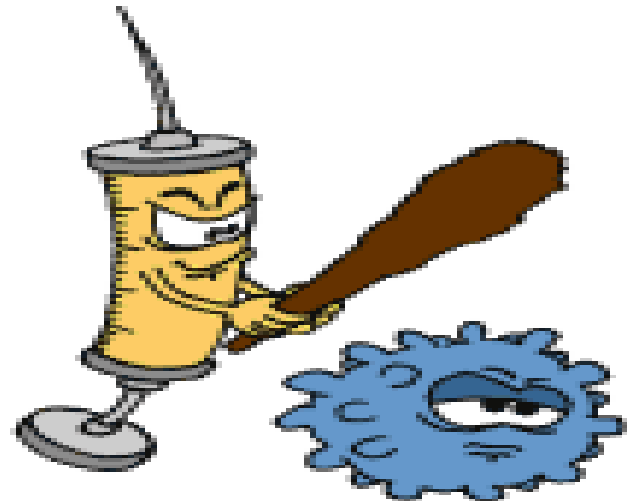
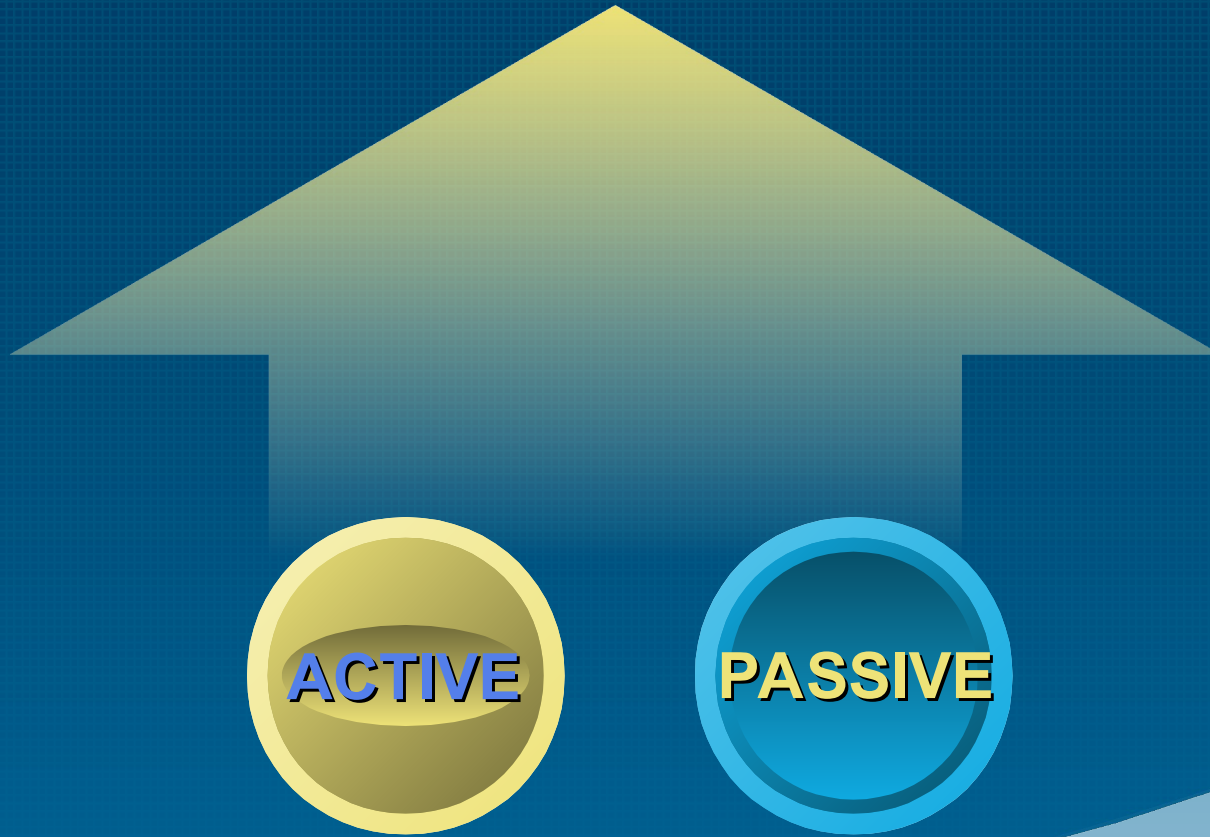


# ***Immunoprophylaxis of infectious diseases***



# *Immunoprophylaxis*



# ***Active immunisation***

- introduction into the body antigens without toxicity and virulence that can stimulate and induce an immune response similar to that produced by natural infection;
- produce an immunity over a long period of time: months or years;
- immunity occurs after a certain latency period, weeks to several months, required to produce its own antibody.

