Vaccination

USA: a hundred years of vaccination programme

	# cases 1900	# cases 1999	% Annual decrease
Smallpox	48,165	0	100
Diphteria	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

R. Gaynes: Germ Theory. ASM Press 2011

Smallpox and Edward Jenner

Variola major:

- vesicles, then firm pustules
- circulatory collapse
  - 50% mortality in children below 1 year of age
  - in Europe 400,000 deaths annually

- scars, blindness

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

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.

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

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

LUCRETIUS.

London:

PRINTED, FOR THE AUTHOR,

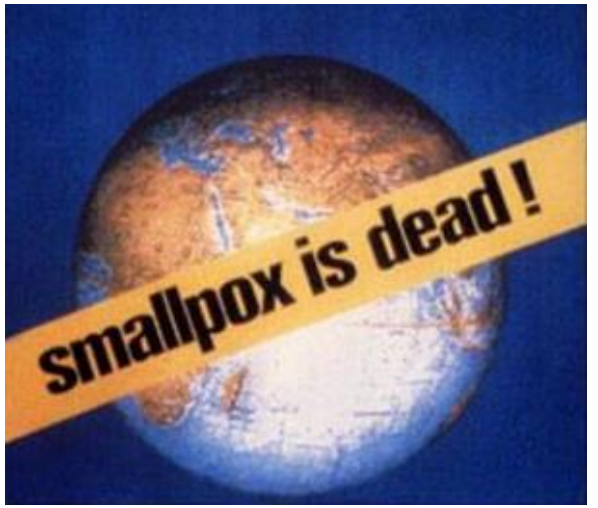
BY SAMPSON LOW, N°. 7, BERWICK STREET, SOHO:

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

1798.

vaccinia virus (hybrid of cowpox and smallpox)

1980: 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)**

Classification of vaccination

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

Regular vaccination

Vaccination schedule CZ, valid from 01/2018

Diphteria
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)

Diphteria
Tetanus
Pertussis
} DTap

Dose 4: year 5 to 6

Diphteria
Tetanus
Pertussis
} Tdap

+ Poliomyelitis IPV

Dose 5: year 10 to 11

for polio, it is dose 4

Tetanus

Dose 6: 25 years of age (and then every 10 to 15 to 20 yrs)

Vaccination schedule CZ, valid from 01/2018

Measles
Mumps
Rubella
} MMR

Dose 1: from month 13 to 18
Dose 2: age 5 - 6

Clostridium tetani

Type of vaccine	Toxoid
Targetting	Tetanospasmin

post-exposure prophylaxis possible and applied when:

