

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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# 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%)



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 IPPIS  
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; IgM production without immunological memory; not mature in children below 2 yrs of age; capsular polysaccharides

--> **conjugate vaccines:**

T-indep. 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** (recombinant, split ...)  
lower occurrence of adverse events

## 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

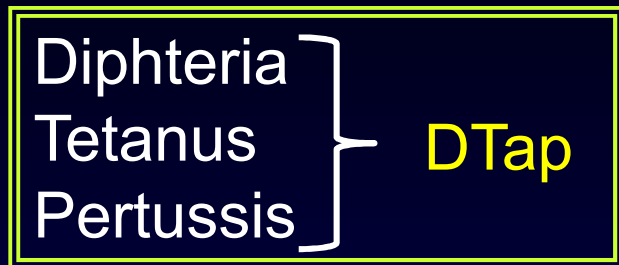
Dose 2: 2 months apart

Dose 3: 6 months apart

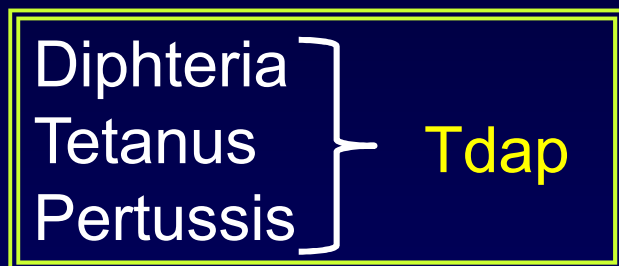
(to complete at 11 to 13 months of age)

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

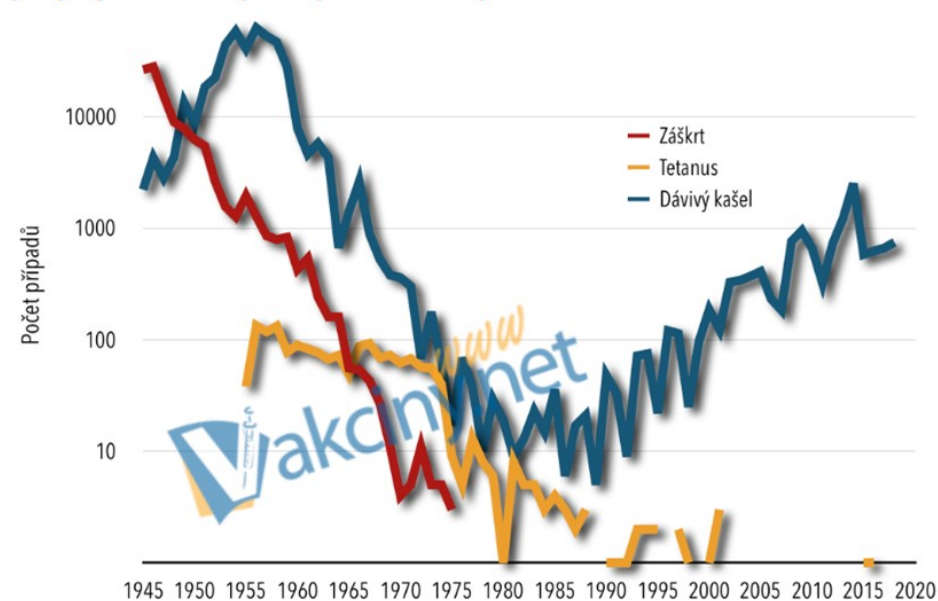
Toxoid

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 acelular)

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

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

BUT

- lower protectivity (fewer childred develop antibodies)
- immunity against selected antigens only

# Clinical picture

## Pertussis (whooping cough)

incubation 4 - 21 days

transmission through droplets or direct

non-invasive disease

Stages:

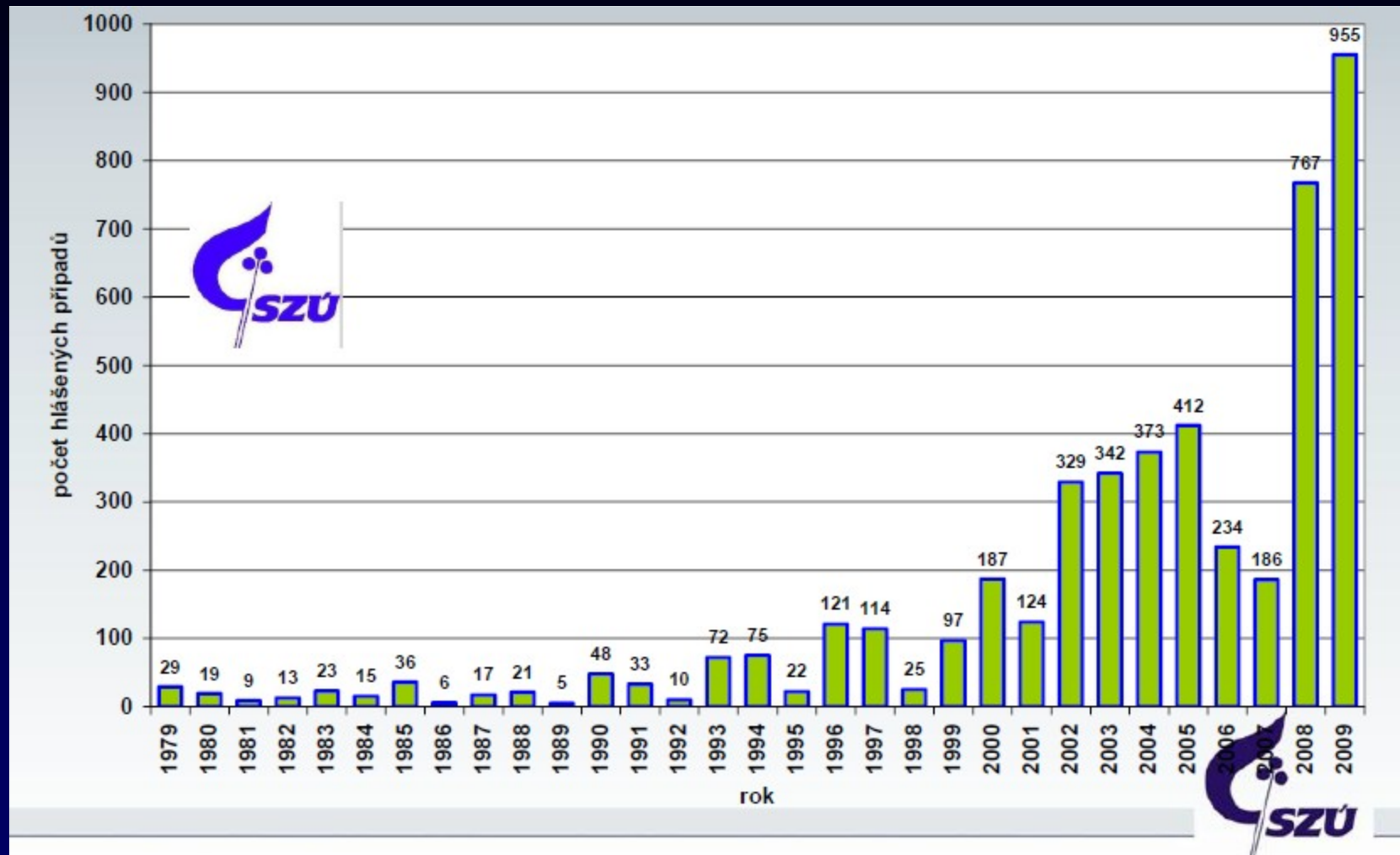
- catarrhal (rhinitis)
- paroxysmal (attacks of cough, dyspnoea, vomiting)
- convalescent (risk of secondary infection, encephalopathy)

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%)