# Vaccines classification

1. By the nature of the antigen

2. By number of antigenic components

3. By the way of the vaccine is prepared

4. By requirement of vaccination

# ***1. By the nature of the antigen***

## **Antiviral v.**

- ✓ flu vaccine,
- ✓ against measles,
- ✓ against rubella,
- ✓ against polio,
- ✓ anti- viral hepatitis A / B.

## **Antibacterial v.**

- ✓ BCG,
- ✓ against diphtheria
- ✓ against tetanus,
- ✓ against typhoid,
- ✓ anti-pneumococcal

## **Antimicelian v.**

- ✓ Anticandidozic vaccine
- ✓ less used.

## **Antiprotozoal v.**

- ✓ candidate antimalarial vaccine.

## 2. *By number of antigenic components*

### Monovalent v.

- ✓ the antigen originates from one microbial species;

- ✓ BCG (antituberculosis).

### Complex v.

- ✓ contain more serotypes of the same species;

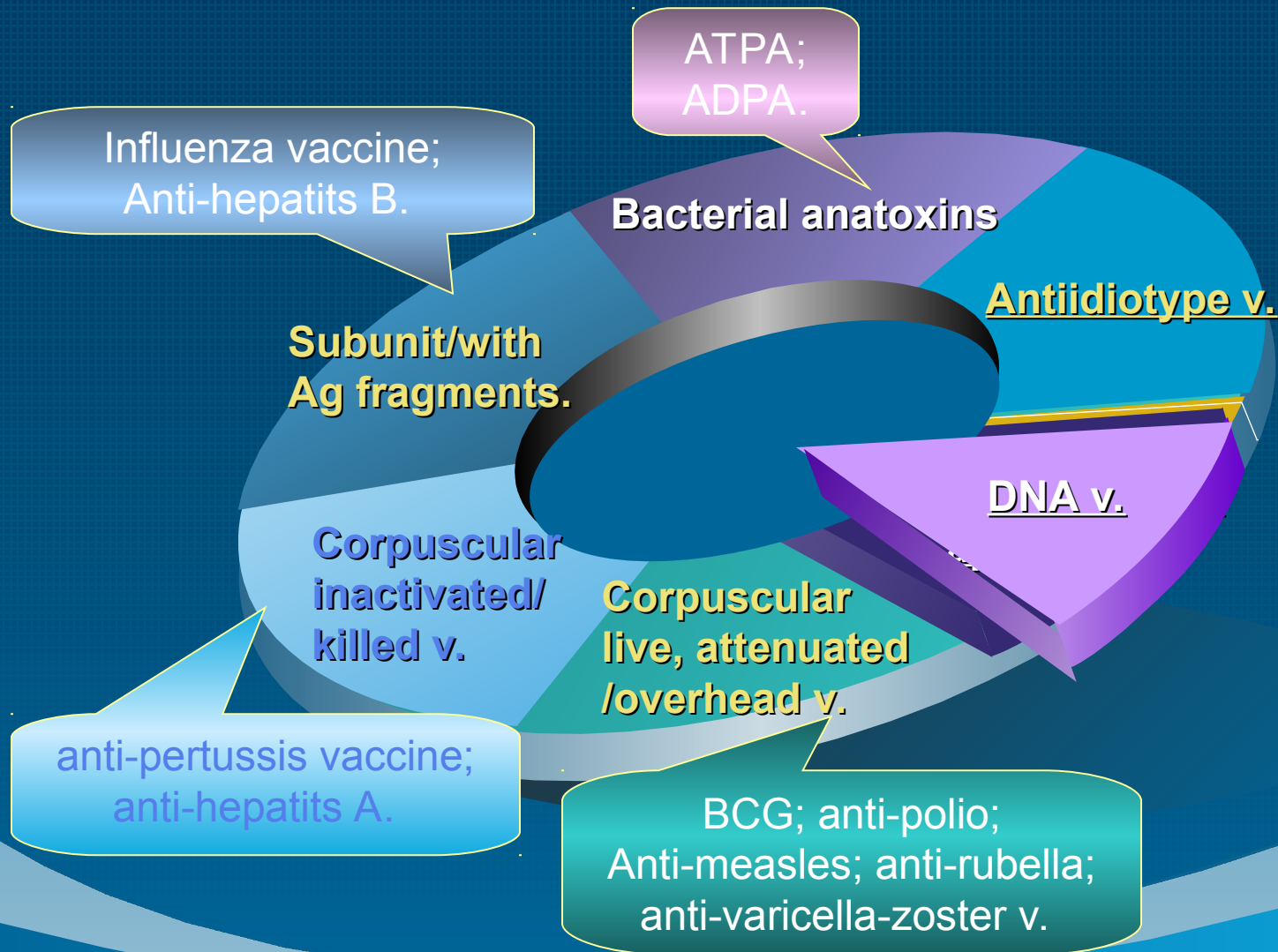
- ✓ Influentza vaccine,
- ✓ Anti-polio v.