> 5 yrs from the last dose

> 10 yrs from the last dose

+ passive immunization

Corynebacterium diphteriae

Type of vaccine	Toxoid
Targetting	Diphteria toxin

Effective also against other corynebacteria producing diphteria toxin

Bordetella pertussis

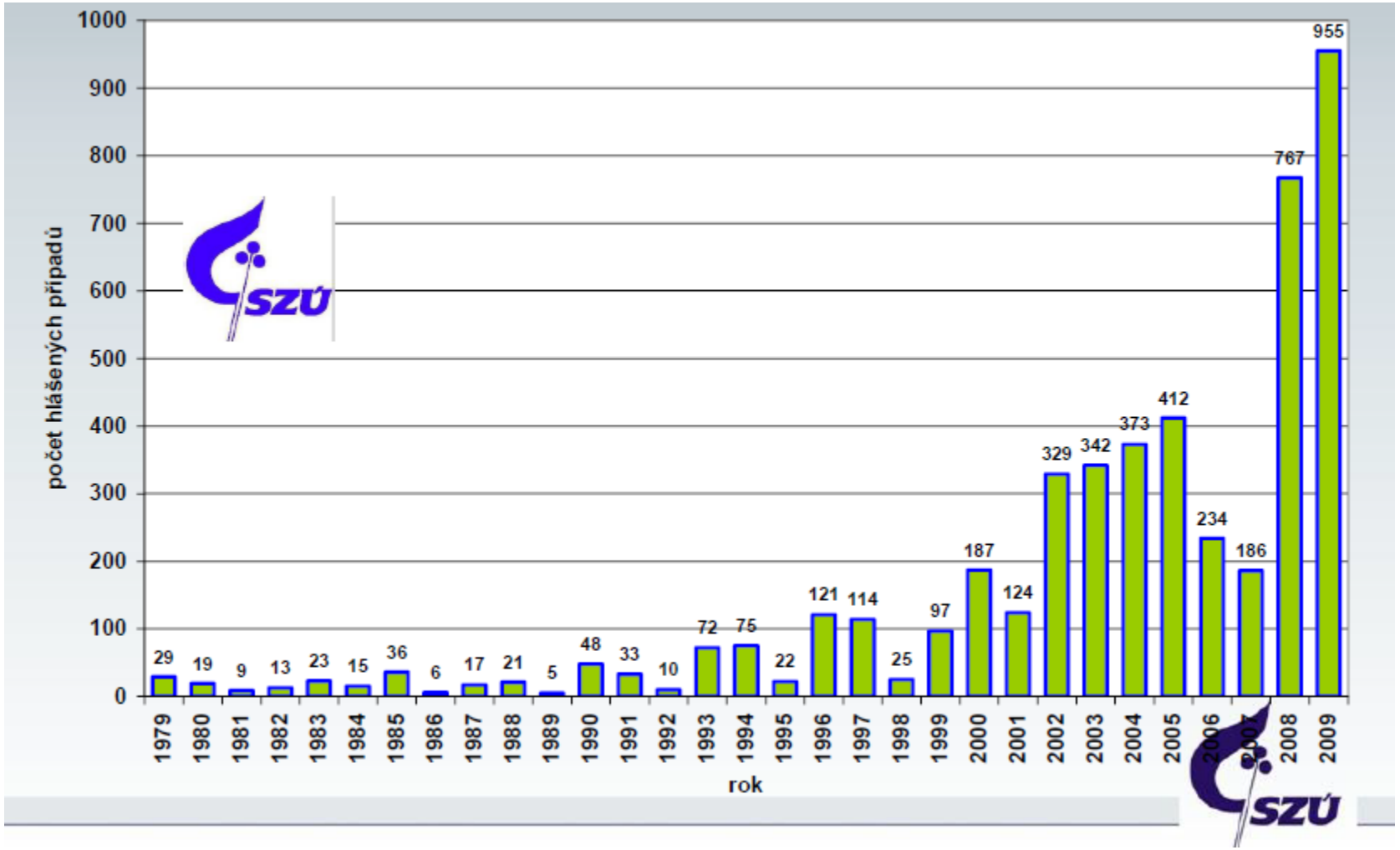
Type of vaccine	whole cell (bacterin) acelullar
Targetting (if acellular)	Pertussis toxin (toxoid) filamentous hemagglutinin pertactin *(not always)*

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

BUT

- lower protectivity (fewer children develop antibodies)
- shorter duration of immunity
- does not protect against colonization of the respiratory tract, and thus against transmission

