

Autism ADHD Asthma Allergies Eczema

**THE BIGGEST LIE  
BIG PHARMA  
EVER SOLD**



**...THAT VACCINES ARE  
SAFE AND EFFECTIVE**

Seizures Obesity Auto-Immune Diabetes



# Vaccination

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## USA: a hundred years of vaccination programme

	# cases 1900	# cases 1999	% Annual decrease
Smallpox	48,165	0	100
Diphtheria	175,885	1	100
Pertussis	147,271	6,279	95.7
Tetanus	1,314	34	97.4
Poliomyelitis	16,316	0	100
Measles	503,282	89	100
Mumps	152,209	606	99.6
Rubella	47,745	345	99.3
Congenital rubella	823	5	99.4
H influenzae b	20,000	54	99.7

# Smallpox and Edward Jenner

Variola major:

- vesicles, then firm pustules
- circulatory collapse
  - 30% mortality
  - in Europe 400,000 deaths annually
- scars, blindness

variolation as an 18<sup>th</sup> century official preventive method (with mortality 5 - 10%)



## Smallpox and Edward Jenner

Milkmaid: „I shall never have smallpox for I have had cowpox. I shall never have an ugly pockmarked face.“



1796: „vaccination“ with cowpox



AN  
*INQUIRY*  
INTO  
THE CAUSES AND EFFECTS  
OF  
THE VARIOLÆ VACCINÆ,  
A DISEASE

DISCOVERED IN SOME OF THE WESTERN COUNTIES OF ENGLAND,

PARTICULARLY

*GLOUCESTERSHIRE,*

AND KNOWN BY THE NAME OF

THE COW POX.

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BY EDWARD JENNER, M. D. F. R. S. &c.

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— QUID NOBIS CERTIUS IPSIS  
SENSIBUS ESSE POTEST, QUO VERA AC FALSA NOTEMUS.

LUCRETIVS.

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London:

PRINTED, FOR THE AUTHOR,

BY SAMPSON LOW, N<sup>o</sup>. 7, BEEWICK STREET, SOHO:

AND SOLD BY LAW, AVE-MARIA LANE; AND MURRAY AND HIGHLEY, FLEET STREET.

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1798.

# Smallpox and Edward Jenner

vaccinia virus (hybrid of cowpox and smallpox)

1979: WHO reported eradication of the disease



## Artificial immunization

- active = vaccination
- passive = Ig application

## Prevention vs. prophylaxis (post-exposure protection)

**Protective antigen:** generates production of protective antibodies that prevent from infection recurrence

**T-independent antigen:** activation of B cells directly; not mature in children below 2 years of age; capsular polysaccharides

--> **conjugate vaccines:**

T-independent Ag attached to carrier protein, resulting in induction of T-dependent response

## Types of vaccines

- **toxoids** (anatoxins)
- **inactivated** (whole cell)
  - bacterial (bacterin)
  - viral

induction of humoral response; short time retention of Ag

- **live attenuated**
  - bacterial
  - viral

induction of humoral + cell-mediated response,  
persistence in the host  
risk of pathogenic effect (in immunodeficiencies)

- **subunit vaccines (incl. conjugate)**  
lower occurrence of adverse events

- **mRNA**
- **viral vector (carrying DNA)**



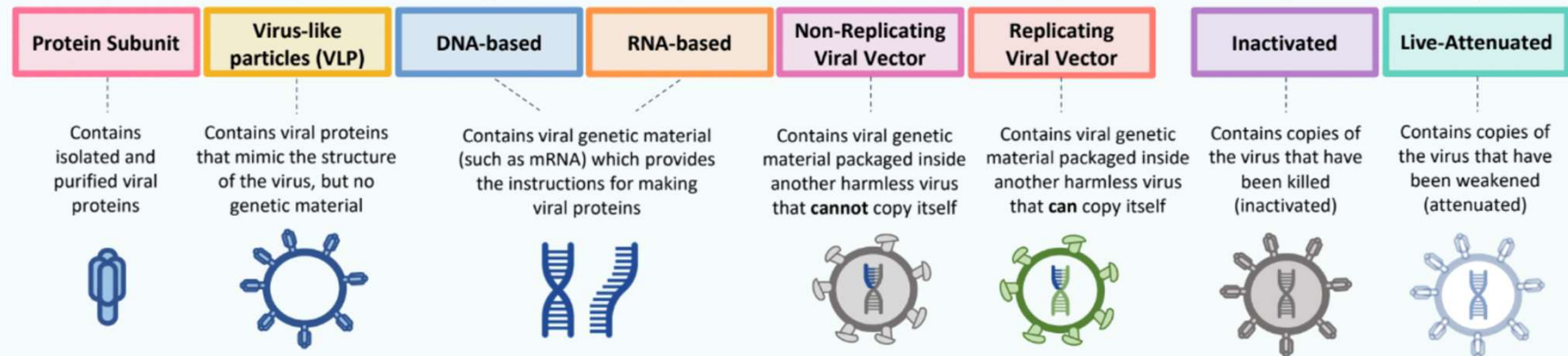
# TYPES OF VACCINES



Vaccine platforms designed to train our immune system

TYPES OF COMPONENT VIRAL VACCINES

TYPES OF WHOLE VIRUS VACCINES



subunit

mRNA

vector

whole cell:

- inactivated

- live attenuated

## Classification of vaccination

- **Regular**
  - vaccination schedule, predisposed individuals
- **Specific**
  - hepatitis A, hepatitis B, rabies, flu
- **Emergency**
  - extraordinary situations
- **Wounds**
  - tetanus, rabies
- **On request**

# Regular vaccination

## Vaccination schedule CZ, valid from 01/2018

Diphtheria  
Tetanus  
Pertussis } **DTaP**; DiTePe

*Hemophilus influenzae* type b (Hib)

Hepatitis B (HBV)

Poliomyelitis (**IPV**)

= Hexavaccine

Dose 1: since week 9

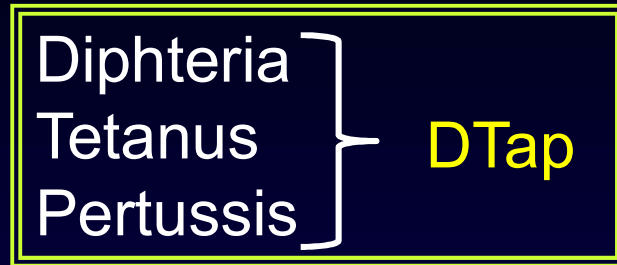
Dose 2: 2 months apart

Dose 3: 6 months apart

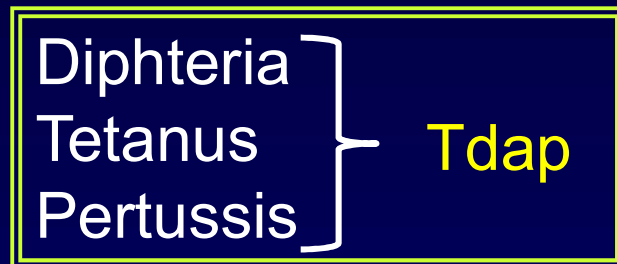
(to complete at 11 to 13 months of age)

the change from 3+1 (year 2010) to 2+1 (year 2018)

# Vaccination schedule CZ, valid from 01/2018



Dose 4: year 5 to 6



+



Dose 5: year 10 to 11

for polio, it is dose 4



Dose 6: 25 years of age (and then every 10 to 15 yrs)