### Associate v.

- ✓ combine more antigens from different species;

- ✓ Trivalent – ROR, DTPa,
- ✓ Tetravalent – Tetraxim,
- ✓ Pentavalent – Pentaxim,
- ✓ Hexavalent – Infanrix Hexa.

### 3. *By the way of the vaccine is prepared*



# 4. *By requirement of vaccination*

## Mandatory

- ✓ applied to the whole populations according to NIP;
- ✓ In Romania, it includes following vaccinations :
  - BCG;
  - VPI;
  - DTPa/dT;
  - anti-*Haemophilus influenzae* type B;
  - antihepatitis B with AgHBs recombinant DNA;
  - ROR and antipneumococic conjugate.

## In situations with increased epidemiological risk

- ✓ tourists who visit **endemic areas**,
- ✓ **natural calamities**, floods, earthquakes, wars,
  - anti-hepatitis A v.,
  - anti-typhoid v.,
  - anti-dysentery.

## Under high individually risk

- ✓ **Professional risk**: medical staff, diplomatic or military;
- ✓ **Biological risk**: over age 65;
- ✓ **Pre-existing pathology**: chronic diseases, immunosuppression, etc.



# NIP (PNI) Romania

Vaccinul	0-7 days	2 months*	4 months*	11 months*	12 months	5 years**	6 years***	14 years
BCG	BCG							
Anti-polio inactivated		VPI	VPI	VPI			VPI	
Diftero-tetano-pertussis		DTPa	DTPa	DTPa			DTPa	DTPa
<i>Haemophilus</i> type B		Hib	Hib	Hib				
Anti-hepatitis B	Hep. B	Hep. B	Hep. B	Hep. B				
Anti-measels-anti-rubella-anti-mumps					ROR	ROR		
Pneumococcal conjugate		PCV	PCV	PCV				

\* concomitantly with the administration of the hexavalent preparation DTPa + VPI + Hib + Hep.B at 2, 4 and 11 months.

\*\* ROR booster at 5 years;

\*\*\* in the tetravalent DTPa + VPI vaccination;

# Vaccination program USA 2015

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13–15 yrs	16–18 yrs
Hepatitis B <sup>1</sup> (HepB)	1 <sup>st</sup> dose	2 <sup>nd</sup> dose			3 <sup>rd</sup> dose											
Rotavirus <sup>2</sup> (RV) RV1 (2-dose series); RV5 (3-dose series)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	See footnote 2											
Diphtheria, tetanus, & acellular pertussis <sup>3</sup> (DTaP: <7 yrs)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	3 <sup>rd</sup> dose			4 <sup>th</sup> dose				5 <sup>th</sup> dose				
Tetanus, diphtheria, & acellular pertussis <sup>4</sup> (Tdap: ≥7 yrs)														(Tdap)		
<i>Haemophilus influenzae</i> type b <sup>5</sup> (Hib)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	See footnote 5		3 <sup>rd</sup> or 4 <sup>th</sup> dose See footnote 5									
Pneumococcal conjugate <sup>6</sup> (PCV13)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	3 <sup>rd</sup> dose		4 <sup>th</sup> dose									
Pneumococcal polysaccharide <sup>6</sup> (PPSV23)																
Inactivated poliovirus <sup>7</sup> (IPV: <18 yrs)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	3 <sup>rd</sup> dose							4 <sup>th</sup> dose				
Influenza <sup>8</sup> (IIV; LAIV) 2 doses for some: See footnote 8					Annual vaccination (IIV only) 1 or 2 doses						Annual vaccination (LAIV or IIV) 1 or 2 doses		Annual vaccination (LAIV or IIV) 1 dose only			
Measles, mumps, rubella <sup>9</sup> (MMR)					See footnote 9		1 <sup>st</sup> dose					2 <sup>nd</sup> dose				
Varicella <sup>10</sup> (VAR)							1 <sup>st</sup> dose					2 <sup>nd</sup> dose				
Hepatitis A <sup>11</sup> (HepA)							2-dose series, See footnote 11									
Human papillomavirus <sup>12</sup> (HPV2: females only; HPV4: males and females)														(3-dose series)		
Meningococcal <sup>13</sup> (Hib-MenCY ≥ 6 weeks; MenACWY-D ≥ 9 mos; MenACWY-CRM ≥ 2 mos)			See footnote 13											1 <sup>st</sup> dose		Booster

Range of recommended ages for all children

Range of recommended ages for catch-up immunization

Range of recommended ages for certain high-risk groups

Range of recommended ages during which catch-up is encouraged and for certain high-risk groups

