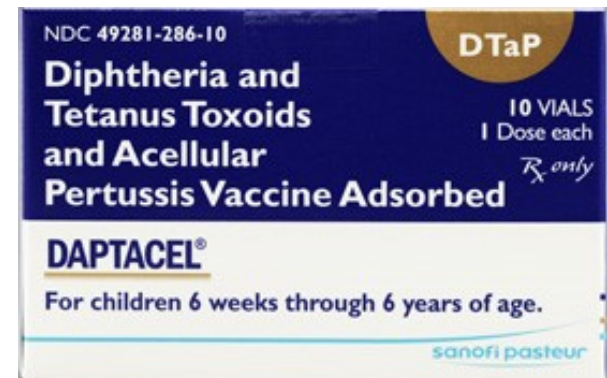
Contain specific antigens of the pathogen

Examples: HBV, HPV

## 4. Toxoid vaccines

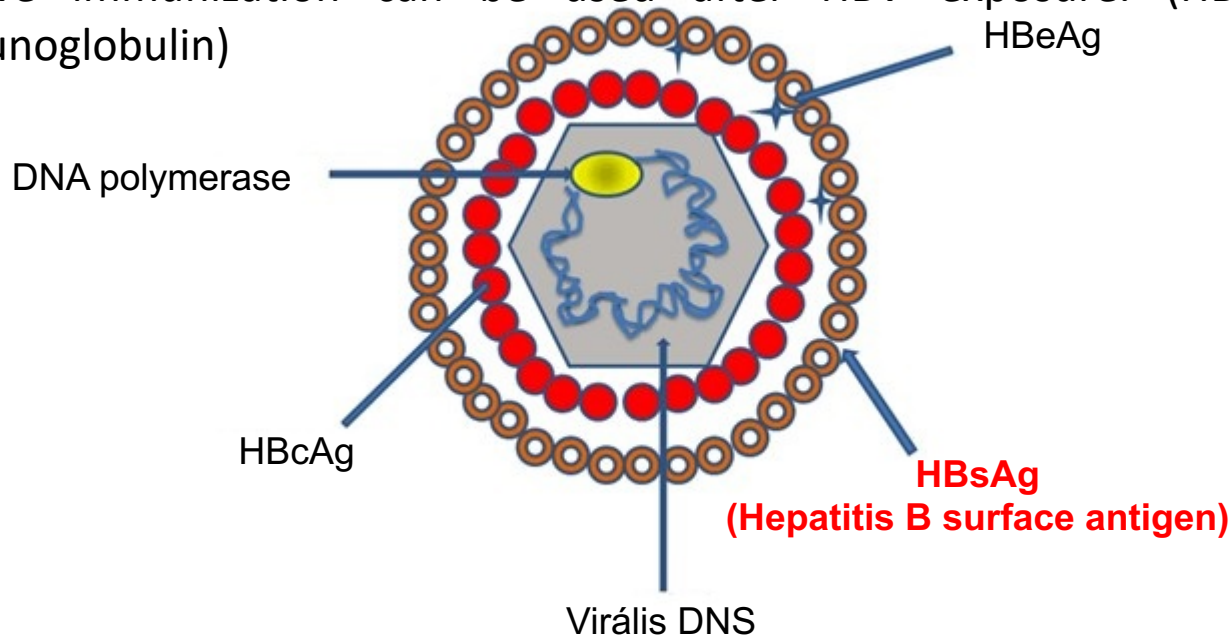
Contain inactivated toxins

Examples: Diphtherie, Tetanus



# HBV vaccine

- Contains the **surface antigen** (HBsAg) of hepatitis B virus (HBV).
- **Recombinant subunit vaccine**, the viral antigen is produced in yeast.<sup>[39.]</sup>
- Needs to be administered multiple times, the produced **anti-HBsAg antibodies** provide protection against the infection. → Long-term protection is variable but the **antibody levels can be measured**.
- It is compulsory in Hungary.
- **Can be combined with other vaccines**<sup>[42,43.]</sup>, e.g. DTaP+IPV+Hib+Hep B.
- Passive immunization can be used after HBV exposure. (HBIG= hepatitis B immunoglobulin)



