

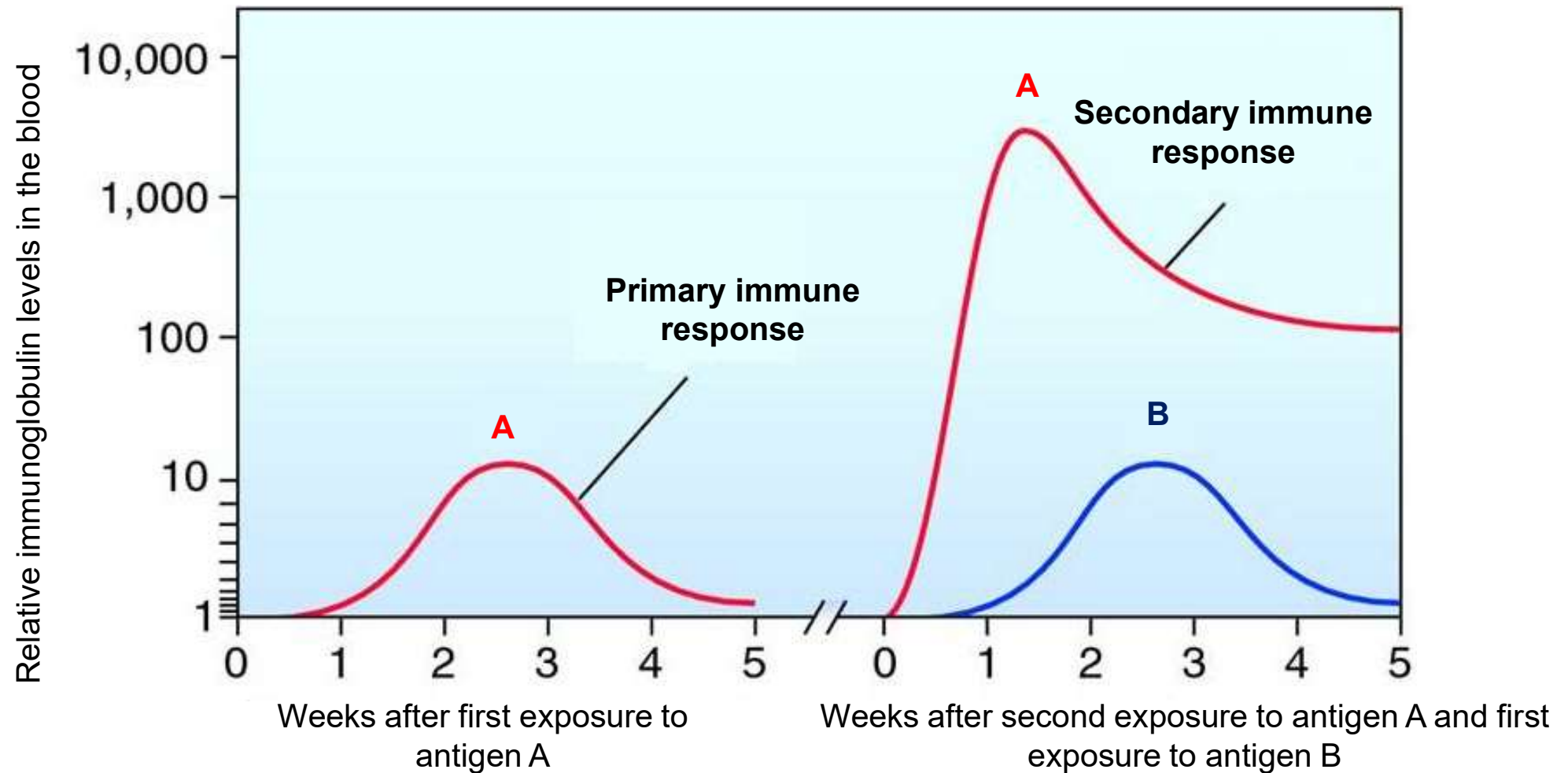
Basic immunology

Lecture 14.