Not routinely recommended

# Adults Vaccination program USA 2015

VACCINE ▼	AGE GROUP ►	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years
Influenza <sup>*,2</sup>		1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>*,3</sup>		Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs					
Varicella <sup>*,4</sup>		2 doses					
Human papillomavirus (HPV) Female <sup>*,5</sup>		3 doses					
Human papillomavirus (HPV) Male <sup>*,5</sup>		3 doses					
Zoster <sup>6</sup>						1 dose	
Measles, mumps, rubella (MMR) <sup>*,7</sup>		1 or 2 doses					
Pneumococcal 13-valent conjugate (PCV13) <sup>*,8</sup>		1-time dose					
Pneumococcal polysaccharide (PPSV23) <sup>8</sup>		1 or 2 doses					1 dose
Meningococcal <sup>*,9</sup>		1 or more doses					
Hepatitis A <sup>*,10</sup>		2 doses					
Hepatitis B <sup>*,11</sup>		3 doses					
Haemophilus influenzae type b (Hib) <sup>*,12</sup>		1 or 3 doses					

\*Covered by the Vaccine Injury Compensation Program

# Adults vaccination program USA 2015

VACCINE ▼	INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV]) <sup>4,6,7,8,13</sup>	HIV infection CD4+ T lymphocyte count <sup>4,6,7,8,13</sup>		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies) <sup>8,12</sup>	Chronic liver disease	Diabetes	Healthcare personnel
			< 200 cells/ $\mu$ L	$\geq$ 200 cells/ $\mu$ L								
Influenza <sup>*2</sup>			1 dose IIV annually		1 dose IIV or LAIN annually	1 dose IIV annually						1 dose IIV or LAIN annually
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>*3</sup>	1 dose Tdap each pregnancy	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs										
Varicella <sup>*4</sup>		Contraindicated		2 doses								
Human papillomavirus (HPV) Female <sup>*5</sup>		3 doses through age 26 yrs		3 doses through age 26 yrs								
Human papillomavirus (HPV) Male <sup>*5</sup>		3 doses through age 26 yrs		3 doses through age 21 yrs								
Zoster <sup>6</sup>		Contraindicated		1 dose								
Measles, mumps, rubella (MMR) <sup>*7</sup>		Contraindicated		1 or 2 doses								
Pneumococcal 13-valent conjugate (PCV13) <sup>*8</sup>						1 dose						
Pneumococcal polysaccharide (PPSV23) <sup>8</sup>						1 or 2 doses						
Meningococcal <sup>*9</sup>						1 or more doses						
Hepatitis A <sup>*10</sup>						2 doses						
Hepatitis B <sup>*11</sup>						3 doses						
Haemophilus influenzae type b (Hib) <sup>*12</sup>		post-HSCT recipients only				1 or 3 doses						

\*Covered by the Vaccine Injury Compensation Program



For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster



Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)



No recommendation



# *Principles of vaccination*

**Who?**

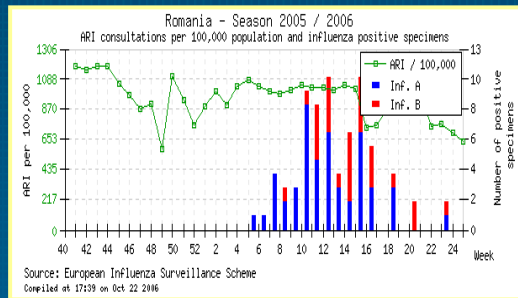


- To protect the age group with maximum receptivity or the highest risk for severe clinical forms of disease.



# Principles of vaccination

When?



■ The vaccination campaign shall be organized before season with the maximum incidence for that disease;

■ Ex: influenza vaccination is being applied in October-November, before a possible winter-spring epidemic (for temperate climates)..



# Principles of vaccination

How?



- It must be count of:
  - the minimal age for vaccination,
  - the route of administration of each vaccine,
  - the number and size of doses,
  - the administration of boosters,
  - the intervals between different immunizations.





# *Principles of vaccination*

## Registration

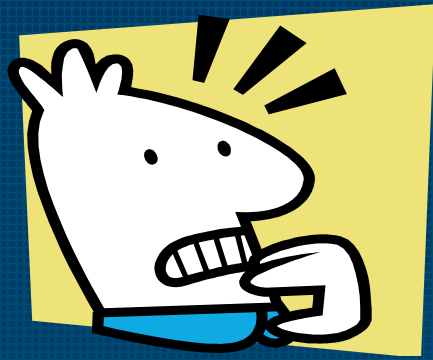


- Newborns receive a vaccination card in maternities;
- They will be recorded both in the individual patient record, in the vaccination card and in the electronic vaccinations register (on-line);
- For adolescents, adults or floating persons, a vaccination certificate is issued.



# Contraindications

DEFINITIVE	TEMPORARY	PRECAUTIONS DTP c/a
1. <u>anaphylactic antecedents at the vaccine or its constituents.</u>	1. <u>Fever conditions above 37.5C.</u>	1. hyperpirexia 40.5C.
2. <u>live, attenuated vaccines - CI of pregnant women and patients with immunodepressions of congenital, acquired or iatrogenic causes.</u>	2. <u>Acute disease with moderate or severe evolution, with or without fever, until the pathological process ceases.</u>	2. crying over 3 hours.
3. Revaccination with DTP c / a - contraindicated for children who developed an encephalopathy within the first 7 days after vaccination.	3. <u>Immunosuppressive treatment: chemo, radiotherapy, high dose corticotherapy.</u>	3. hypotonic-hyporesponsive status within the first 48 hours after vaccination..
	4. <u>Administration of blood preparations and immunoglobulins.</u>	4. febrile / afebrile seizures within the first 3 days after vaccination.