## Vaccination schedule CZ, valid from 01/2018

Measles	}	MMR
Mumps		
Rubella		

Dose 1: from month 13 to 18

Dose 2: age 5 - 6

# *Clostridium tetani*

Diphtheria  
Tetanus  
Pertussis

Type of vaccine

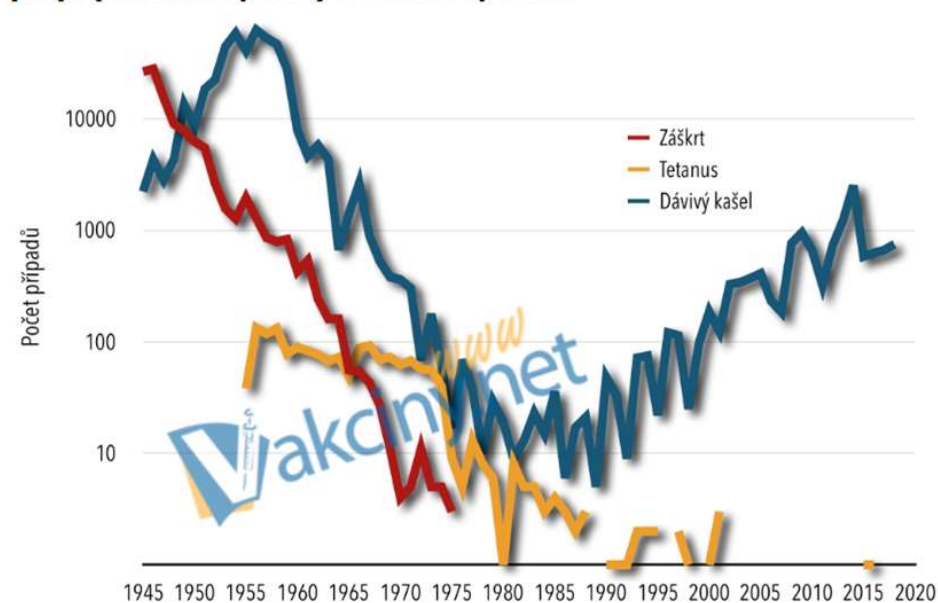
Toxoid

Targetting

Tetanospasmin

Booster every 10 – 15 yrs  
post-exposure prophylaxis  
possible and applied when:  
> 5 yrs from the last dose  
> 10 yrs from the last dose  
+ passive immunization

Výskyt (absolutní počet) v České republice



# *Corynebacterium diphtheriae*

Diphtheria  
Tetanus  
Pertussis

Type of vaccine

Toxoid

Targetting

Diphtheria toxin

Effective also against other corynebacteria producing diphtheria toxin



# *Bordetella pertussis*

Diphtheria  
Tetanus  
Pertussis

Type of vaccine

whole cell (bacterin)  
acelullar

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Targetting (if acellular)

Pertussis toxin (toxoid)  
filamentous hemagglutinin  
pertactin (*not always*)

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transition to acelullar in 2007 – elimination of LPS, decrease of adverse events

BUT

- lower protectivity (fewer children develop antibodies)
- shorter duration of immunity

# Clinical picture

## Pertussis (whooping cough)

incubation 4 - 21 days

transmission through droplets or direct

non-invasive disease

Stages:

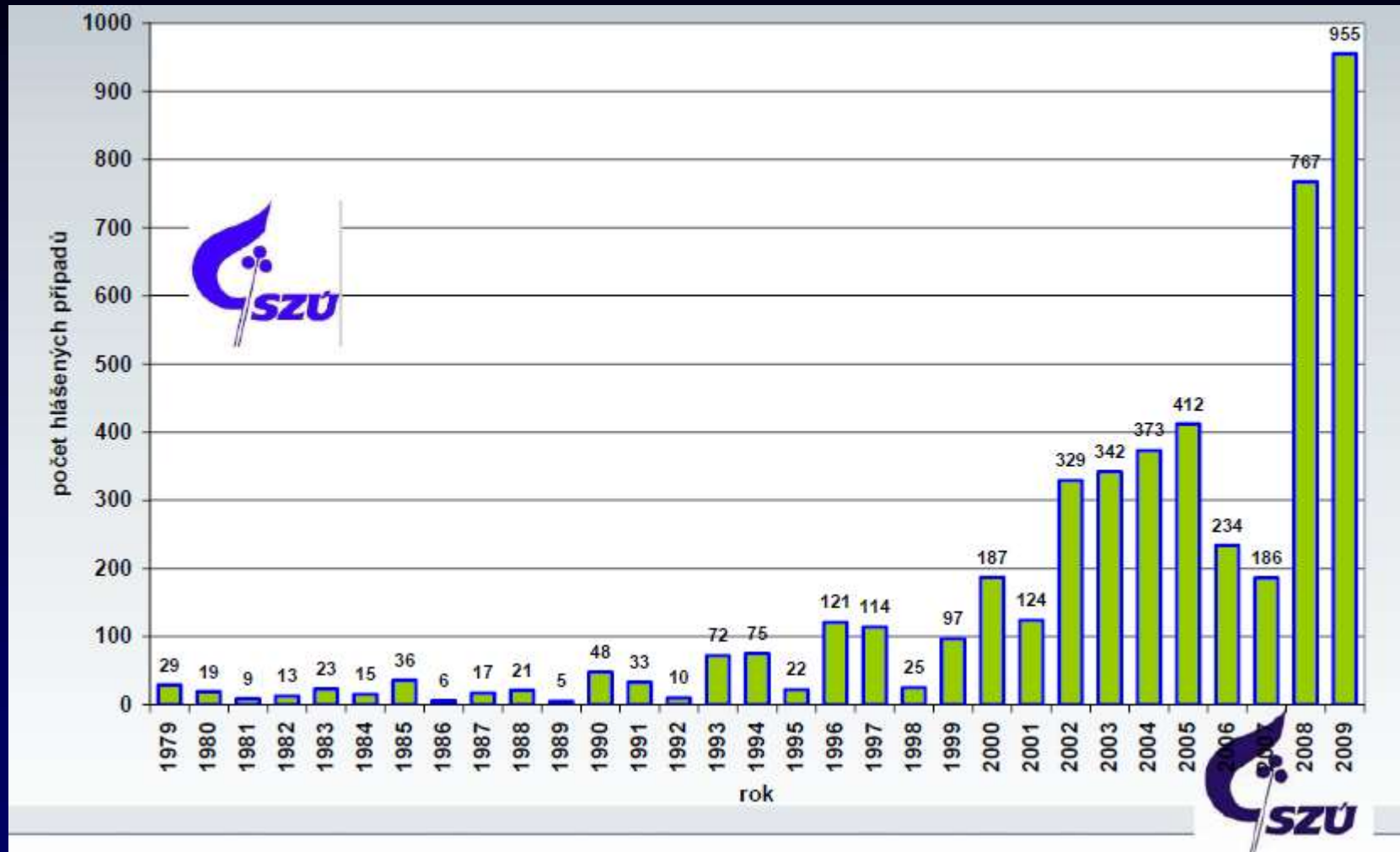
- catarrhal (rhinitis)
- paroxysmal (attacks of cough, dyspnoea, vomiting)
- convalescent (risk of secondary infection, encephalopathy)

In the era of vaccination:

- atypical course (persistent cough in adults)
- modified route of transmission (from adult on child)