Vaccines

Péter Engelmann

Primary and secondary immune response



Vaccines

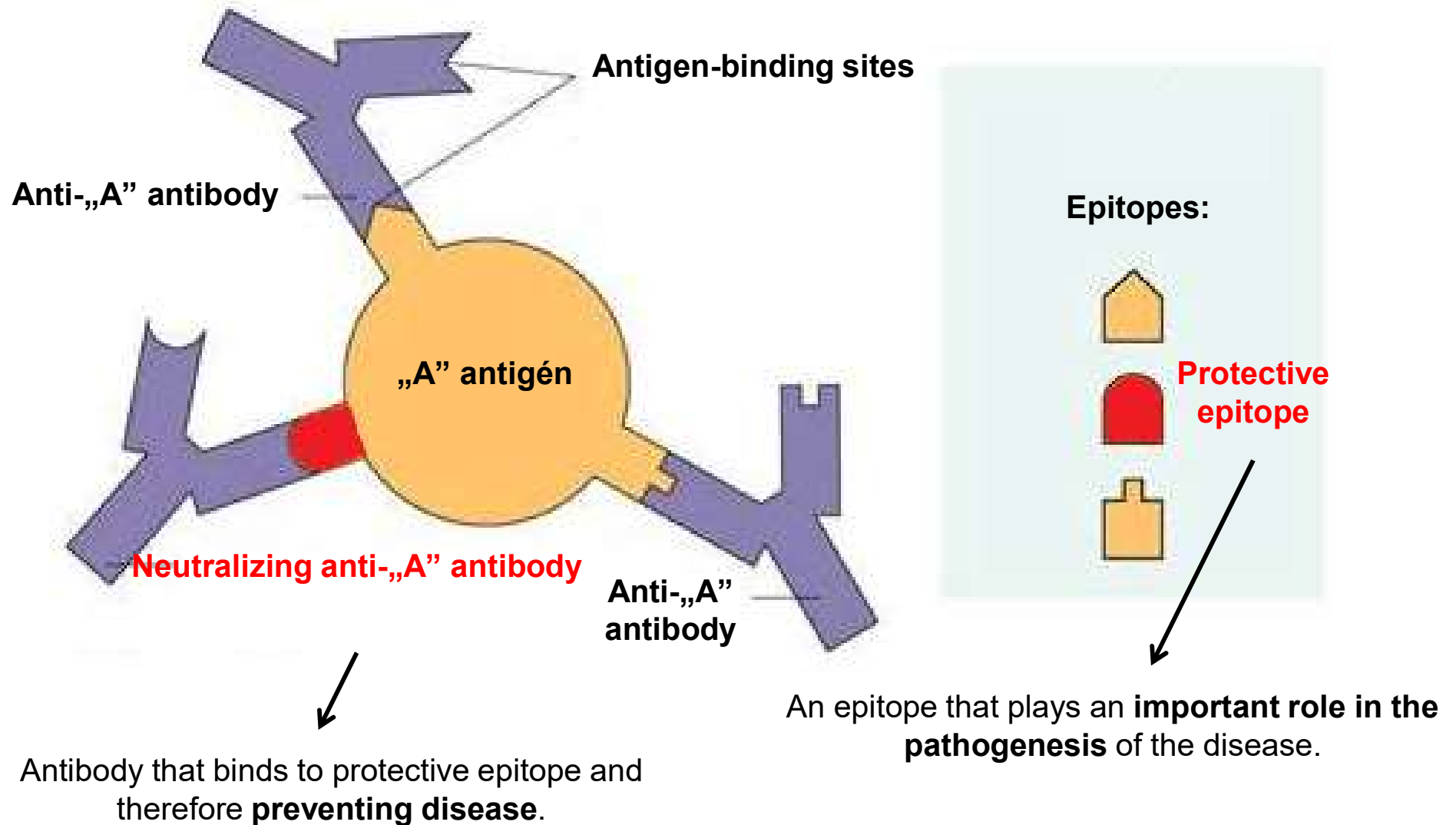
- Vacca, -ae (f): Cow
- Edward Jenner – 1796
- Variolation - Vaccination



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)