# ***There are NO contraindications:***

- mild or moderate local reactions;
- mild respiratory affection, in afebrility;
- mild diarrheal diseases;
- antibiotic treatment;
- convalescence after acute illness;
- severe post-vaccination history in the family;
- prematurity;
- natural infant feeding;
- allergic antecedents to penicillin or other non-specific allergies;
- contact with a pregnant person.

# ***Post-vaccination adverse reactions***

- medical accident occurred within 1 month after vaccination;
- Only after BCG, some side effects can be spread over a period of 12-16 months postvaccination;
- Undesirable post-vaccination adverse reactions are reported by phone, UPVR (RAPI) system.



# Reporting UPVR (RAPI)

Severe local reactions	CNS reactions	Other severe side effects
✓ Lymphangitis/local, regional lymphadenitis;	✓ acute paralysis (peripheral motor neuron syndrome) post VPO;	✓ anaphylactic reactions; ✓ toxico-septic syndrome;
✓ abscesses at the site of inoculation;	✓ Guillain-Barre syndrome;	✓ collapse; ✓ hyperpyrexia; ✓ arthralgia; very strong myalgia with serious alteration of the general condition;
✓ erythema and extensive swelling / lasting over 3 days / requiring hospitalization.	✓ Encephalopathies / encephalitis; ✓ meningitis; ✓ seizures.	✓ death of the vaccinated person.

# ***Reporting UPVR (RAPI)***

## **LOCAL**



## **CNS**



# REVIEW

1. Which of the following vaccines are corpuscles live attenuated:  
(multiple answer question)

- ☐ anti-pertussis vaccine;
- ☐ anti-measels vaccine;
- ☐ anti-tetanus vaccine;
- ☐ anti-rubella vaccine;
- ☐ BCG.

4. Choose the complex vaccines from the following : (multiple answer question)

- ☐ pentavalent vaccine;
- ☐ influenza vaccine;
- ☐ hexavalent vaccine;
- ☐ antipolio vaccine;
- ☐ BCG.

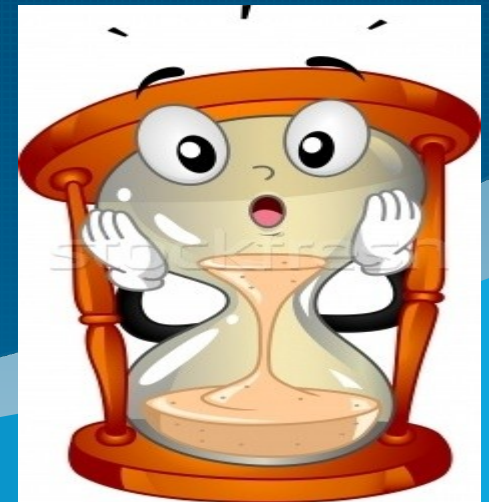


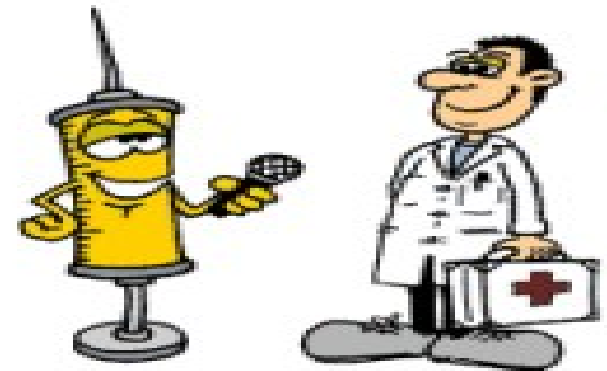


# REVIEW

## 3. Undesirable post-vaccination adverse reactions (the reactions to be declared) are : (multiple answer question)

- erythems / hardening strictly in the place of inoculation;
- erythema / swelling extended to the adjacent joint;
- erythema / swelling severe over 3 days;
- local reactions that require patient hospitalization;
- all of the above.





# **National Immunization Programme Romania**

## **I. Obligatory vaccinations**





# I. BCG Antituberculosis Vaccination



- live strains of *Mycobacterium tuberculosis bovis* with attenuated virulence;

## Presentation form:

- ampoules with 2 mg of live, freeze-dried, lyophilized bacterial mass, white powder, non-adherent to the vial walls;
- As a solvent - medium Sauton, a clear, colorless liquid, supplied in separate vials;
- 1 BCG vaccine = 20 vaccine doses.