## Epidemiology: 30 - 50 mil cases a year (mortality 1%)

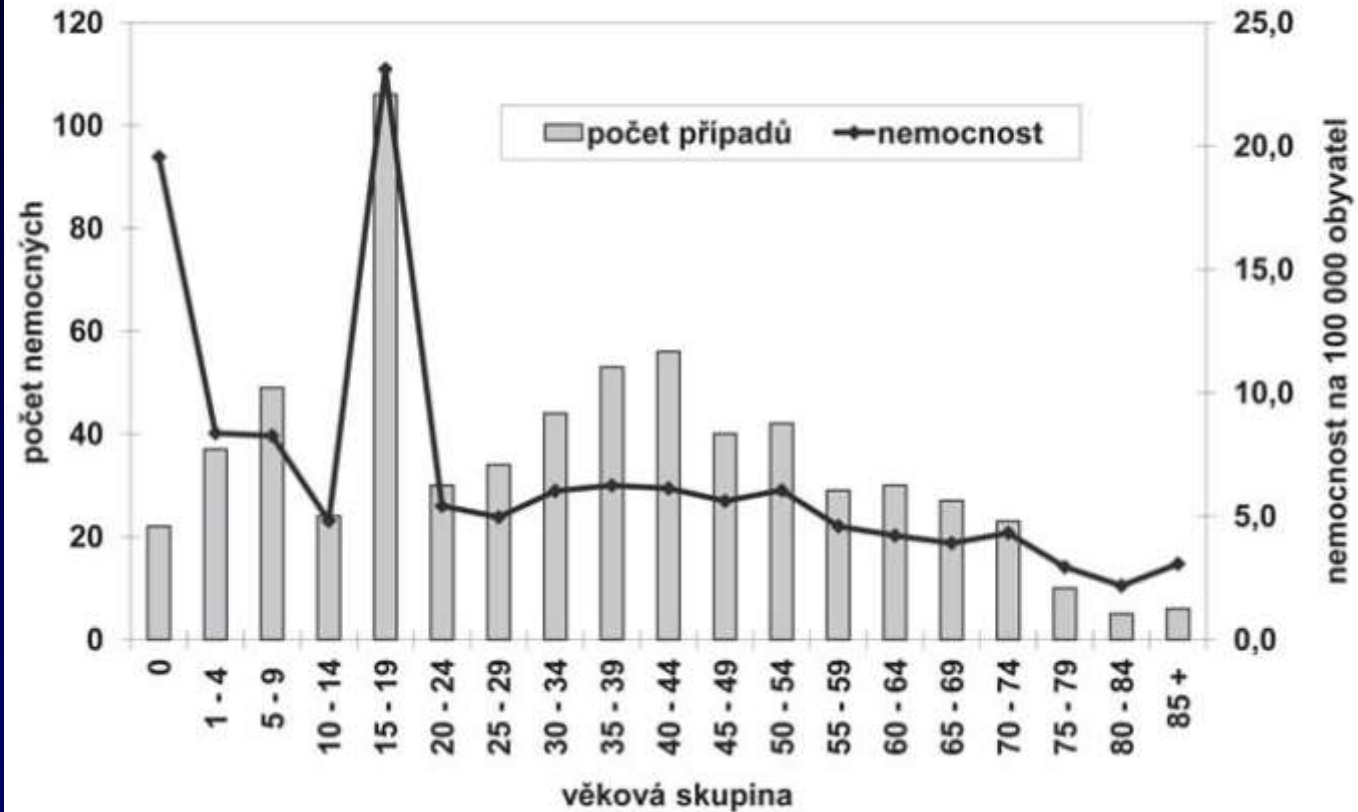


2014: 2,300 cases  
2018: 750 cases  
2019: 1,347 cases

2020: 696 cases  
2021: 51 cases  
2022: 87 cases

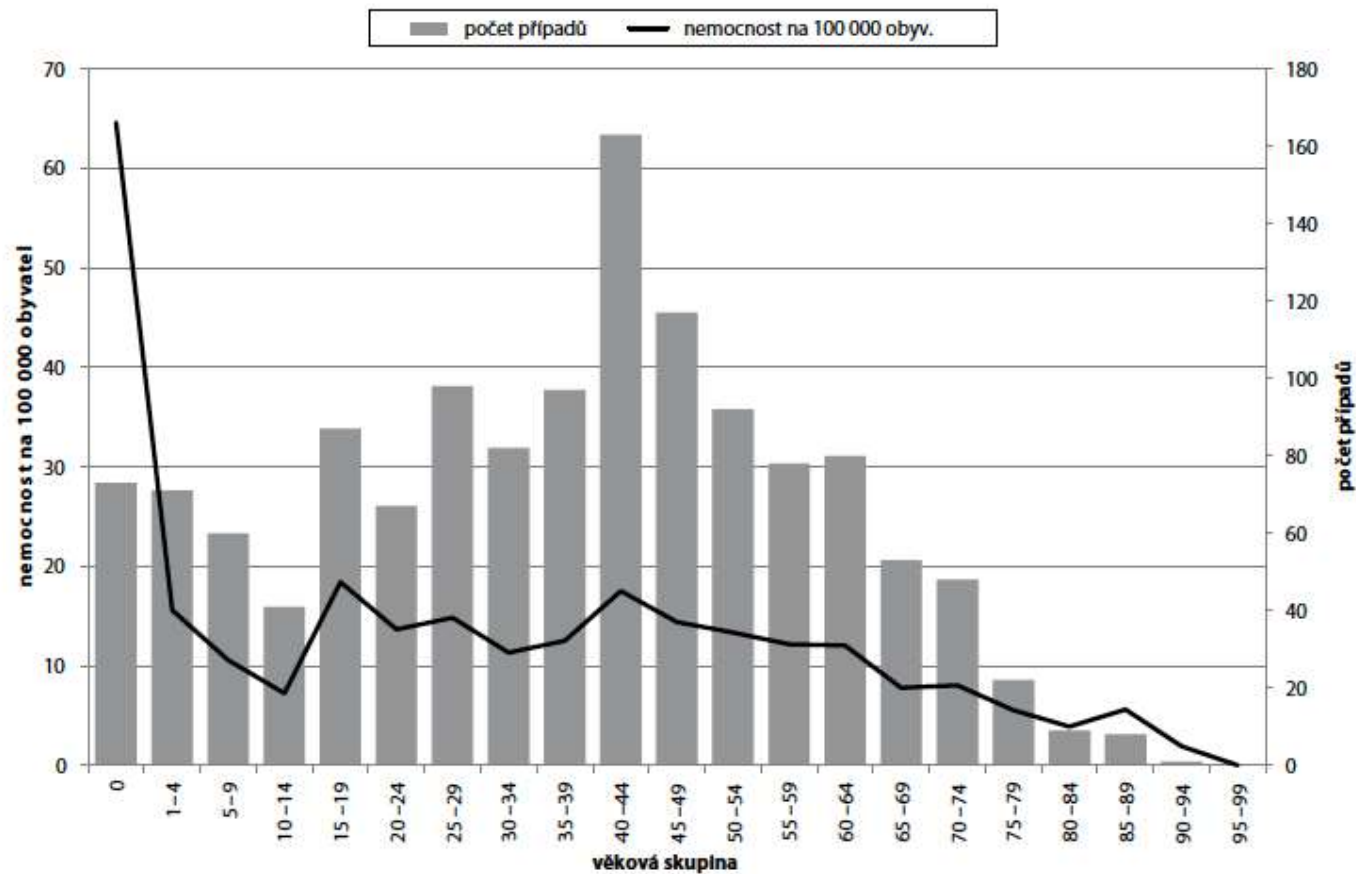
## Epidemiology and year 2017 in CZ: Morbidity by age

Graf 3: PERTUSE, ČR, 2017, POČET PŘÍPADŮ A NEMOCNOST NA 100 000 OBYVATEL, PODLE VĚKU



# Epidemiology and year 2019 in CZ: Morbidity by age

Graf 4: PERTUSE, ČR, 2019, počet případů a nemocnost na 100 000 obyvatel, podle věku



Fabiánová et al. Zprávy CEM 2020.