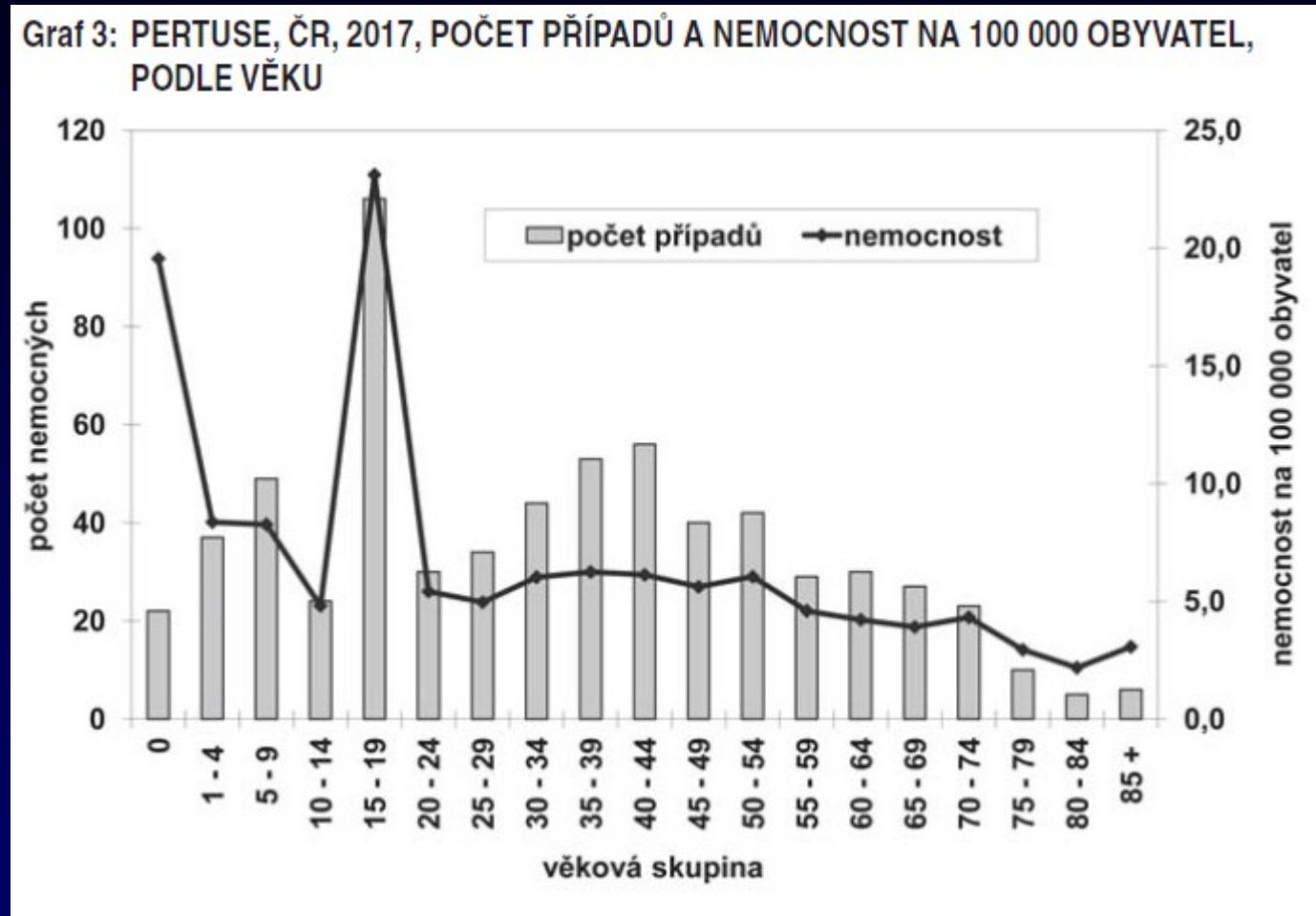


2014: 2,300 cases

2018: 750 cases



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



Fabiánová et al. Zprávy CEM 2018.

## 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

(Warfel et al. Acellular pertussis vaccines protect against disease but fail to prevent infection and transmission in a nonhuman primate model. PNAS 2014)

  - 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)
- Non-vaccinated children
- Difficult diagnostics in early stages of disease
- Bacterial evolution driven 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

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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## OPV:

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

## IPV:

- no risk to people with immunodefects
- no risk of getting a circulating vaccine-derived poliovirus
- effect of vaccine not lowered when co-infection with other enterovirus occurs

# 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

# *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 or 13 serotypes

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

Vaccination for patients after splenectomy !

# 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")

# Other vaccines

**Live attenuated**

# Virus chickenpox herpesvirus VZV, HHV3

Type of vaccine

live attenuated

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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

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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