# I. BCG Antituberculosis Vaccination



## Administration:

- strictly id. 0.1 ml of suspension in the postero-external area of the left arm,
- formation of a 5-6 mm diameter papule, which persists for 30 minutes.;
- erythematous, glossy - pustular, with or without subsequent fistulization - central crust.
- After removing the crust - a depigmented and slightly uneven scar.



# I. BCG Antituberculosis Vaccination

## Efficiency:

- for the prophylaxis of disseminated tuberculosis or meningitis in tuberculosis for children under 5 years of age;
- Can not prevent the spread of Koch bacillus strains in the population!

## Vaccination scheme:

- BCG first vaccination - in maternity, in the first 2-7 days of life or until the age of 2 months - W under 2500g;
- Read postvaccinal scar - 5 to 10 months.



# I. BCG Antituberculosis Vaccination

## **Definitive contraindications:**

- Newborns from HIV+; mothers;
- tuberculin positive reactions.

## **Temporary contraindications:**

- W under 2500 g at birth;
- acute febrile illness;
- the period of infectious disease status;
- Dystrophies / malnutrition;
- transient immune deficiencies.

## **Postvaccinal Complications:**

- Abscesses at the site of inoculation;
- Local or regional lymphadenopathies;
- Osteitis / osteomyelitis - 8-16 months after vaccination;
- Disseminated infection with the vaccine strain of *M. tuberculosis bovis* 1-12 months after vaccination.



# I. BCG Antituberculosis Vaccination

Most of the World's population is covered by universal BCG vaccination

2011

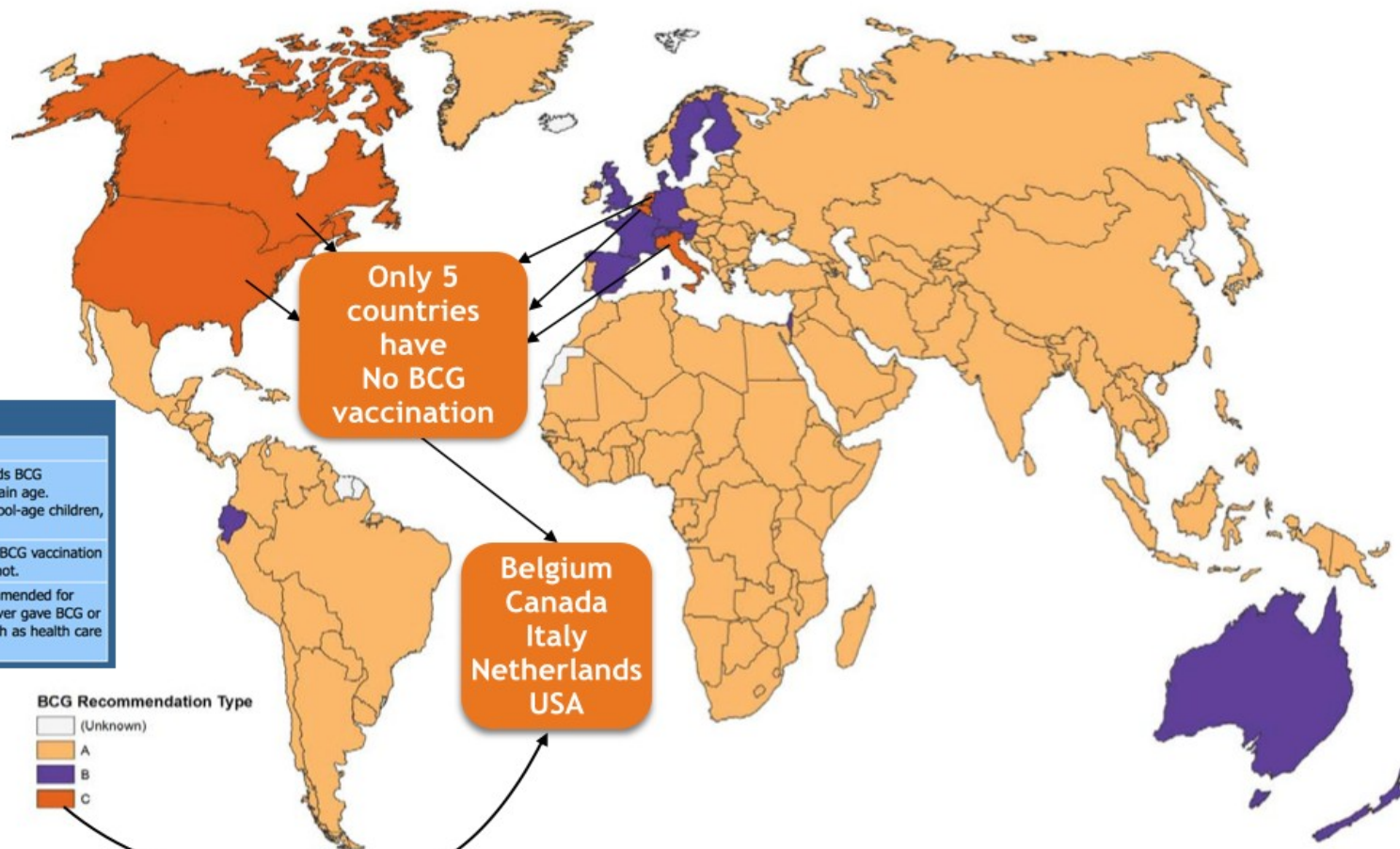
Only 5 countries have No BCG vaccination