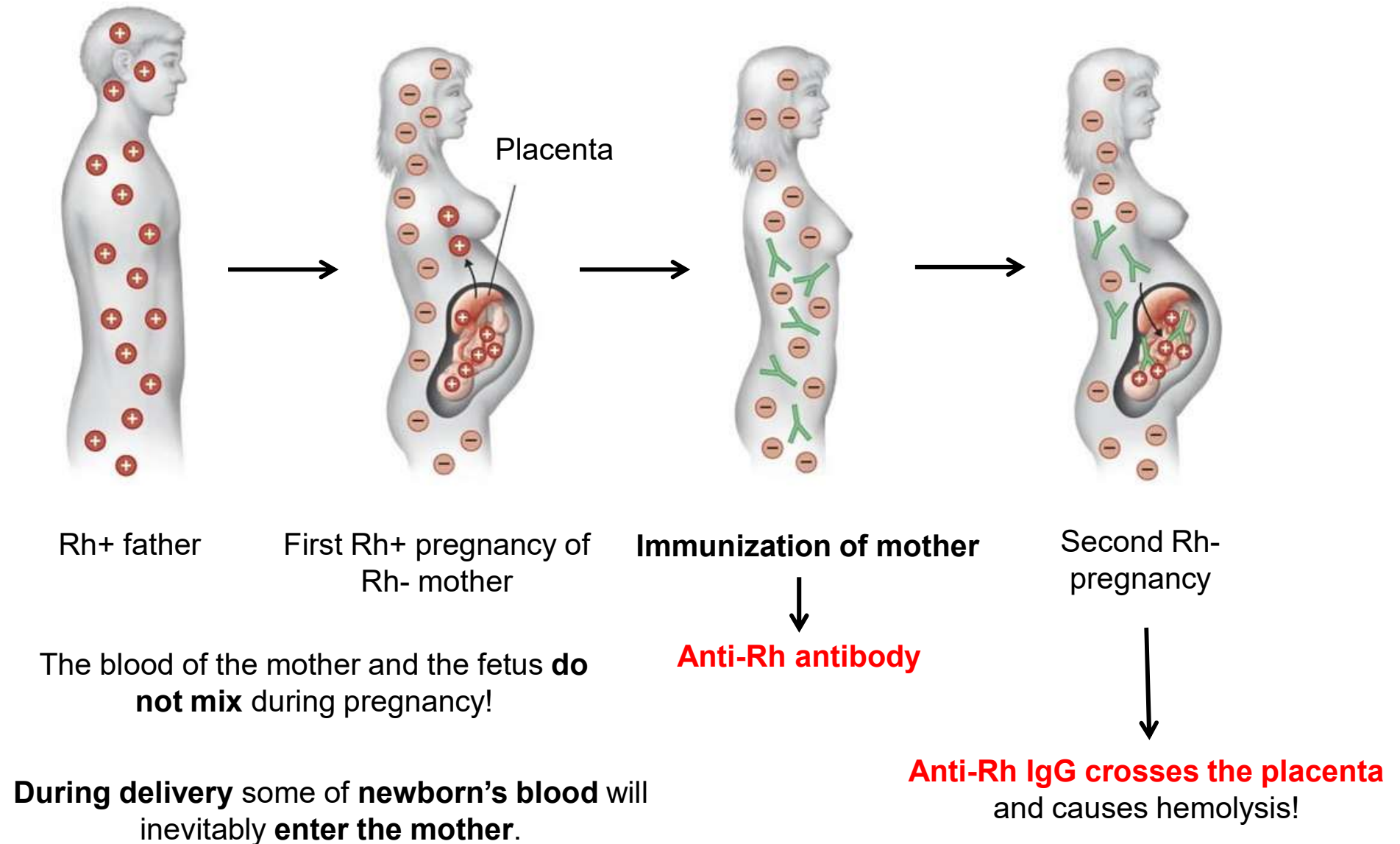


**Quick but only temporary
protection**

Passive Immunisation

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

Rh alloimmunization



Prevention of Rh alloimmunization

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



Human anti-Rh(D)
immunoglobulin

↓

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.