## Questionmarks with regard to acellular vaccine

- Immunization on selected antigens only  
PT (+ FHA (+ PRN (+ FIM)

  - *B. parapertussis* does not have PT

  - *B. pertussis* and its adoption on selective pressure
    - new strains with no antigens present in the vaccine

- aP does not protect against colonization of the respiratory tract, and thus against transmission

  - vaccination of pregnant women

# Epidemic in the era of vaccination

California, 2010:

9,477 cases

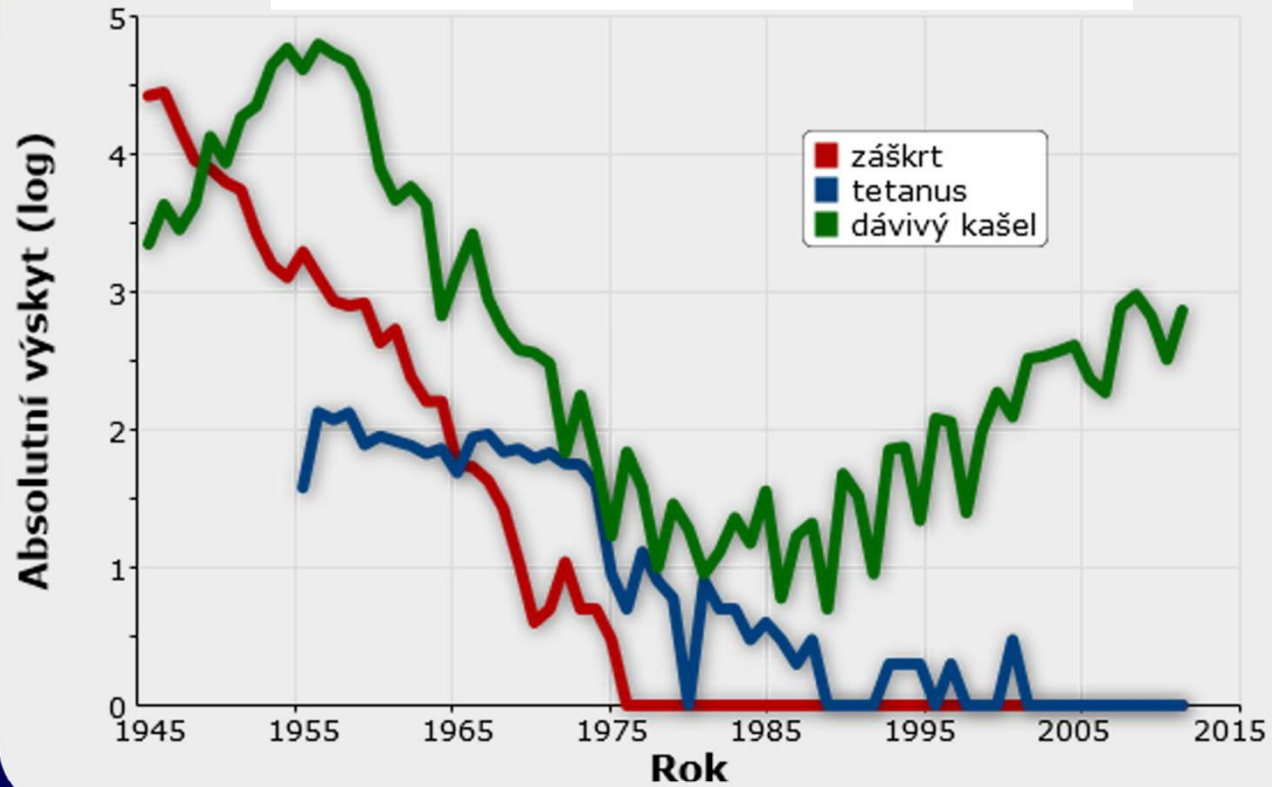
10 deaths (children by 2 mo age)



## Predisposing factors:

- Adults no longer protected (booster dose in adulthood)
- Epidemic in cycles (every 3 to 5 years)
- Non-vaccinated children
- Difficult diagnostics in early stages of disease (culture and PCR vs. serology)
- Bacterial evolution driven by vaccination

## Absolute occurrence since 1945



Least controlled disease that is preventable by vaccination



# *Haemophilus influenzae*

Diphtheria  
Tetanus  
Pertussis

*Hemophilus influenzae* type b (Hib)  
Hepatitis B (HBV)  
Poliomyelitis (IPV)

Type of vaccine

subunit

Targetting

Polyribosylribitolphosphate  
(PRP)  
= capsular polysaccharide

T - independent Ag → conjugate vaccine (with tetanus anatoxin)

**BUT: other serotypes of *H. influenzae* can be pathogens**  
*H. influenzae* type e, f, nontypable

# Virus hepatitis B

Diphtheria  
Tetanus  
Pertussis

*Hemophilus influenzae* type b (Hib)  
Hepatitis B (HBV)  
Poliomyelitis (IPV)

Type of vaccine

subunit (recombinant)

Targetting

HBsAg

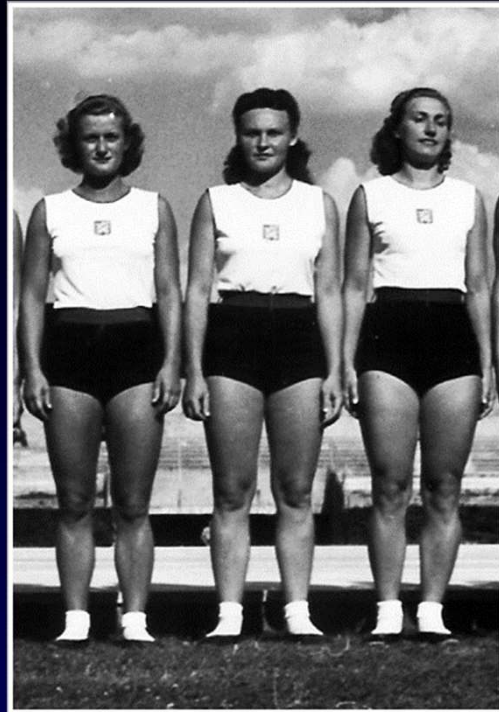
## Indications:

- children (regular vaccination)
- newborns of HBsAg positive mothers (+ passive immunization)
- increased risk
  - medical students, laboratories with biolog. material ...

postexposure prophylaxis possible

# Poliovirus

- asymptomatic infection
- aseptic meningitis
- paralytic form
  - spinal
  - bulbospinal



1925 – 1948



Eliška Misáková

Gold medal in gymnastics  
in memoriam London, 1948

Last case in Czechoslovakia in 1960  
European region declared polio-free in 2002

## Endemic Countries

Polio remains endemic in two countries Afghanistan and Pakistan. Until poliovirus transmission is interrupted in these countries, all countries remain at risk of importation of polio, especially vulnerable countries with weak public health and immunization services and travel or trade links to endemic countries.