Belgium  
Canada  
Italy  
Netherlands  
USA

BCG Recommendation Types	
Type	Description
A	This country currently recommends BCG vaccination for everyone at a certain age. (Example: BCG at birth or for school-age children, etc.)
B	This country used to recommend BCG vaccination for everyone, but currently does not.
C	BCG vaccination was never recommended for everyone in this country. (i.e.: never gave BCG or given only to high risk groups such as health care workers.)

BCG Recommendation Type

- (Unknown)
- A
- B
- C

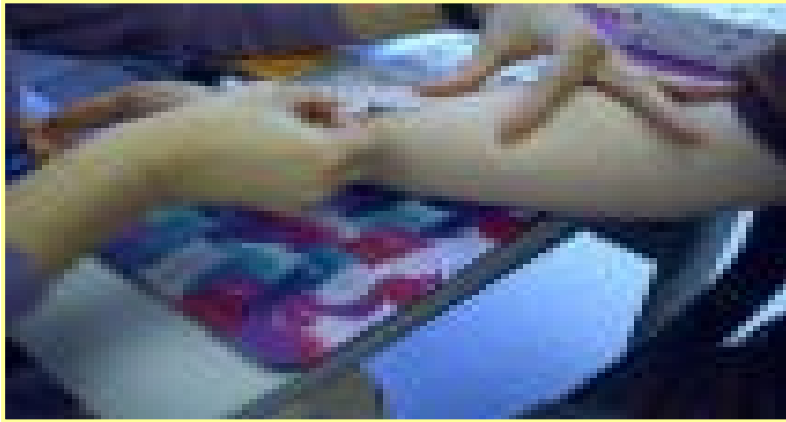


**Figure 2. Map displaying BCG vaccination policy by country.** A: The country currently has universal BCG vaccination program. B: The country used to recommend BCG vaccination for everyone, but currently does not. C: The country never had universal BCG vaccination programs.  
doi:10.1371/journal.pmed.1001012.g002





# I. BCG Antituberculosis Vaccination



## Tuberculin IDR (Mantoux test)

- i.d., 2 units / 0.1 ml PPD, purified tuberculin protein fraction,
- ampoules with 1 ml of product serving on average for 6 tests.





# I. BCG Antituberculosis Vaccination



## Reading the reaction:

- at 72 h,
- the transverse diameter of the induced dermal papule
- its appearance of fistulae, necrosis, ulceration, without taking into account simple erythematous reactions.





# I. BCG Antituberculosis Vaccination

- **Negative reaction:** the diameter of the induced papule is 0 to 9 mm;
- **Positive reactions:** age and presence of the vaccine scar
  - **In the absence of the vaccine scar:** positive reaction = bacillary infection;
  - **In the presence of the vaccine scar:**
    - children between 0-5 years of age are controlled by radiography in case of tuberculin reactions of 10-14 mm, with consistent induration, necrosis, flicthene, general affection, or in case of reactions greater than 15 mm;
    - children over the age of 5 years and young people are controlled by radiographs in case of 10-19 mm reactions with harsh induration, necrosis, flickering, general damage or in case of reactions greater than 20 mm.





(a)



(b)

	✓	Inner square lighter than outer circle. <i>If the expiry date has not been passed, USE the vaccine</i>
	✓	At a later time, inner square still lighter than outer circle. <i>If the expiry date has not been passed, USE the vaccine</i>
	✗	Discard point: Inner square matches colour of outer circle. <i>DO NOT use the vaccine. Inform your supervisor</i>
	✗	Beyond the discard point: Inner square darker than outer circle. <i>DO NOT use the vaccine. Inform your supervisor</i>



## II. Anti-polio vaccination

### IPV

- strains of serotypes 1,2,3 inactivated with formalin;
- in countries with high economic standards in Europe, USA, Canada;
- Romania introduced it into the prime vaccination of infants from 2008, and from 2010 for boosters.

### OPV

- living strains of serotypes 1,2,3 of the poliomyelitis virus;
- is easy to administer orally, has a low cost price;
- **Disadvantage: post-vaccinal paralysis accidents – flaccid acute paralysis FAP.**

From April  
2016, bivalent  
recommendation of  
1.3!



