Active and passive immunization

Active and passive arteficial immunisation

	Active immunisation	**Passive immunisation**
Speed of response	**Delayed**	**Prompt**
Length of response	**Long-term**	**Short-term**
Clinical use	**Long-term prophylaxis**	**Treatment, short-term prophylaxis**

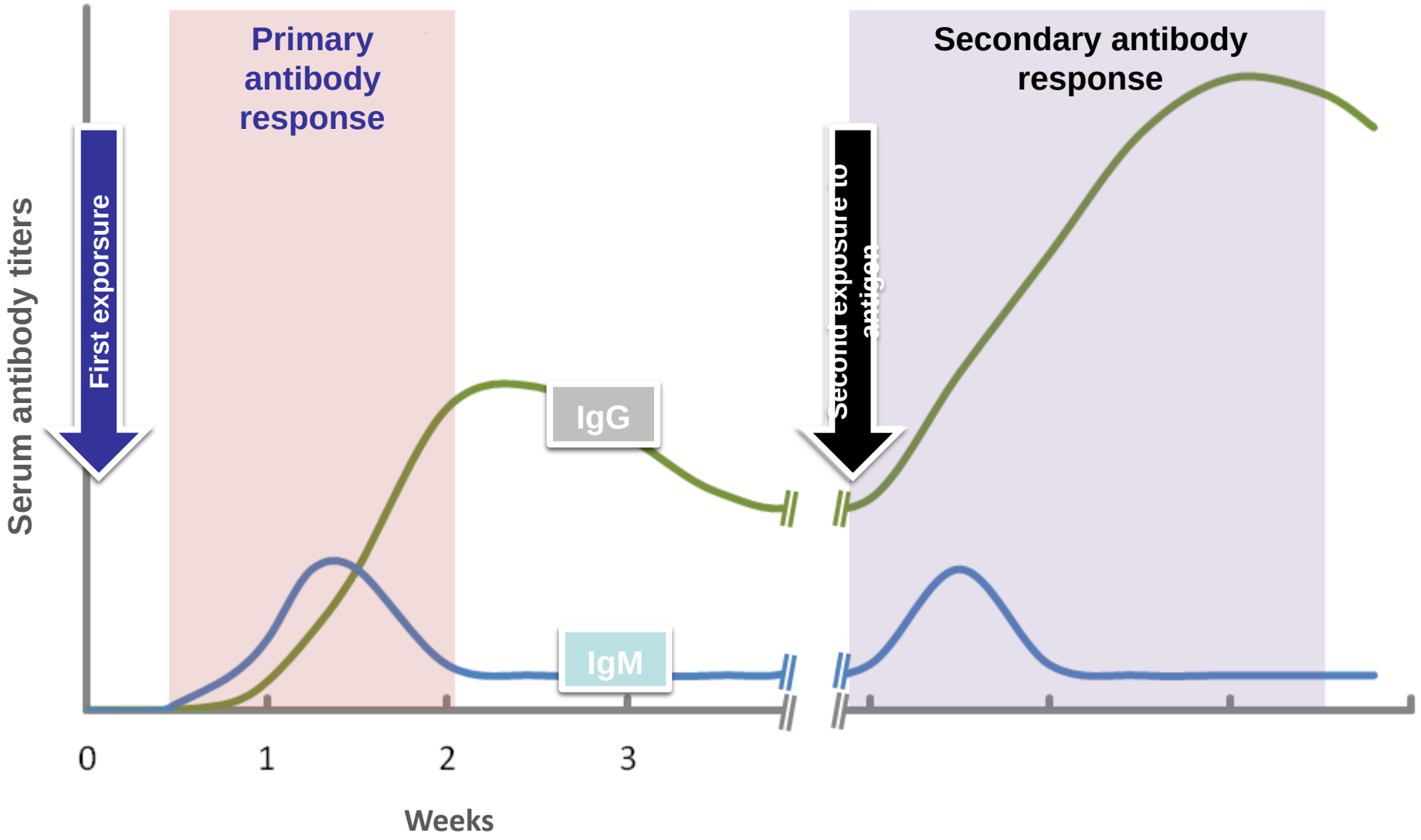
Active immunization (vaccination)

- Induction of immune memory by a harmless antigen.
- In the case of infection by a pathogen prompt secondary immune response protects the immunized person from the disease.
- Has protective, but no therapeutic effect.