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



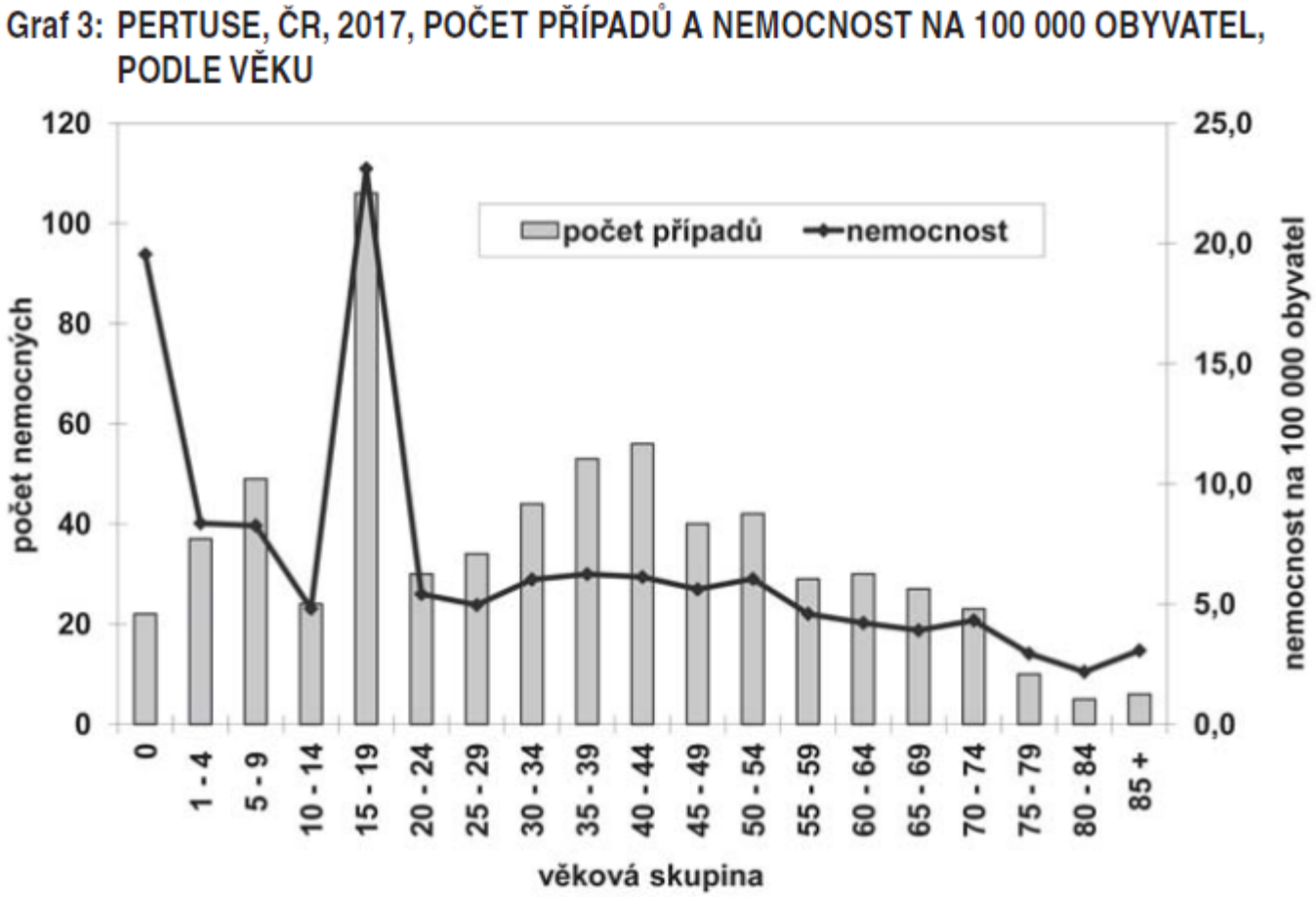
Epidemics in cycles:
every 3 to 5 years

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

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

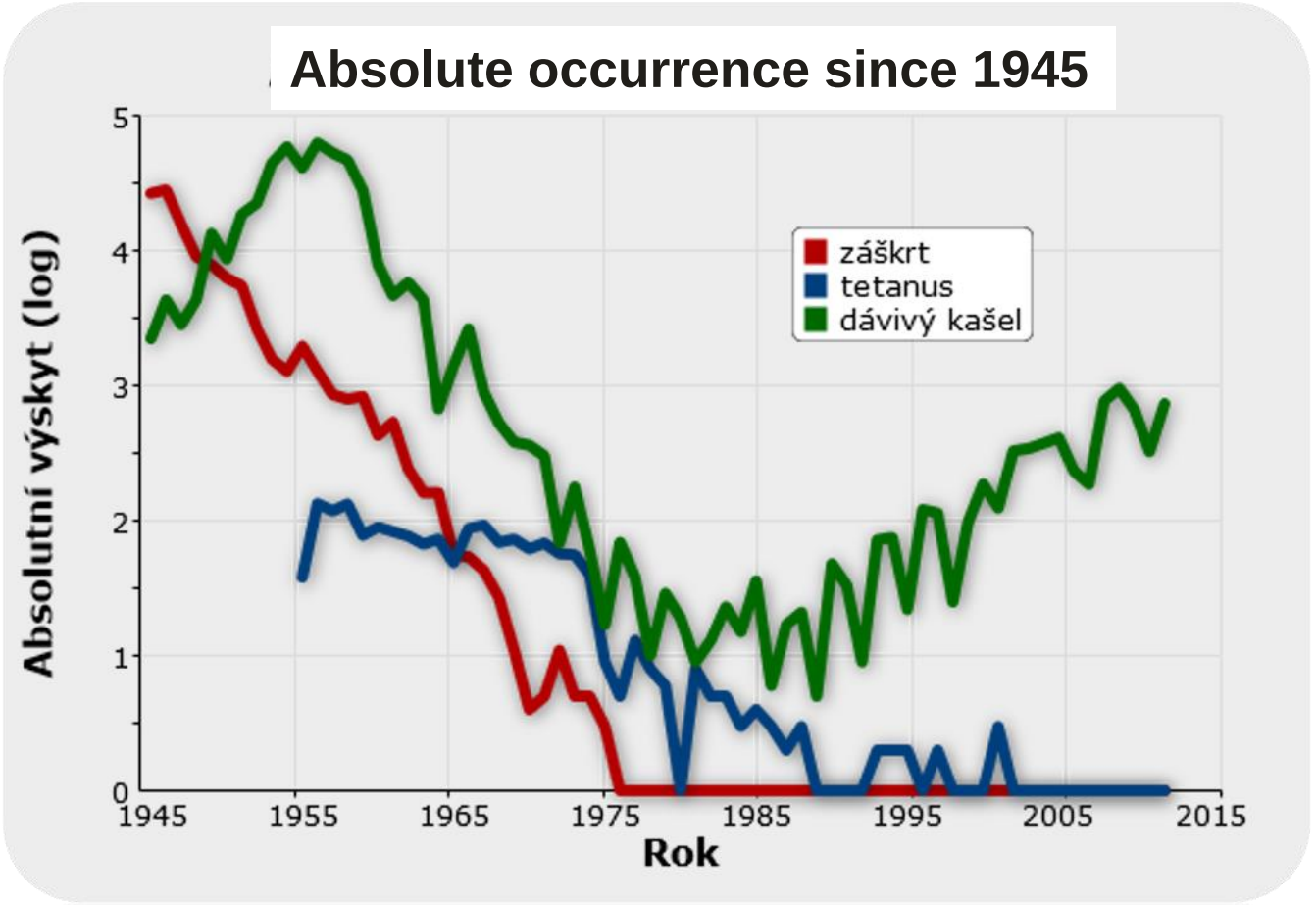
2023: 494 cases
2024: 37,000 cases
2025: 3,700 cases

Epidemiology and year 2017 in CZ: Morbidity by age



Fabiánová et al. Zprávy CEM 2018.