# Poliovirus

Diphtheria  
Tetanus  
Pertussis

*Hemophilus influenzae* type b (Hib)  
Hepatitis B (HBV)  
Poliomyelitis (IPV)

Type of vaccine

live attenuated (OPV) Sabin  
inactivated (IPV) Salk

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Targetting

2 serotypes

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## advantages of OPV:

- mimicks infection with the wild strain, generates mucosal gut immunity
- „booster“ to others (through elimination of vaccine strains from vaccinated)

## advantages of IPV:

- no risk to people with immunodefects
- no risk of getting a circulating vaccine-derived poliovirus (cVDPV)

# Measles, Mumps, Rubella

Rod Morbilivirus, Rubulavirus, Rubivirus

Measles  
Mumps  
Rubella

Measles: pneumonia, encephalitis, SSPE

Mumps: orchitis, pancreas

Rubella: teratogenic

Type of vaccine

live attenuated

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WHO Goal: eradication of measles + rubella in Europe by 2015

-- > "Herd immunity" (95 % immunized)

+ even distribution of non-immunized

but in 2010 in Europe: ~ 30,000 cases

most at risk: children < 1 year of age (SSPE)

**Voluntary, covered by insurance**

valid from 01/2018

pneumococcal  
vaccine

dose 1: from week 9  
dose 2 : 2 months apart  
dose 3 : 6 months apart

HPV vaccine

2 doses at the age of 13 to 14

valid from 05/2020

meningococcal  
vaccine

2-3 doses against B  
1 dose against A,C,W, Y

# *Streptococcus pneumoniae*

Type of vaccine                      subunit

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Targetting                              capsular polysaccharides

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T - independent Ag → conjugate vaccine

combined vaccines for more serotypes:

conjugated: 10, **13 and 15 serotypes**

(2016 and CR: covers invasive pneumococcal infections > 40 %)

polysaccharide: **23 serotypes**

Vaccination for patients after splenectomy !



# *Neisseria meningitidis*

Type of vaccine

subunit

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Targetting

capsular polysaccharide:  
serogroups A, C, W135, Y

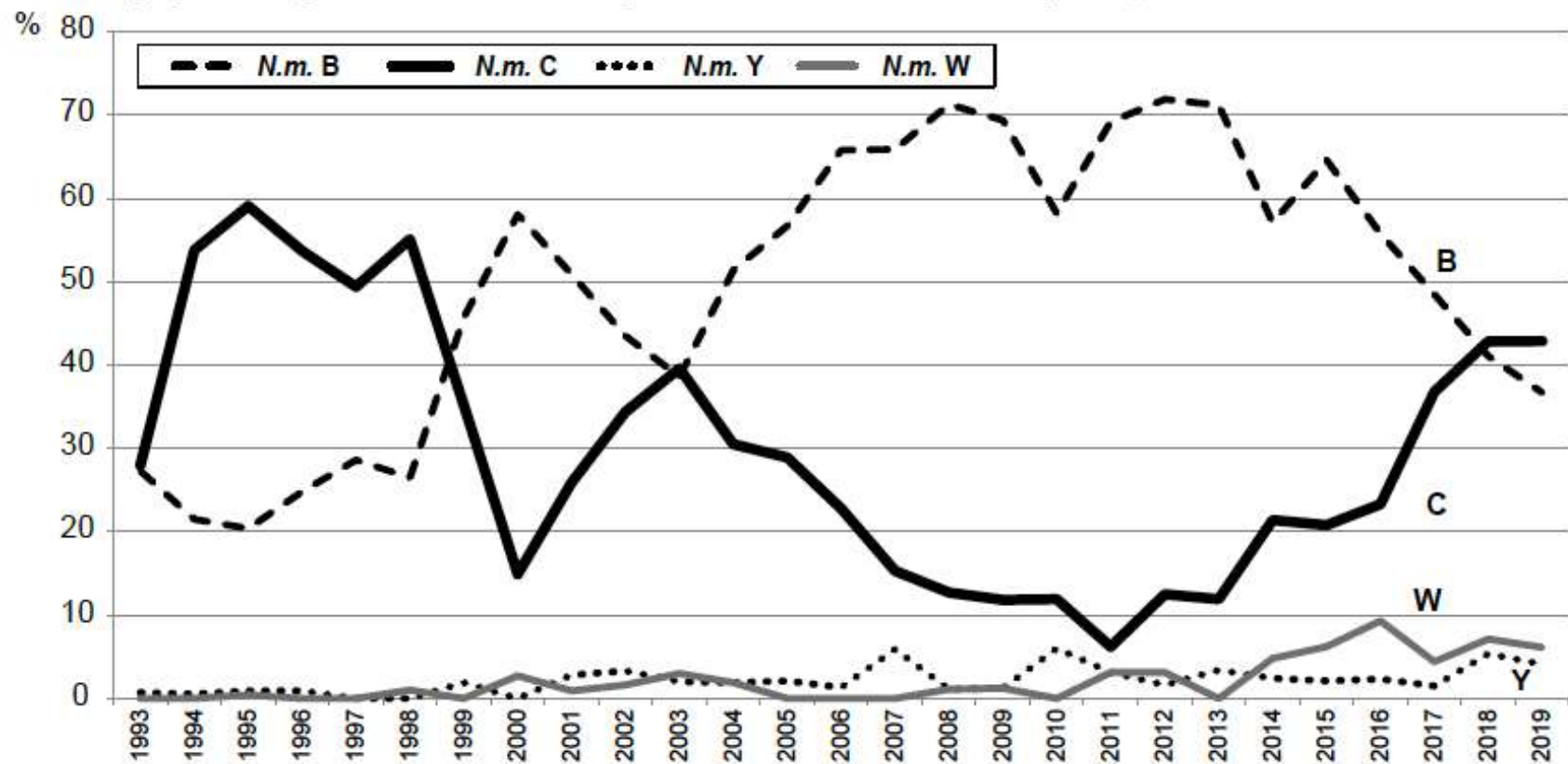
Proteins: group B (not all  
subtypes covered)