Edward Jenner

Discovery of small pox vaccine

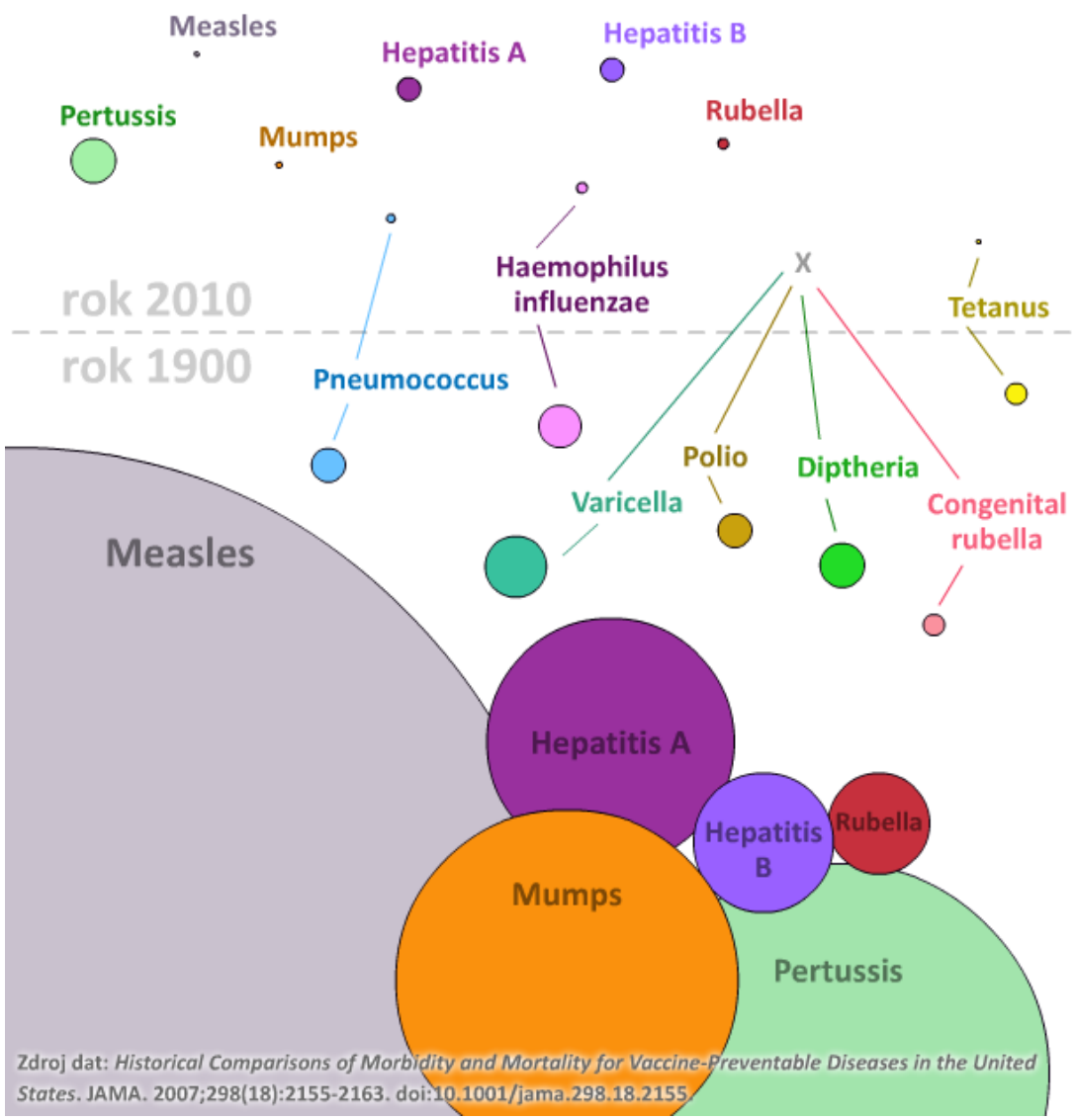
Antibody response after primary and secondary antigen exposure



Adjuvants

- Substances, that, when mixed with antigen, non-specifically enhance immune reaction against the antigen.
- Alum precipitate - $AL(OH)_3$ - used in human medicine.
- Mechanisms: improved prezentation of the antigen, fixation of the antigen in the place of application.
- Various adjuvants are used in modern vaccines, but the are patent-protected and very little is known about them.