# HPV vaccine

- **Recombinant subunit vaccine**, contains the antigens of some selected strains of HPV. Not compulsory in Hungary.<sup>[44.]</sup>
- Three vaccines have been approved<sup>[45.]</sup>:
  - Cervarix®: against **HPV-16** and **18** (bivalent)
  - Gardasil®: against **HPV-16, 18** and **6, 11** (quadrivalent)
  - Gardasil 9®: against 9 different strains of HPV (for both men and women)
- HPV-16 and 18: Cause **70% of cervical cancer**, 80% of anal cancer and 60% of vaginal cancer.<sup>[46.]</sup>
- HPV-6 and 11: Cause 90% of **genital warts**.
- WHO: Young, 9-13 year old girls should be vaccinated **before sexual activity**.<sup>[45.]</sup>



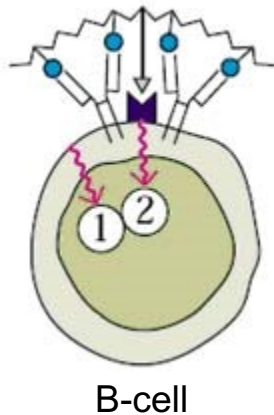
# Active immunization

## 5. Conjugated vaccines

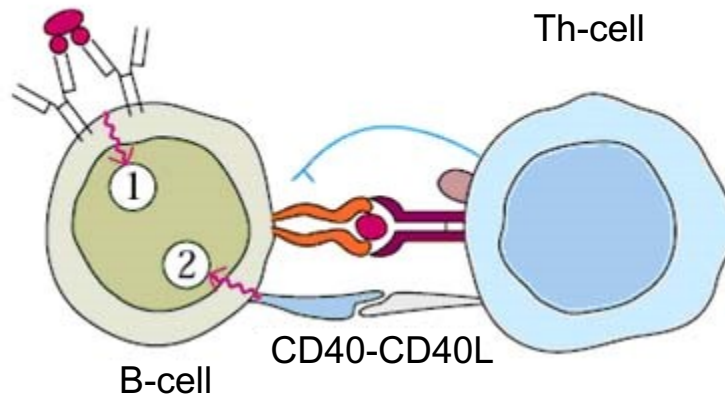
Contain pathogens with polysaccharid capsules (=T-independent antigens, do not induce immunological memory). Solution: conjugation of polysaccharides to protein carriers.

Examples: *Haemophilus influenzae* B, *Neisseria meningitidis*

**T-independent Ag**



**T-dependent Ag**



# Some notable cases in the past



December of 2014.: Measles outbreak in the American Disneyland with 189 patient, most of them did not receive vaccination against Measles.<sup>[54.]</sup>

## First Case of Diphtheria in Spain Since 1986 After Parents Shun Vaccination

**TIME**

June of 2015.: A 6 year old boy died of Diphtheria in Spain where this disease haven't been encountered since 1986. The parents did not allow the child to receive vaccination as an infant.<sup>[55.]</sup>