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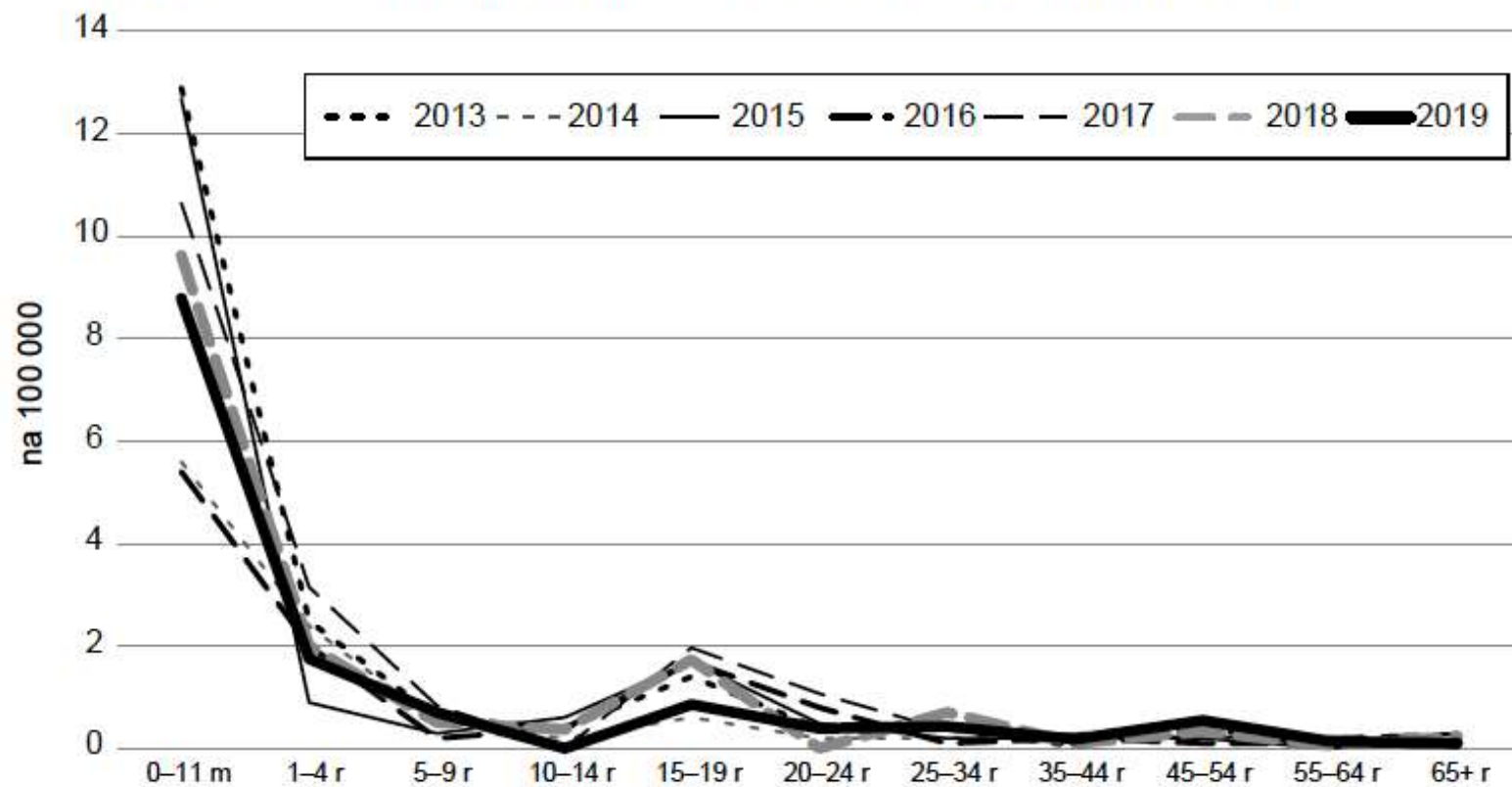
T - independent Ag → conjugate vaccine for children below 2 yrs

combined vaccines A + C + W135 + Y  
vaccine against serogroup B

Graf 4: Séroskupiny *N. meningitidis* u invazivního meningokokového onemocnění Česká republika, 1993–2019



Graf 5: Specifická věková nemocnost invazivního meningokokového onemocnění Česká republika, 2013–2019



# Papillomaviruses

cervix cancer, laryngeal cancer

Type of vaccine

subunit (recombinant)

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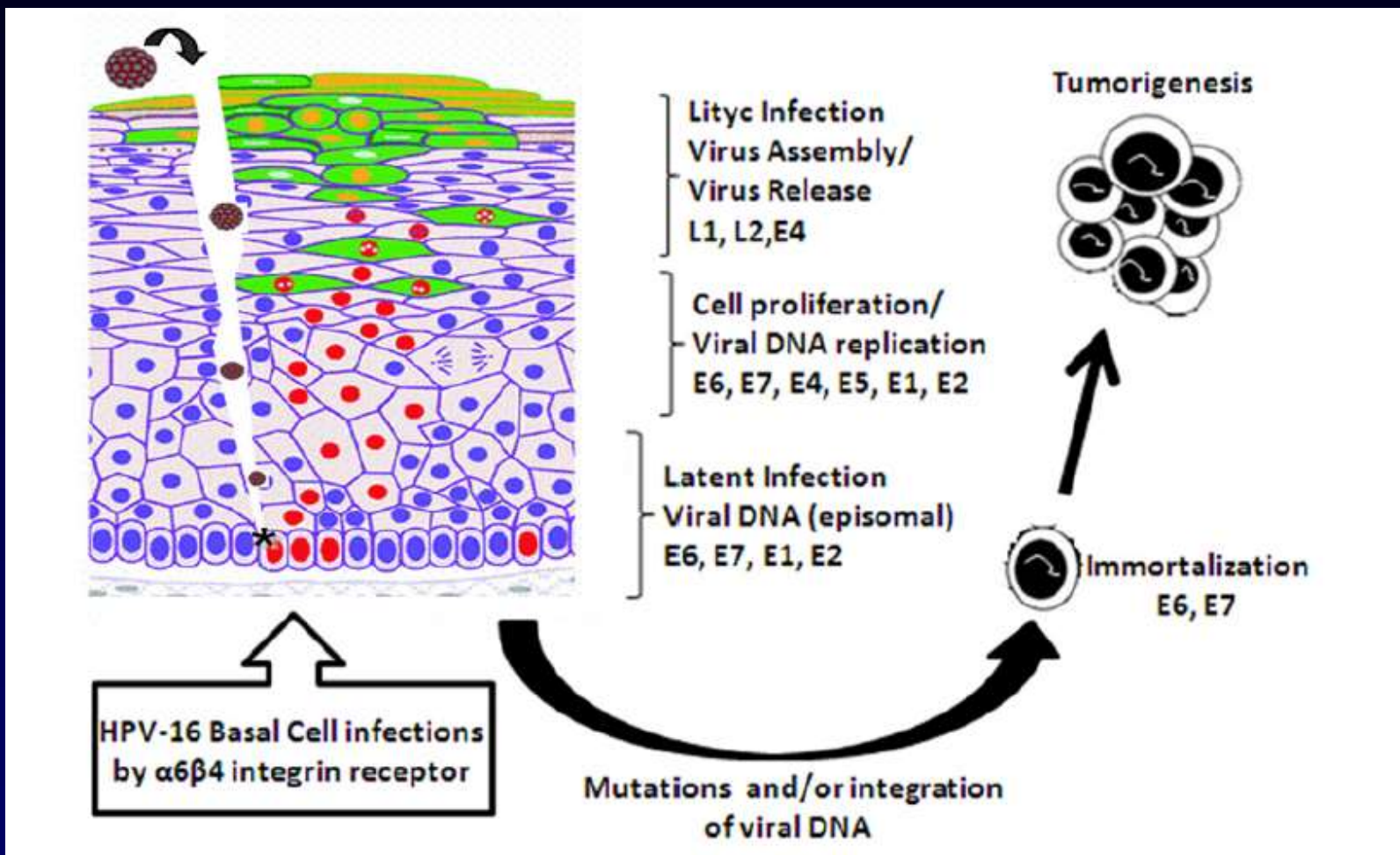
Targetting

L1 capsid protein

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Vaccine bivalent (serotypes 16, 18 - oncogenic), tetravalent (6, 11 – condylomata accuminata, 16, 18), nonavalent ("universal")

# vaccination as a prevention of latent infection with a risk of cancer



# Other vaccines

**Live attenuated**

# Virus chickenpox herpesvirus VZV, HHV3

chickenpox, shingles (herpes zoster)

primary pneumonia, encephalitis, congenital visceral varicella

Type of vaccine

live attenuated

---

Vaccine against HHV3 is part of combined MMR (MMRV) or separate

indication:

children older than 1 yr

very reasonable: susceptible adults (planned parenthood in particular)

prevention of recurrent herpes zoster



# Rotaviruses

Type of vaccine

live attenuated

---

Vaccine against rotaviruses per os  
For children 6 wks - 8 months

# Yellow Fever Flavivirus

Type of vaccine

live attenuated

YF vaccine compulsory or recommended

- before entry to endemic countries
- upon arrival from endemic countries to non-endemic with the mosquito



# *Mycobacterium tuberculosis*

Type of vaccine

live attenuated BCG

---

Th1 cell immunity

prevents from dissemination of BK from site of primo infection

partial cross reactivity with NTM

since 1953:

4 day (till 6 wks) newborns + 2-year + 11-year old (tuberculin neg)



# **Inactivated vaccines (whole cell)**

# Virus tick-borne encephalitis Flavivirus

Type of vaccine

inactivated

---

Vaccine against TBE effective against all subtypes  
(Western , Eastern, Siberian)



# Virus hepatitis A HAV, Hepatovirus

Type of vaccine

inactivated

---

Vaccine against HAV for travellers

# Rabies

Rod Lyssavirus

Type of vaccine

inactivated

---

Vaccine against rabies for prevention and prophylaxis (+ passive immunization with anti rabies serum)

- bites, scratches, lick of wounded skin

(not contact with blood, urine or faeces of animals)



# *Vibrio cholerae*

Type of vaccine

inactivated (serotype O1) - p.o.