The effect of vaccionation in USA



1900:	29 005	100%	Varicella
2010:	0		
1900:	21 053	100%	Diphtheria
2010:	0		
1900:	16 316	100%	Polio (paralytic)
2010:	0		
1900:	152	100%	Congenital rubella
2010:	0		
1900:	580	99%	Tetanus
2010:	8		
1900:	530 217	99%	Measles
2010:	61		
1900:	47 745	99%	Rubella
2010:	6		
1900:	20 000	99%	Haemophilus influenzae
2010:	270		
1900:	162 344	98%	Mumps
2010:	2 528		
1900:	117 333	91%	Hepatitis A
2010:	11 049		
1900:	200 752	89%	Pertussis
2010:	21 291		
1900:	66 232	83%	Hepatitis B (acute)
2010:	11 269		
1900:	16 069	74%	Pneumococcus
2010:	4 167		<5 years of age

(From World Health Organization.)

Consequence of polio

(From the Centers for Disease Control and Prevention, Atlanta, GA.)

Tetanus neonatorum

Iron lungs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THE J.H. EMERSON CO.
IRON LUNG
Rare Historical Photos.com

Ten Great Public Health Achievements in the 20th Century (CDC)

- **Vaccination to reduce epidemic diseases**
- **Improved motor vehicle safety**.
- **Safer workplaces**
- **Control of infectious diseases**
- **Decline in death from cardiovascular disease**
- **Food Safety**
- **Improvements in maternal and child health**
- **Family planning**
- **Fluoridation of drinking water**
- **Reductions in prevalence of tobacco use**

WHO: top 10 threats to global health in 2019

1. **Air pollution and climate change**
2. **Noncommunicable diseases (NCDs)**
3. **Global influenza pandemic**
4. **Fragile and vulnerable settings**
5. **Antimicrobial resistance**
6. **Ebola and other high-threat pathogens**
7. **Weak primary healthcare**
8. **Vaccine hesitancy**
9. **Dengue**
10. **HIV**

First generation vaccines – use of „Whole“ microbes

- **Atenuated microbes**: mumps, measles rubella (MMR vaccine), rotavirus varicella, BCG (against TBC),cholera, yellow fever, poliomyelitis,
- Excellent immunogenicity, danger of reversal into pathogenic strains (repeatedly observed in live polivirus vaccine)

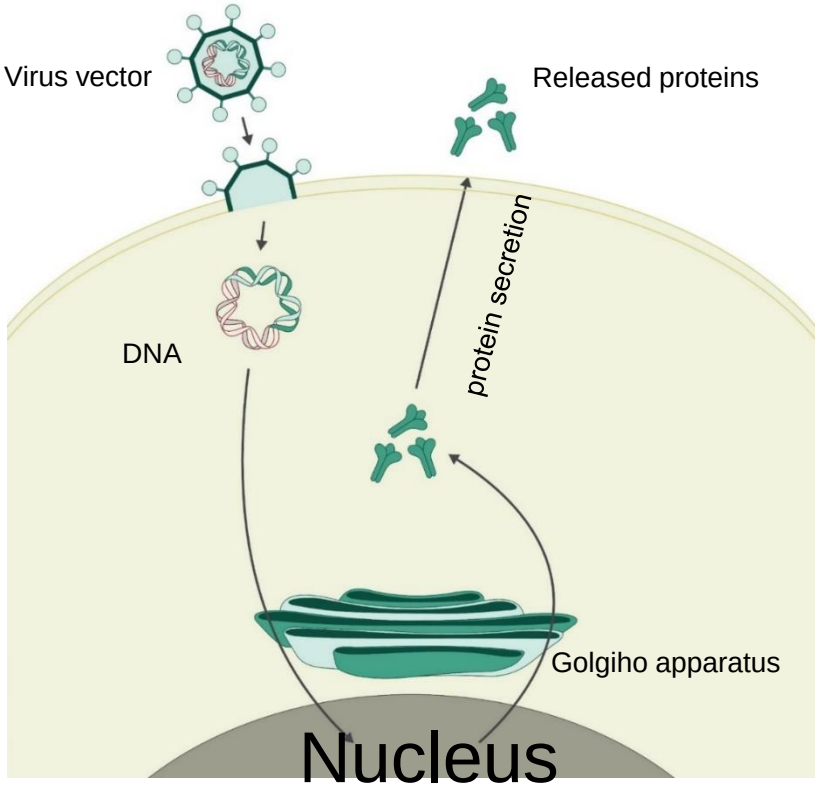
- **Inactivated microorganisms**: rabies, hepatitis A, tick-born encephalitis, poliomyelitis, cholera, plague. Formerly pertussis.
- Also SARS-Cov-2 vaccines, not aprooved in Europe.
- Because of realatively weak immunogenicity, repeated vaccination is usually necessary