Booster in adulthood?
vaccination in pregnancy



Least controlled disease that is preventable by vaccination

www.vakciny.net

Haemophilus influenzae

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

Type of vaccine	subunit (recombinant)
Targetting	HBsAg

Indications:

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

postexposure prophylaxis possible

Poliovirus

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

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

Type of vaccine	live attenuated (OPV) Sabin inactivated (IPV) Salk
Targetting	2 serotypes

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: pneumonia, encephalitis, SSPE
Mumps: orchitis, pancreas
Rubella: teratogennic

Type of vaccine live atenuated

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missed WHO Goal: eradication of measles + rubella in Europe by 2015
-- > “Herd immunity“ (95 % immunized)
+ even distribution of non-immunized

Voluntary, covered by insurance

pneumococcal vaccine

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

meningococcal vaccine

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

HPV vaccine

2 doses at the age of 11 to 15

Streptococcus pneumoniae

Type of vaccine	subunit
Targetting	capsular polysaccharides

T - independent Ag → conjugate vaccine

combined vaccines for more serotypes:
conjugated: 10, 13 and 15 serotypes (children)
(2016 and CR: covers invasive pneumoccal infections > 40 %)
polysaccharide: 23 serotypes (adults)

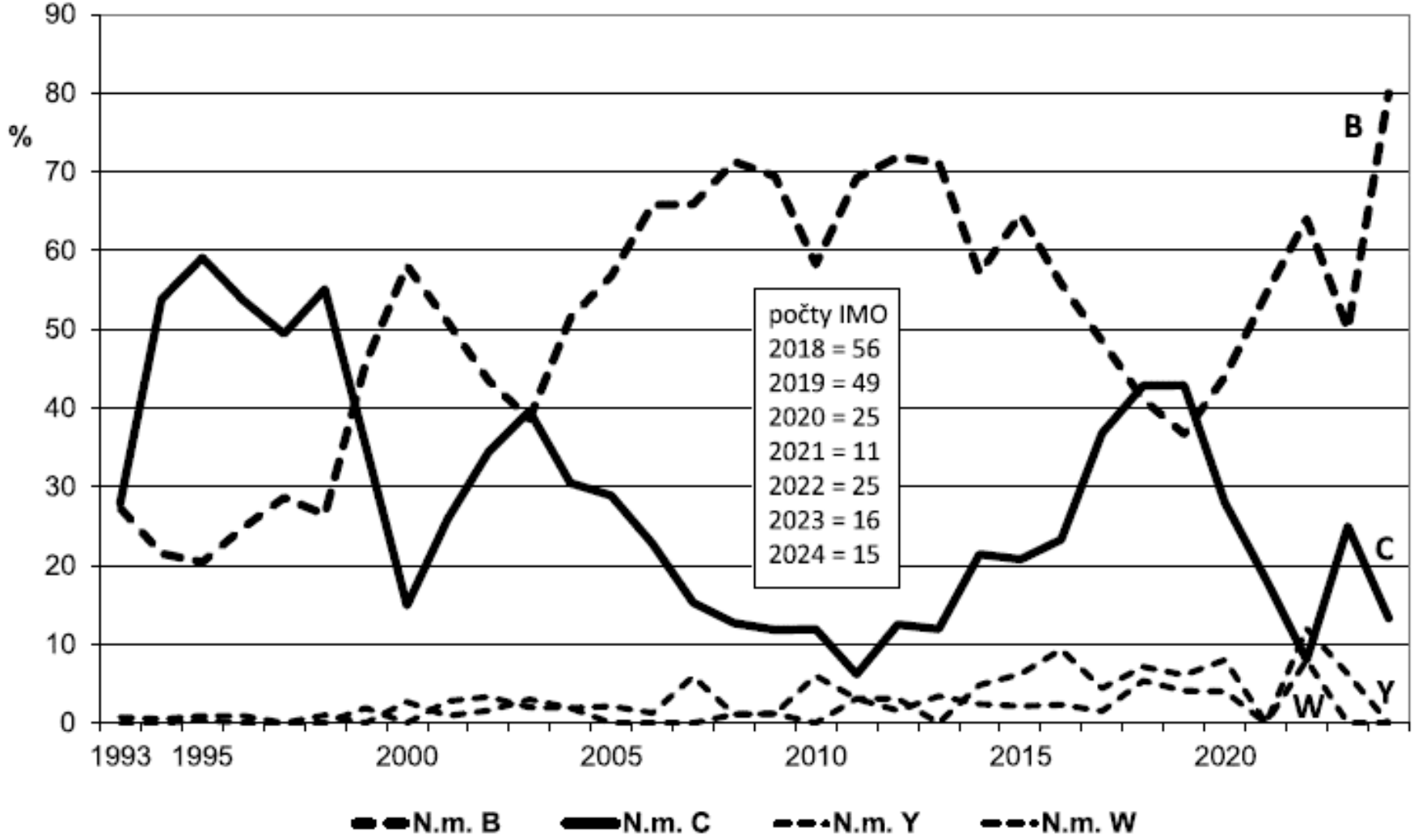
Vaccination for patients after splenectomy !