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Vaccine against cholera with low protectivity, short-term  
not protective against other *V. cholerae* like O139

# Subunit vaccines

# Virus influenza

Influenzavirus A, Influenzavirus B

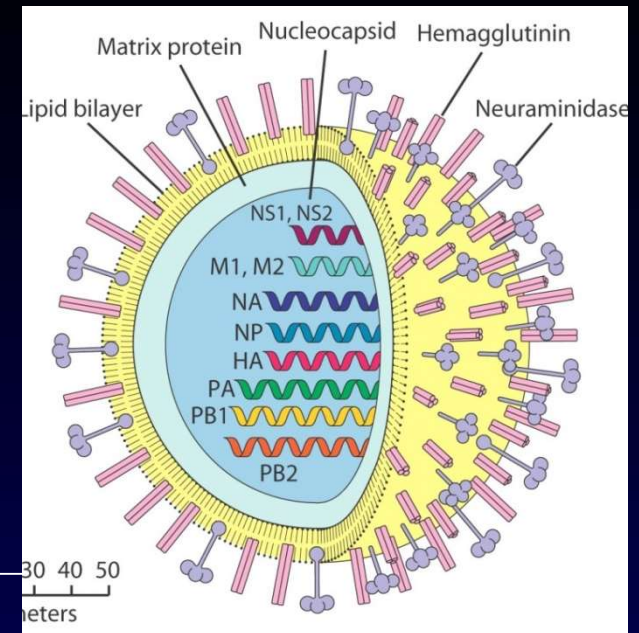
Type of vaccine      subunit, split  
Live attenuated

Targetting      Haemagglutinin (HA)

re-vaccination every year (because of antigen drift)

contains 3-4 strains reflecting current epidemiological situation:

- type B (one or two strains)
- type A H1N1 (protection against pandemic H1N1)
- type A H3N2



# *Salmonella Typhi*

Type of vaccine

subunit

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Targetting

Capsular Vi

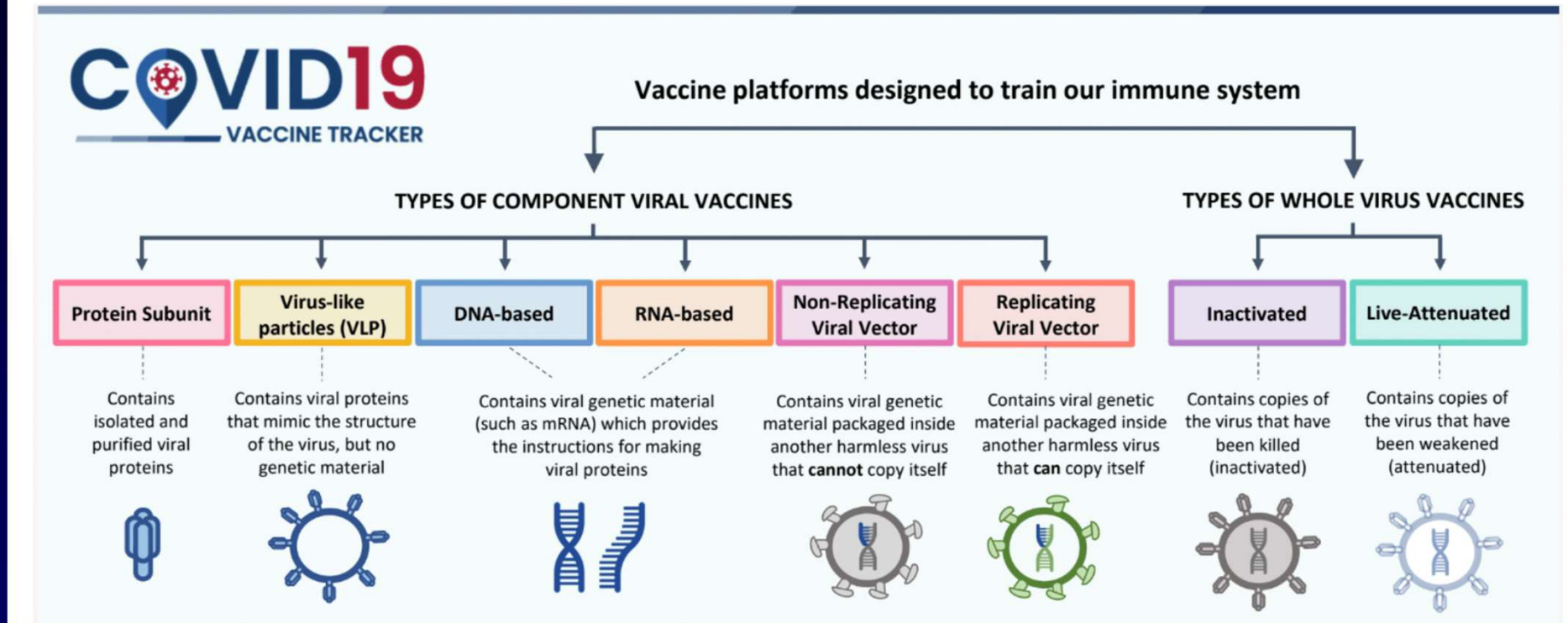
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# what about SARS-CoV-2

## Types of vaccines

- toxoids (anatoxins)
- inactivated (whole cell)
- live attenuated
- subunit
  
- viral vector (non-replicating) with DNA
- lipid nanoparticles with DNA or RNA

# TYPES OF VACCINES



Nuvaxovid (Novavax)

Vaxzevria (AstraZeneca)  
Jcovden (Janssen)