Second generation vaccines

Fragments, parts of microbes are used, prepared either directly from microbes or by recombinant technologies

- **Toxoids**: tetanus, diphteria
- **Subunit vaccines :**influenza vaccines, pertussis, Novavax (anti SARS-Cov_2)
- **Polysaccharide vaccines – either native polysaccharide** – insufficient immunogenicity, mainly in the first 2 years of life, or conjugated with protein carriers (most frequently. tetanic or diphteric toxoids): Heamophilus influenzae B (conjugated), Meningococcus (conjugated, non, conjugated), Pneumococcus (conjugated)
- **Recombinant**: hepatitis B
- **Virus-like particles** (virion without nucleic acid): papillomavirus
- **Vector vaccines – genetic information about antigens is included by recombinant technologies into viruses** (which are unable to proliferate in the human body), Johnson & Johnson vaccine, former Astra-Zeneca vaccine

Adenovirus vector vaccine



Third generation vaccines

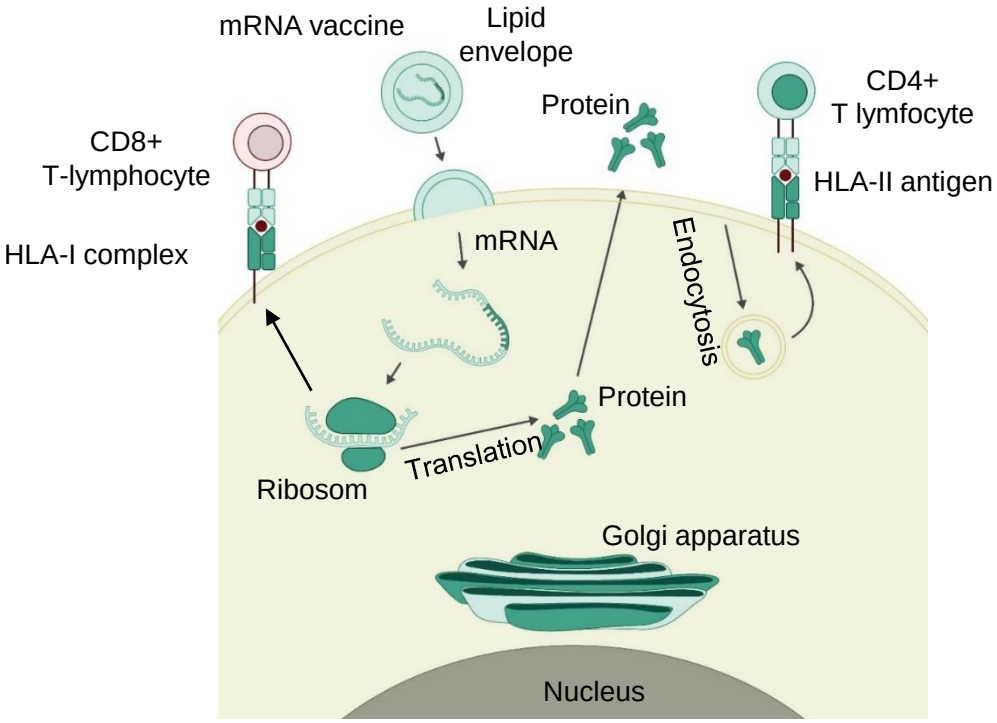
- DNA vaccines
- RNA vaccines

RNA vaccines

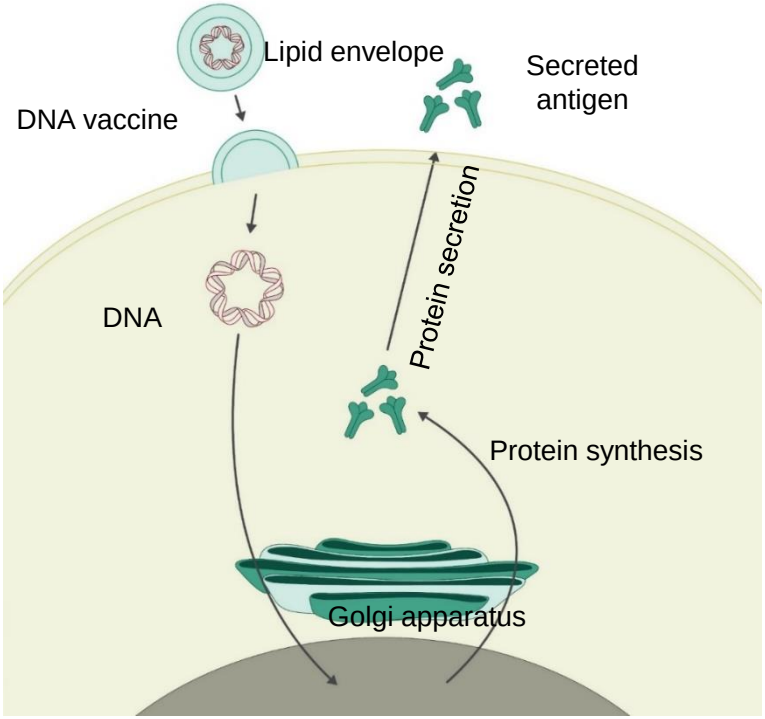
- RNA with information for synthesis of protective antigens is included into the cells, these cell become producers of the antigens (short time).