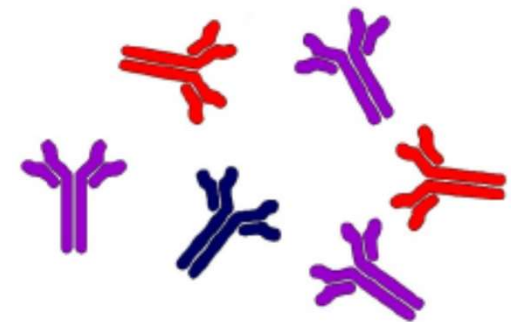
Antivenoms



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

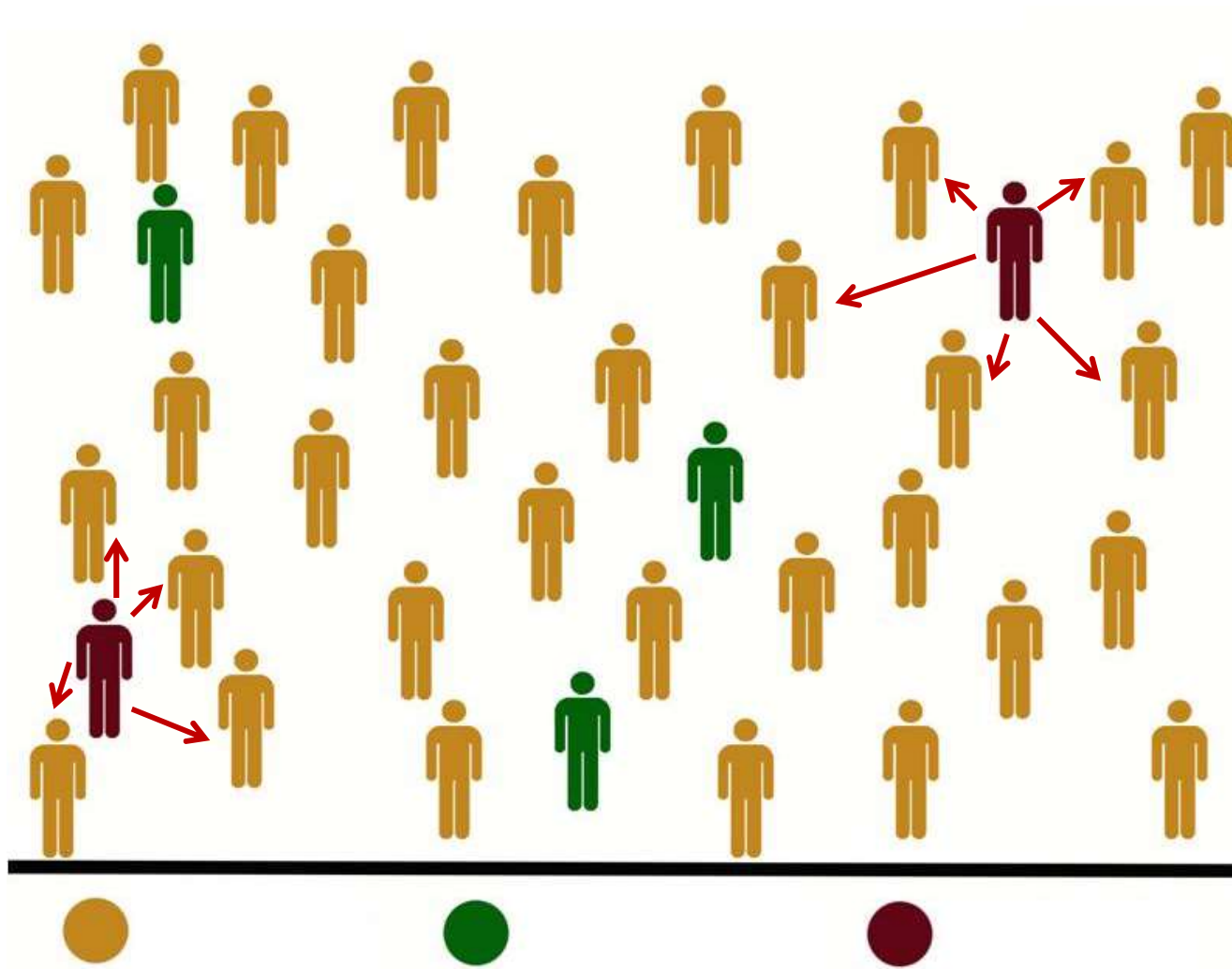
- **Administration of an antigen** in order to **provoke an immune response** against the antigen.
- In case of research animals:
 - **Production of antibodies** (e.g. hybridoma technique, antivenoms)
 - **Triggering autoimmunity** (e.g. human cartilage proteoglycan-induced arthritis in mice) for the **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 ↑^[9.] (see 3rd practice)
- **Herd immunity**: Non-immunized are also protected.^[10.]
- First vaccine: **Edward Jenner** vaccinated people with cowpox to prevent smallpox. vacca = cow in Latin

↓
Vaccination



Edward Jenner (1749-1823)

Herd immunity I.