Neisseria meningitidis

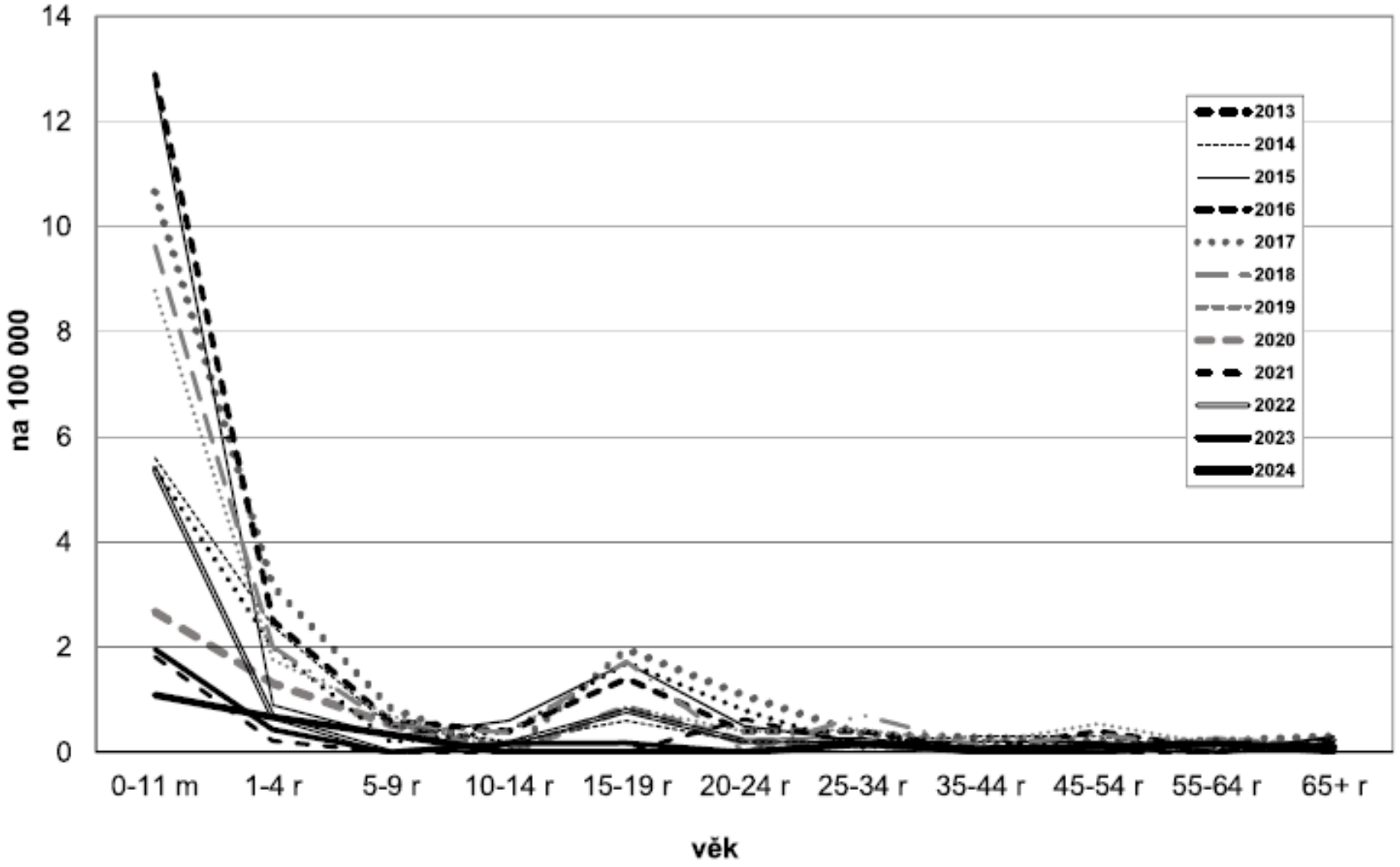
Type of vaccine	subunit
Targetting	capsular polysaccharide: serogroups A, C, W, Y Proteins: group B (not all subtypes covered)

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

combined vaccines MenACWY
vaccine against serogroup B MenB



Okonji et al. Zprávy CEM 2025.