- Comirnaty (Pfizer-BioNTech), Moderna,

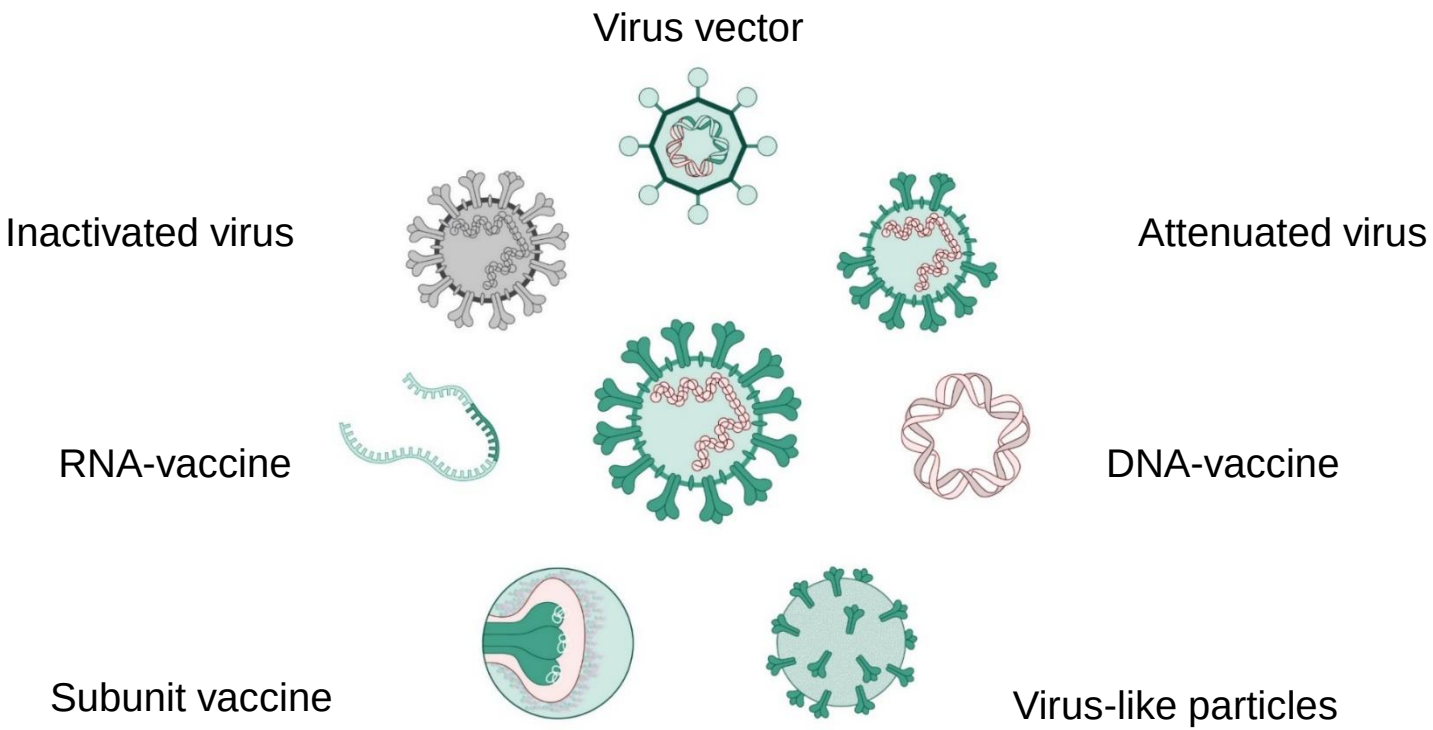
RNA vaccine


mRNA vaccine
Lipid envelope
Protein
CD4+ T lymfocyte
CD8+ T-lymphocyte
HLA-II antigen
HLA-I complex
mRNA
Endocytosis
Protein
Translation
Ribosom
Golgi apparatus
Nucleus

DNA vaccine


Lipid envelope
Secreted antigen
DNA vaccine
DNA
Protein secretion
Protein synthesis
Golgi apparatus
Nucleus

The most frequenty used approches in preparation of anti-Covid19 vaccienes



BCG (Bacille Calmette Guérin) vaccine

- Prepared in 1921 - after 13 years of passage of Mycobacterim bovis, on potatoes with glycerin and beef bile.
- It has been and is used in protection against M. tuberculosis and partly also other mycobacteria.
- It protects mainly against severe disseminated forms of tuberculosis.
- It is a live vaccine that stimulates T-lymphocytes, it was given on the 4th day after birth. However, administration was sometimes accompanied by BCG infection, most often BCG lymphadenitis, so most European countries gradually withdrew from routine administration of BCG vaccine in general population.
- Efforts have been made to use BCG in the treatment of tumors (non-specific immunostimulator); currently, local BCG is a treatment of choice in bladder cancer.

Other (possible) uses of vaccination approach

- Anti-tumour vaccination – both preventive to therapeutic approaches are used
- Prevention ant treatment of Alzheimer disease – anti β-amyloid or τ-protein
- Contraception – most frequently anti-HCG
- Treatment of high blood pressure – enzymes of angiotensin-renin-aldosterone system
- Vaccination against autoimmune diseases – e.g. against autoimmune TCR.
- Vaccination against drugs (cocaine, possibly nicotine)

Passive immunization

- Substitution of missing specific antibodies protecting against infectious disease or treating the infectious disease.