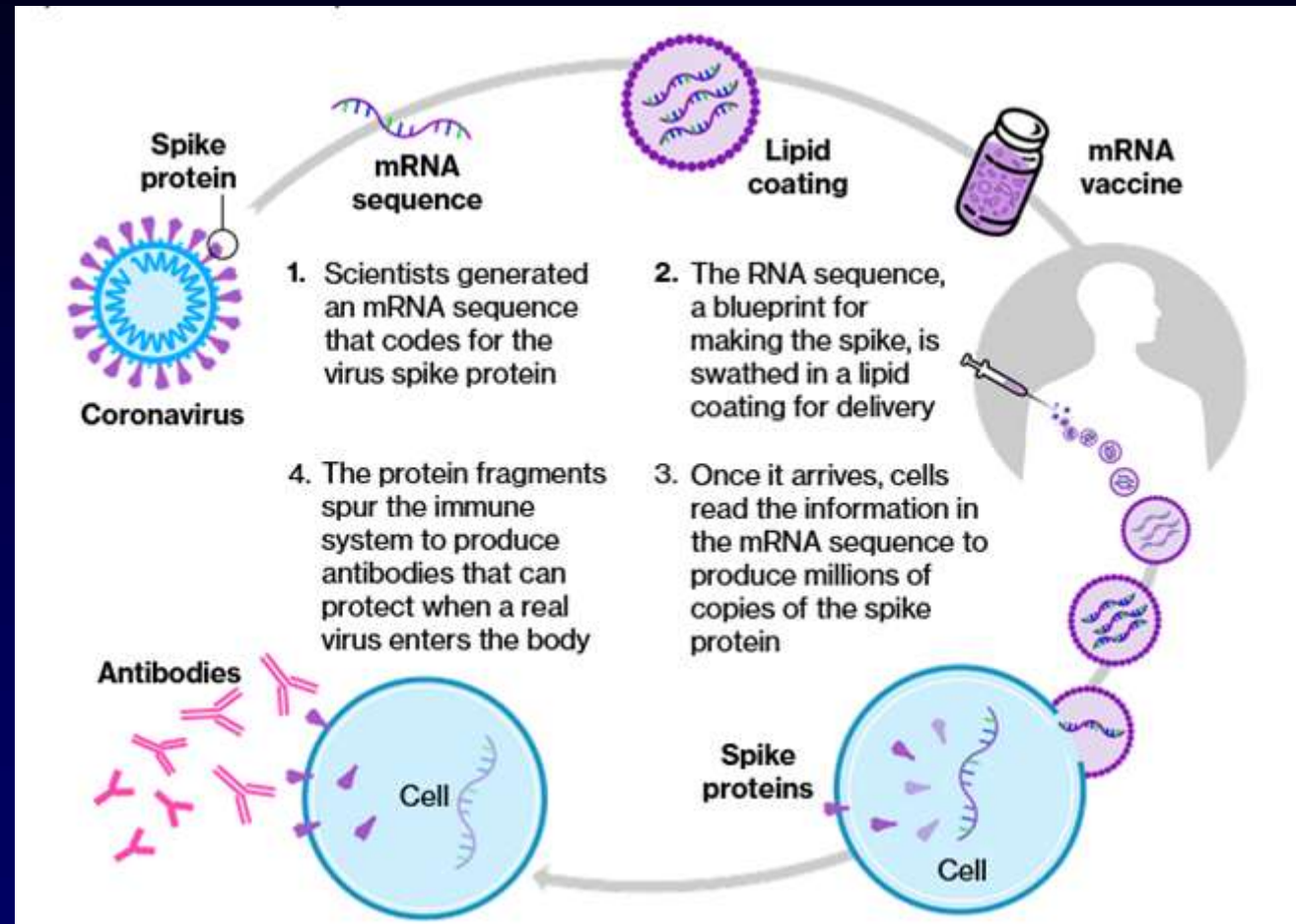
Comirnaty (Pfizer/BioNTech)  
Spikevax (Moderna)

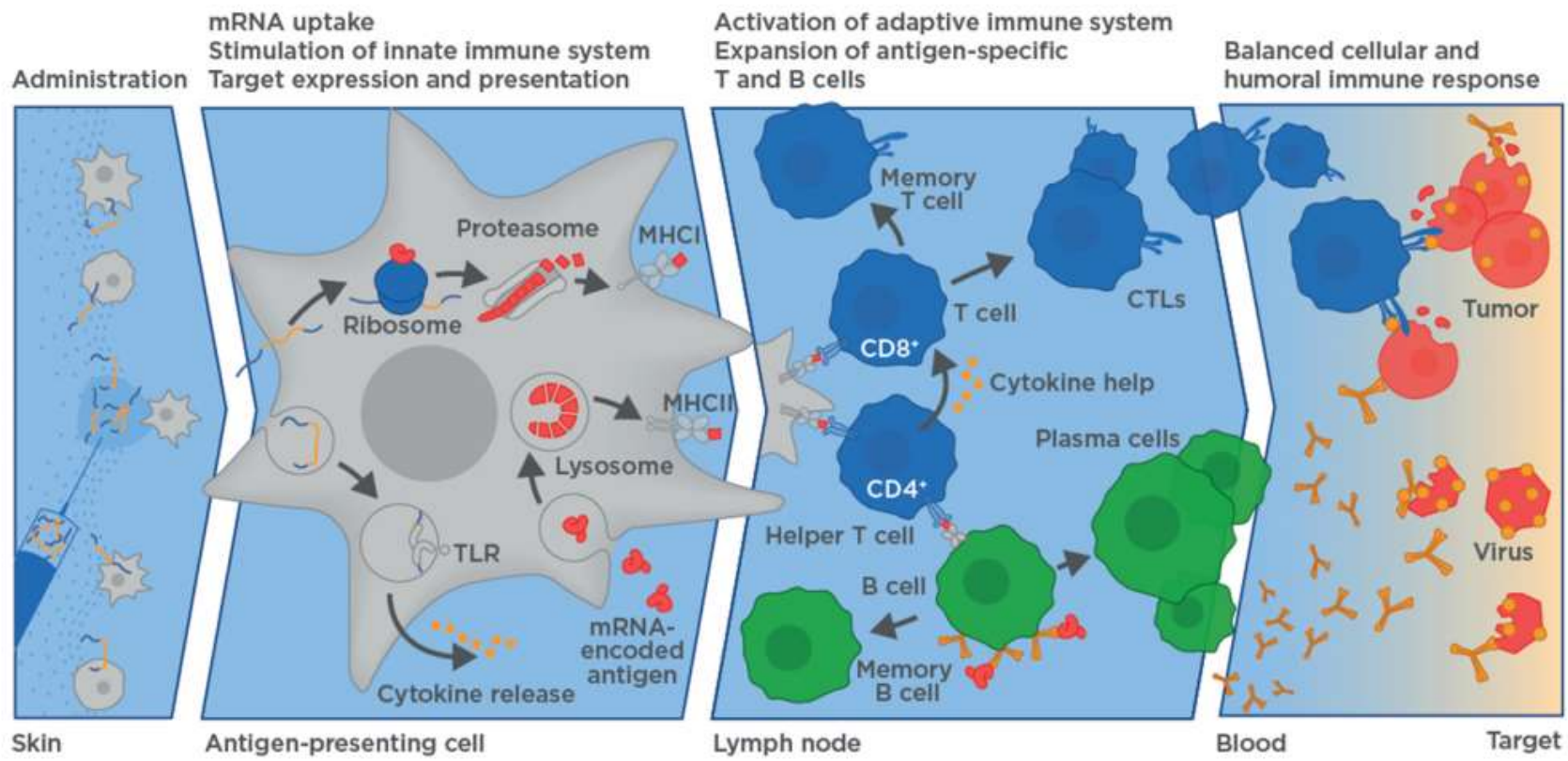
→ bivalent Original/Omicron BA.4-5

# mRNA

- ssRNA encoding full length S protein
- coated in lipids

- stimulation of both humoral and cell immunity







# Last slide

live attenuated vaccine	inactivated (subunit) vaccine
measles, mumps, rubella, VZV	diphtheria, tetanus, pertussis
tuberculosis	Hib
poliomyelitis OPV	poliomyelitis IPV
rotaviruses	hepatitis A, B
yellow fever	pneumococcus, meningococcus
	tick borne encephalitis
	influenza
	rabies
	papillomaviruses
	typhoid fever
	cholera

CAVE patients with immunodefects