Okonji et al. Zprávy CEM 2025.

Papillomaviruses

cervix cancer, laryngeal cancer

Type of vaccine	subunit (recombinant)
Targetting	L1 capsid protein

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

Other vaccines

Live attenuated

Virus chickenpox herpesvirus VZV, HHV3

chickenpox, shingles (herpes zoster)
primary pneumonia, encephalitis, congenital visceral varicella

Type of vaccine live atenuated

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)
- no longer for a prevention of recurrent herpes zoster
  - in such case, subunit vaccine (for adults)

Rotaviruses

Type of vaccine	live atenuated

Vacine against rotaviruses per os
mono or pentavalent

Yellow Fever Flavivirus

Type of vaccine live atenuated

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 atenuated BCG

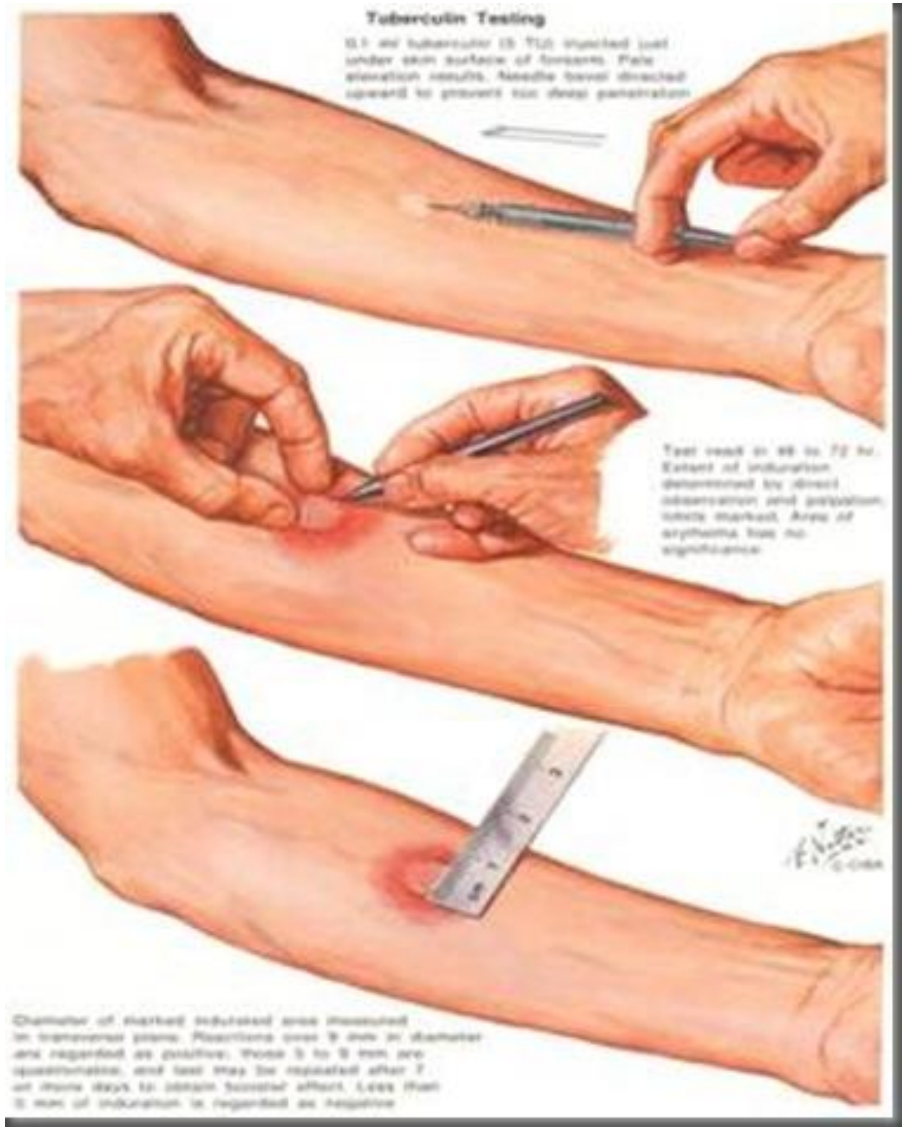
Th1 cell immunity
prevents from dissemination of BK from site of primo infection

partial cross reactivity with NTM

since 1953:
newborns + 2-year + 11-year old (tuberculin neg)

Tuberculin test (Mantoux):
PPD i.d., reading in 48-72 hrs

Nov 2010:
cancelled
(mandatory for groups at risk)



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 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)