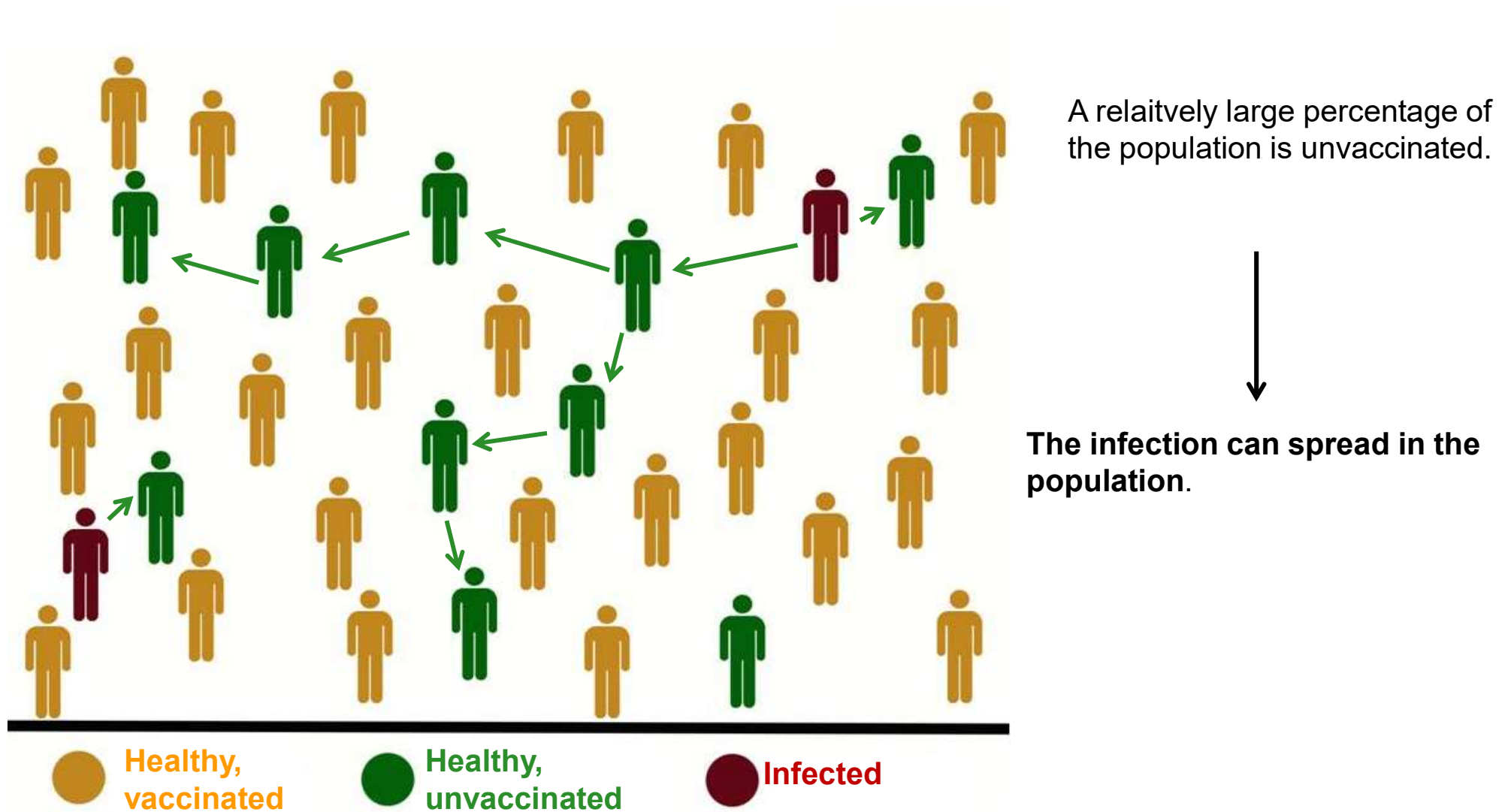


A large percentage of the population is vaccinated.



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

Herd immunity II.



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**.^[22.]
- 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^[23.], 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.^[24,25,26.]
- Ten of the twelve co-authors retracted the article in 2004, and the **article was fully retracted** by Lancet in 2010.^[27.]
- Wakefield was **struck off the UK medical register** by the GMC in 2010.^[28.]



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^[29.]”



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).^[32.]
- Administered intradermally, **leaves a scar**.
- **Efficacy is variable** and somewhat controversial.^[33,34,35.]
- 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**.^[36.]
- Provides some protection against **Leprosy** as well.^[37.]