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Th1 cell immunity

prevents from dissemination of BK from site of primo infection

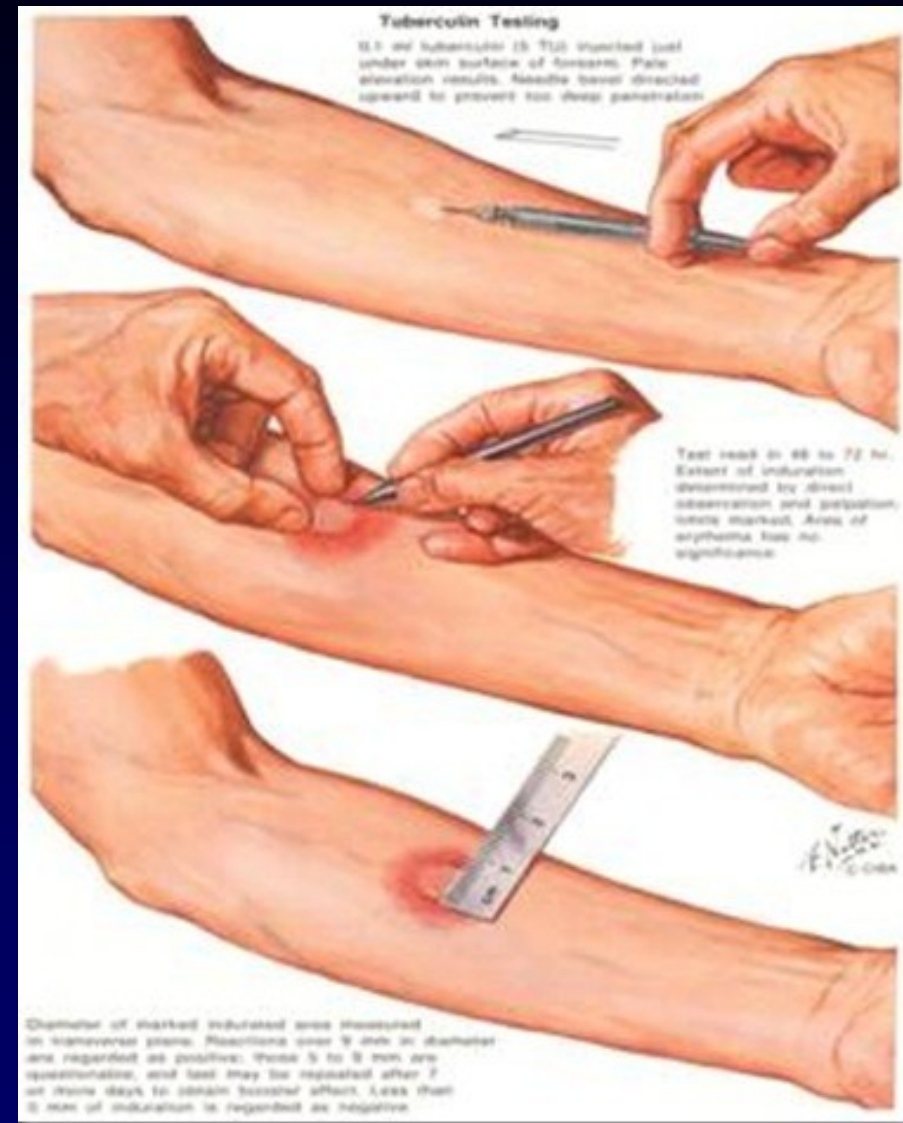
partial cross reactivity with NTM

since 1953:

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

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

Nov 2010:  
cancelled  
(mandatory for groups at risk)



# Subunit vaccines

# Virus influenza

Influenzavirus A, Influenzavirus B

Type of vaccine      subunit, split

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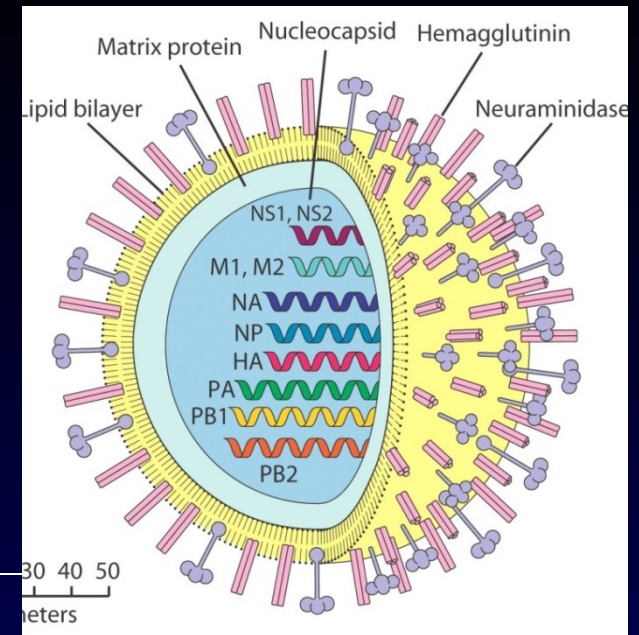
Targetting              Haemagglutinin (HA)  
                                  Neuraminidase (NH)

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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



# *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 available

„meningitis belt“

# *Salmonella Typhi*

Type of vaccine

subunit

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Targetting

Capsular Vi

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# **Inactivated vaccines (whole cell)**

# Virus tick-borne encephalitis Flavivirus

Type of vaccine

inactivated

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





# Virus hepatitis A HAV, Hepatovirus

Type of vaccine

inactivated

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Vaccine against HAV for travellers

# Rabies

Rod Lyssavirus

Type of vaccine

inactivated

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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* (O139)

# 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

## Last slide 2

### active immunization after exposure:

- rabies
- tetanus
- hepatitis B
- hepatitis A
- VZV
- measles

### passive immunization:

- rabies
- tetanus
- hepatitis B
- hepatitis A