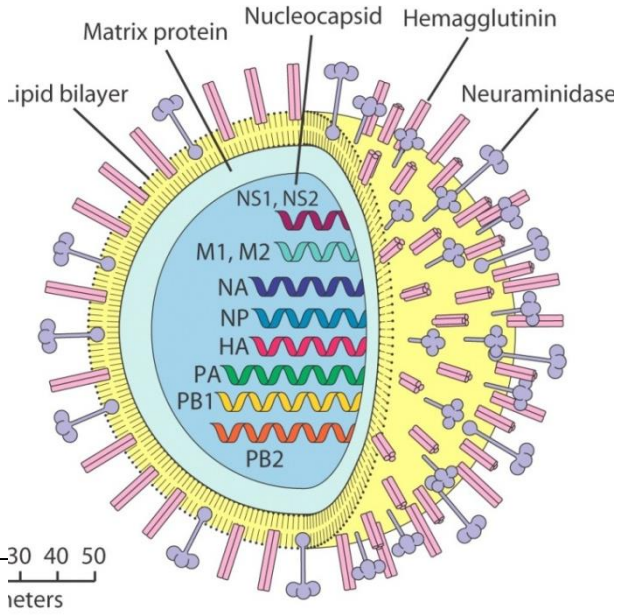
Subunit vaccines

Salmonella Typhi

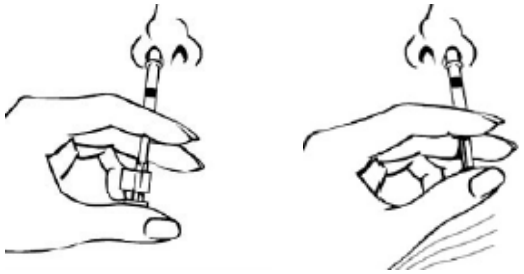
Type of vaccine	subunit
Targetting	Capsular Vi

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 strains reflecting current epidemiological situation:

- type B
- type A H1N1 (protection against pandemic H1N1)
- type A H3N2

RSV

Paramyxovirus

Type of vaccine	subunit
Targetting	Fusion protein

for adults (and pregnant women)

children by 6 months of age: nirsevimab (monoclonal antibody)