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

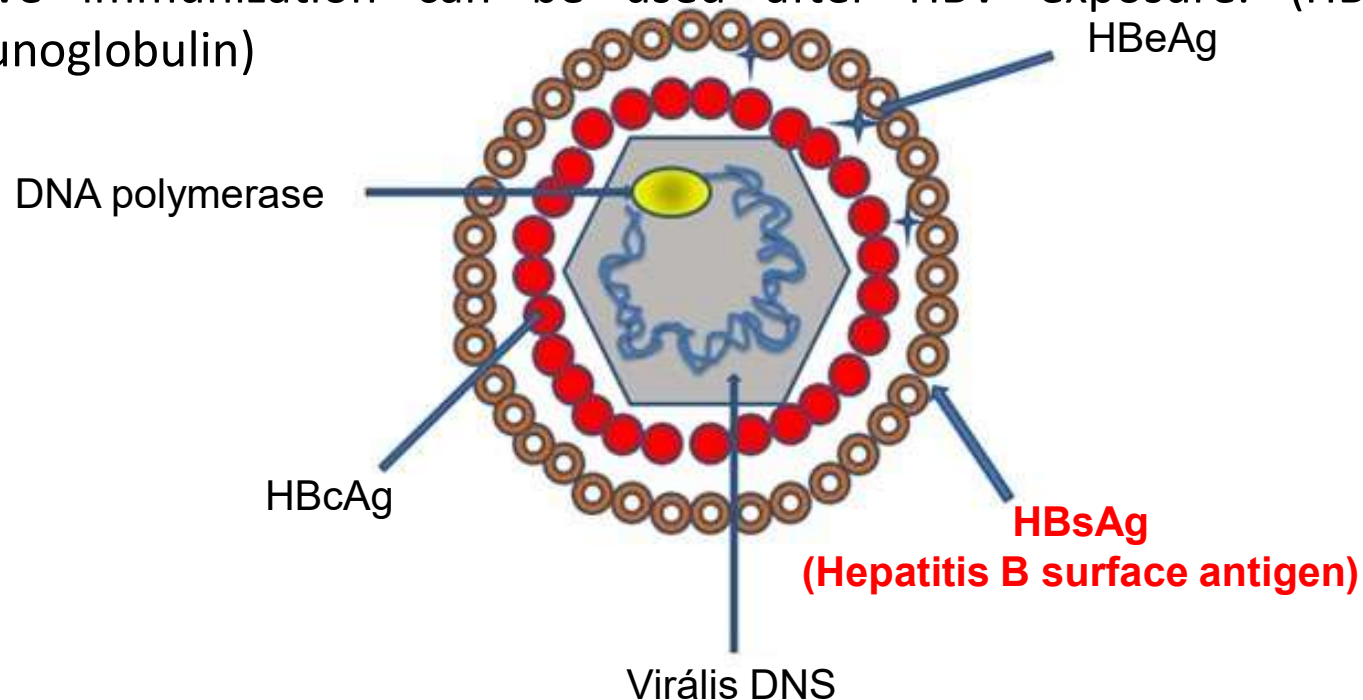
Contain inactivated toxins

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.^[39.]
- 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**^[42,43.], 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.^[44.]
- Three vaccines have been approved^[45.]:
 - 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.^[46.]
- HPV-6 and 11: Cause 90% of **genital warts**.
- WHO: Young, 9-13 year old girls should be vaccinated **before sexual activity**.^[45.]



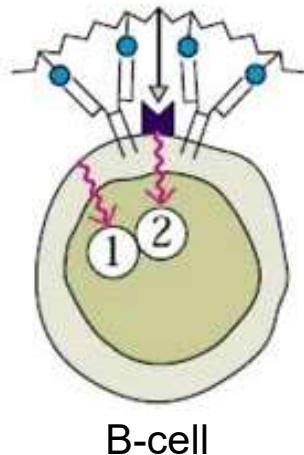
Active immunization

5. Conjugated vaccines

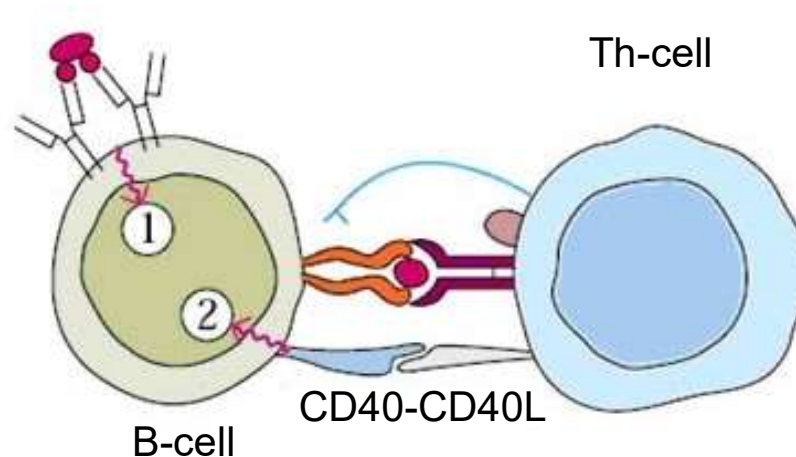
Contain pathogens with polysaccharid capsules (=T-independent antigens, do not induce immunological memory). Solution: conjugation of polysaccharides to protein carriers.