- Used mainly in infectious diseases or diseases caused by toxins.
- Prompt but short-term effect.
- No immunological memory is induced.

Antisera used in human medicine

- Against bacterial infections: Tetanus (human), Diphteria (equine), Botulism (equine)
- Against viral infetions: Hepatitis B (human), Rabies (equine), Varicella-zoster (human), CMV (human), tick-born encephalitis (human), hepatitis A, measles and other viral infections (pooled human immunoglobulin)
- Against snake or black widow spider toxins
- Anti Rh

Monoclonal antibodies used for passive immunisation against microbes

- Various derivatives directed against SAR-Cov-2 virus – both therapy and prevention
- Monoclonal antibody against RS virus (palivizumab) is used as a prevention of RS infection in premature and othere severely affected infants.

Non-specific immunoglobulin derivates

- Obtained from donors´ plasma by ethanol extraction.
- Contains almost exclusively IgG, other isotypes are present only in traces.
- Currently only derivates for intravenous or subcutaneous application are used.

Therapeutic use of immunoglobulin derivates - I

- Replacement treatment in patients with hypogammaglobulinemia .
- It is only IgG substitution, other isotypes are not present.
- In patients with primary hypogammglobulinemia it is usually a life-long treament.

Therapeutic use of immunoglobulin derivates - II

- High-dose intravenouss immunoglobulin treatment can be used in severe inflammatory or autoimmune diseases.
- The mechanism is complex (inhibition of phagocytosis, suppression of B-cells function, effete on T-cell functions) .
- The efficacy is variable and in situation difficult to predict.
- Most effective in Kawasaki disease and immune thrombocytopenic purpura (ITP).