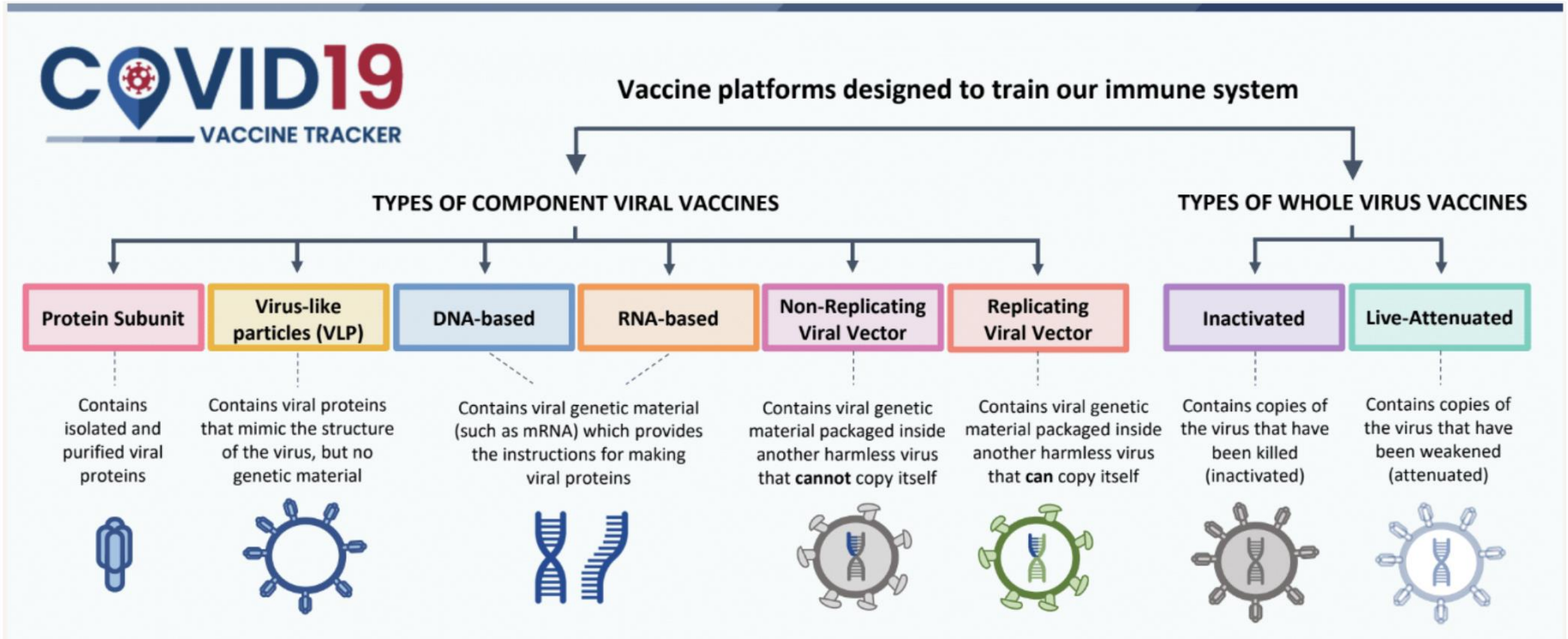
SARS-CoV-2

Types of vaccines

- ~~toxoids (anatoxins)~~
- inactivated (whole cell)
- live attenuated
- subunit

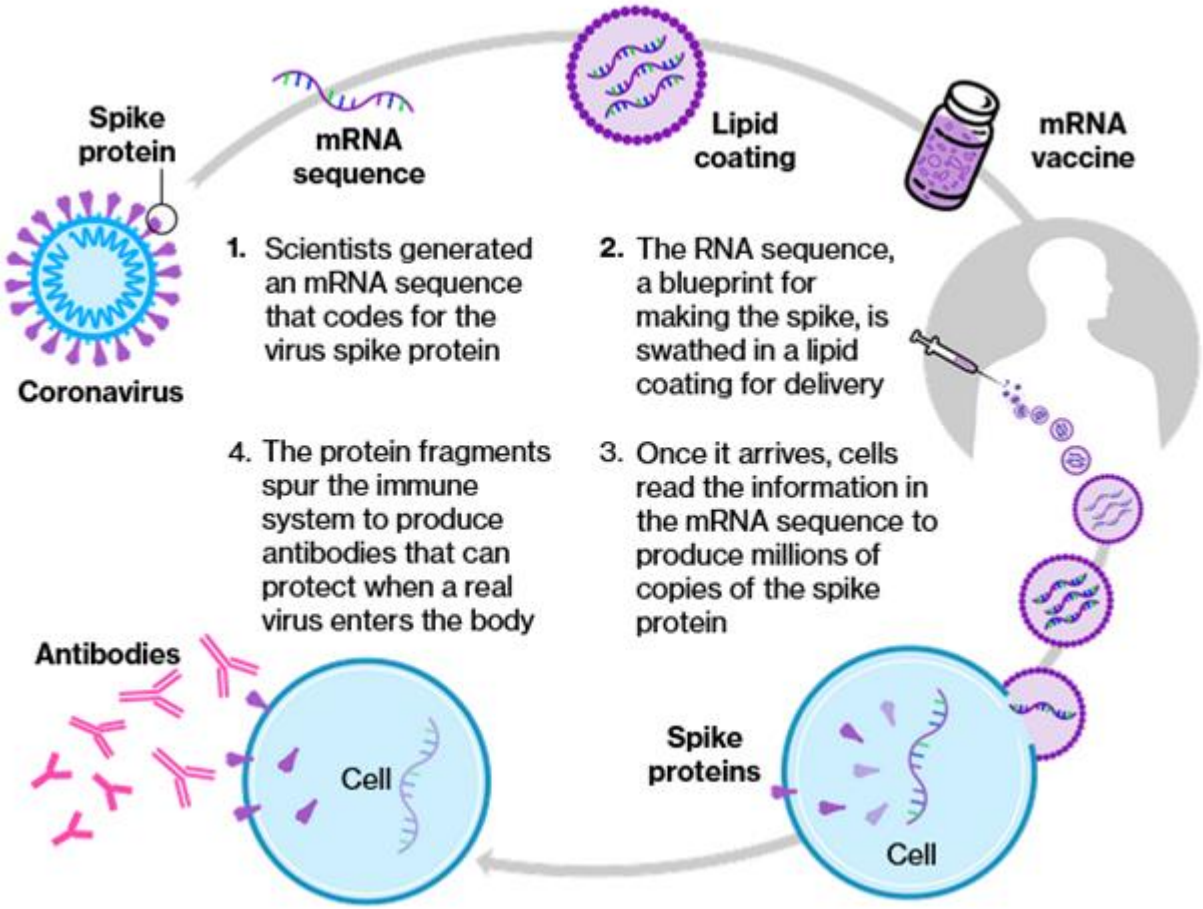
- viral vector (non-replicating) with DNA
- lipid nanoparticles with DNA or RNA

TYPES OF VACCINES



→ monovalent Omicron LP.8.1

mRNA



ww.bloomberg.com

Last slide

live attenuated vaccine	inactivated (subunit) vaccine
measles, mumps, rubella, VZV	diphteria, tetanus, pertussis
tuberculosis	Hib
poliomyelitis OPV	poliomyelitis IPV
rotaviruses	hepatitis A, B
yellow fever	pneumococcus, meningococcus
	tick borne encephalitis
	influenza
	RSV
	SARS-CoV-2
	rabies
	papillomaviruses
	typhoid fever
	cholera

CAVE patients with immunodefects