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

T-independent Ag

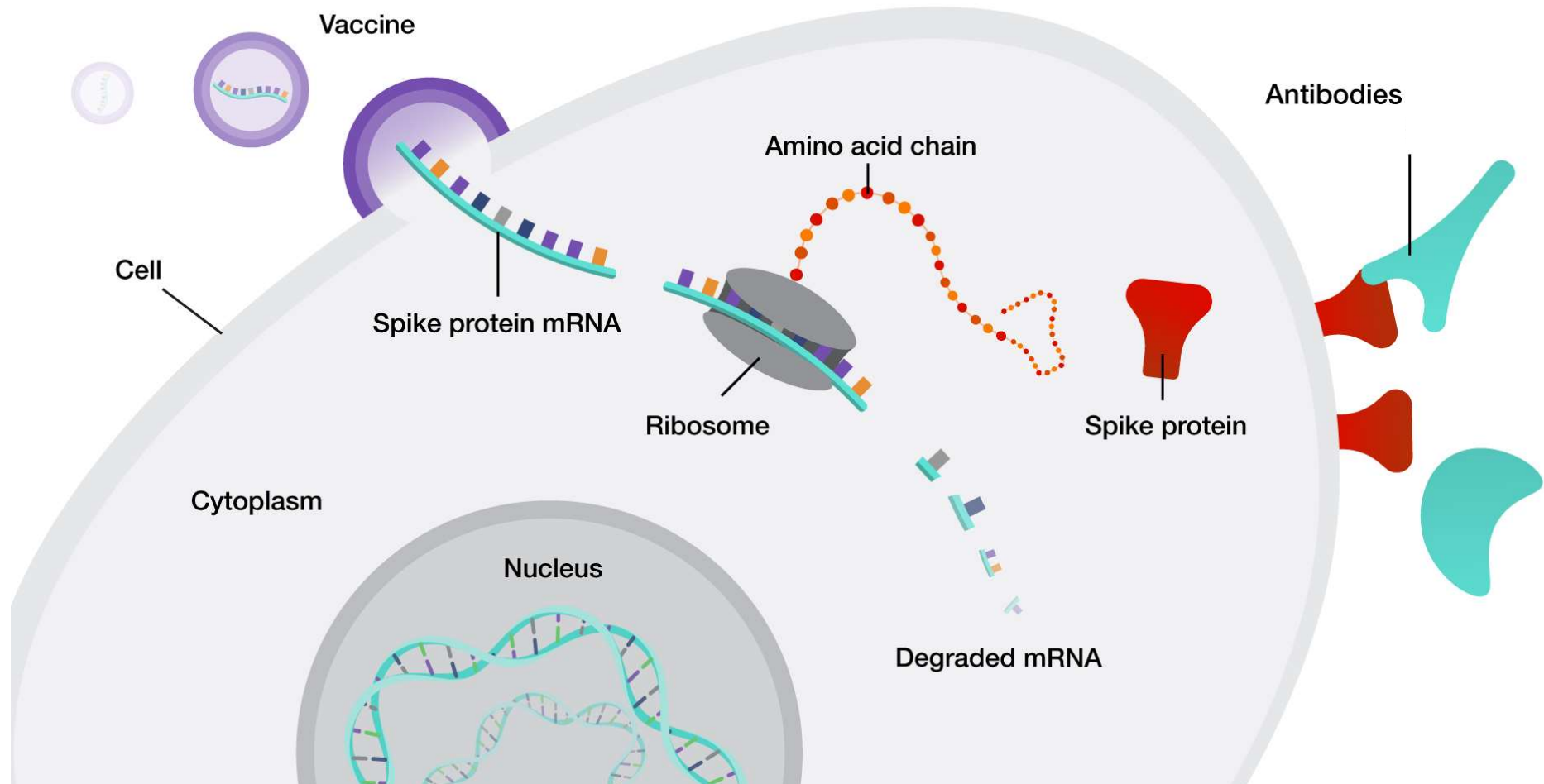


T-dependent Ag



Active immunization

5. Nucleic acid vaccines



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.^[54.]

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.^[55.]