## Children paralysed in Ukraine polio outbreak

**BBC**

By James Gallagher  
Health editor, BBC News website

🕒 2 September 2015 | Health

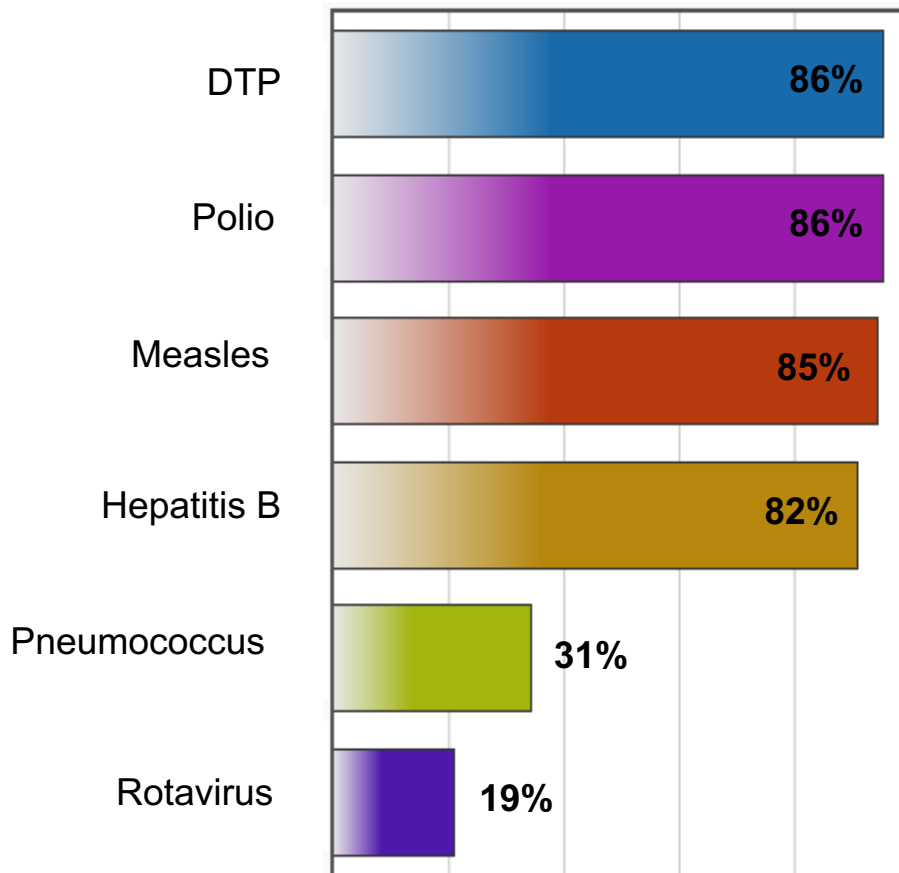
Poliovirus showed up in Europe again after 5 years.<sup>[56.]</sup>

# Achievements of the WHO



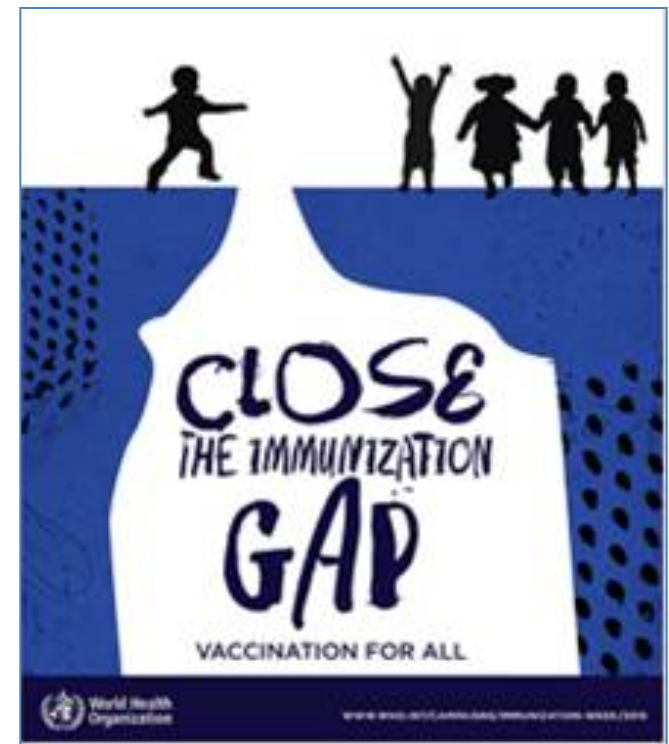
World Health  
Organization

Global immunization coverage in 2014<sup>[57.]</sup>:



**Goals of the Global Vaccine Action Plan:**

- >90% coverage
- **ERADICATION OF POLIO**



# Thank you for your attention!



Emil Adolf von Behring

Was awarded the 1901 Nobel Prize in Physiology and Medicine: For his work on serum therapy, especially its application against diphtheria.<sup>[58.]</sup>



Max Theiler

Was awarded the 1951 Nobel Prize in Physiology and Medicine: For his discoveries concerning yellow fever and how to combat it.<sup>[59.]</sup>