Children paralysed in Ukraine polio outbreak

BBC

By James Gallagher
Health editor, BBC News website

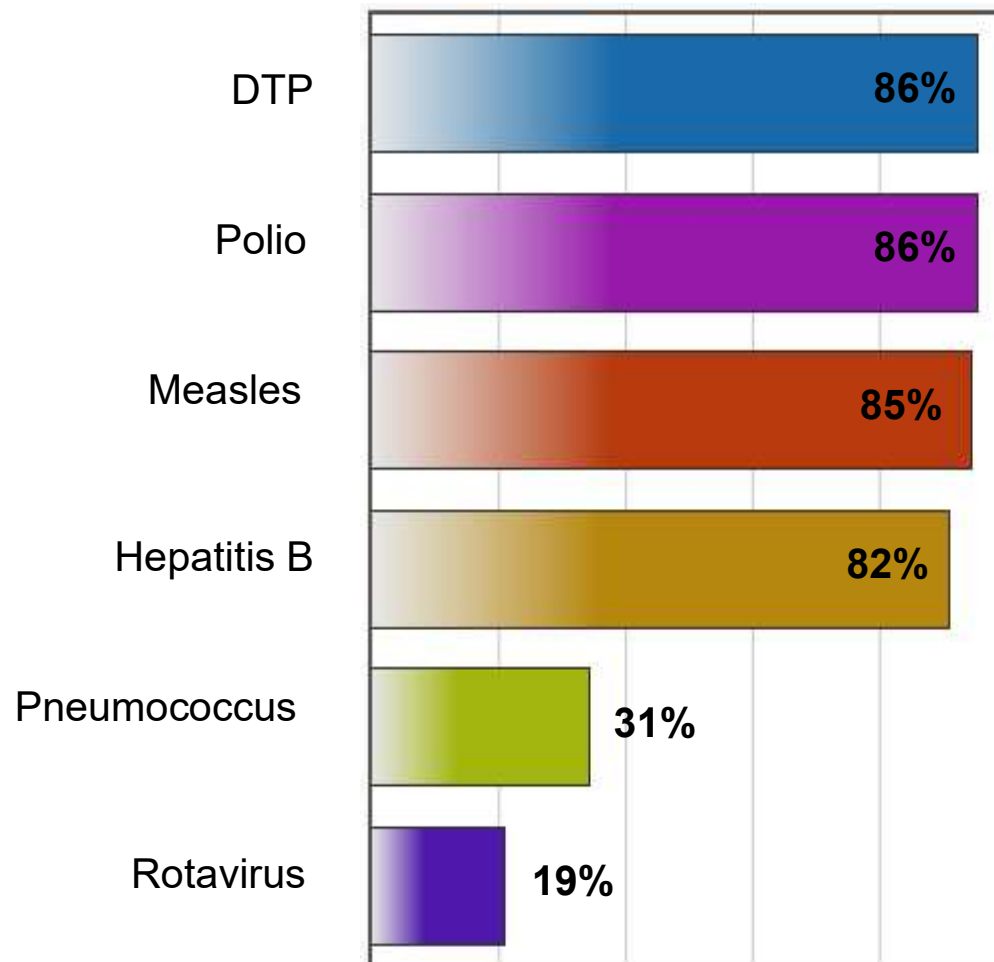
🕒 2 September 2015 | Health

Poliovirus showed up in Europe again after 5 years.^[56.]

Achievements of the WHO

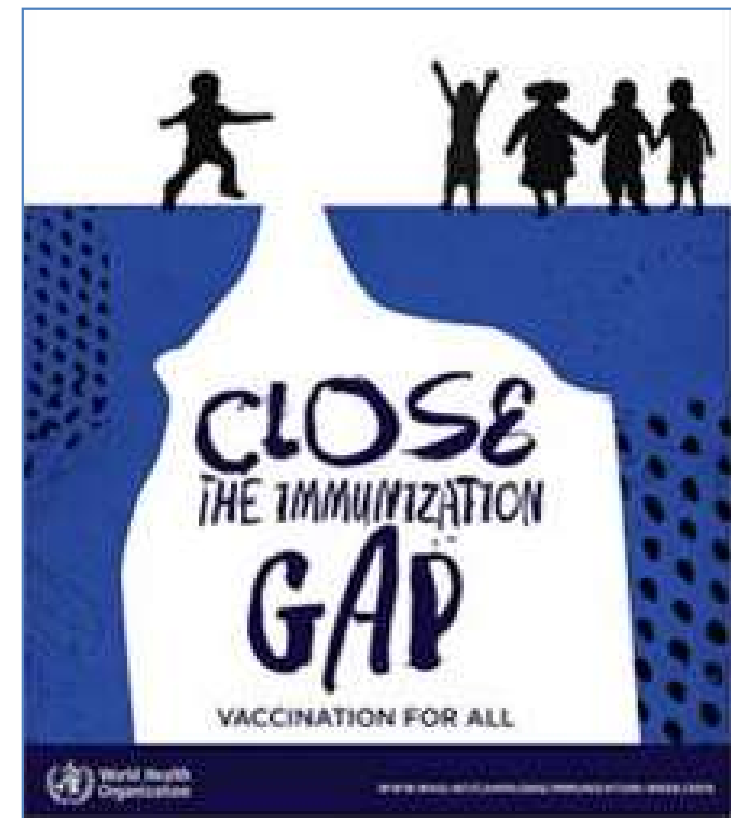


Global immunization coverage in 2014^[57.]:



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.^[58.]



Max Theiler

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