## II. Anti-polio vaccination





## II. Anti-polio vaccination

### Presentation form:

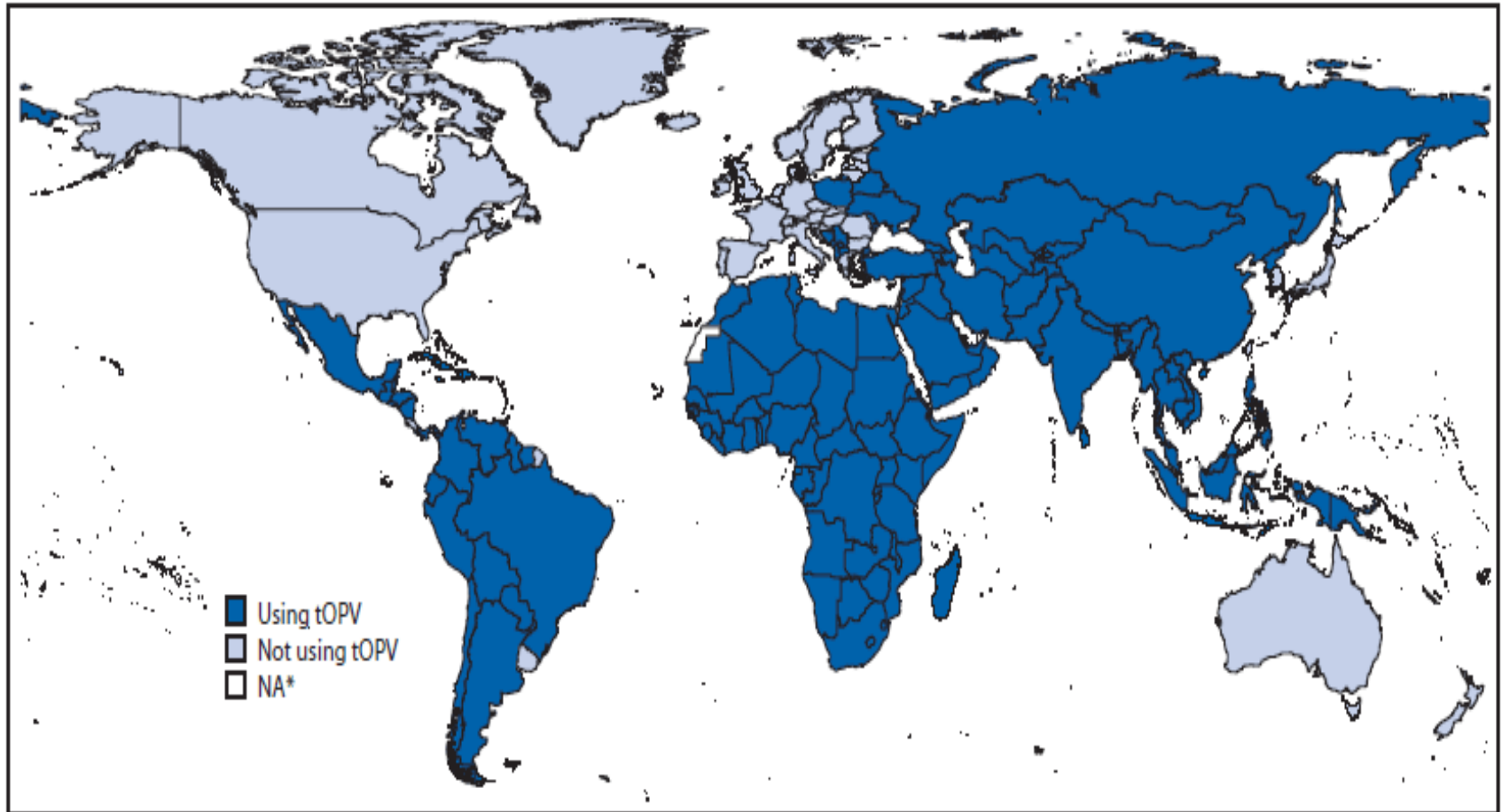
- Inactivated vaccine - pre-filled syringes;
- Sabin Vaccine - vials with clear, light pink liquid;
- It is not allowed to get turbid or become yellow-citrin!

### Vaccination scheme:

- First vaccination - 3 doses (0.5ml) at 2, 4, 11 months as a component in the hexavalent vaccine);
- Boosters of 1st dose of IPV (tetraivalent preparation) i.m., at 6 years. In those vaccinated with DTPa at 4 years, monovalent revaccination with IPV, i.m., at 8 years, is maintained until 2015.



## II. Anti-polio vaccination





## II. Anti-polio vaccination

### Administration rules :

#### OPV

- ✓ If regurgitation or vomiting occurs after administration - repeat the vaccination at the same session;
- ✓ Do not take the mother's milk 3 hours before and after taking the vaccine;
- ✓ **Contraindicated intramuscular injections or surgical interventions that may be delayed for 30 days postvaccinal (any treatment will be given intravenously);**
- ✓ febrile states will be treated with antipyretics in the first 6 weeks of vaccination.



## II. Anti-polio vaccination

### Definitive contraindications for OPV:

- HIV infected children or immunodeficiency of any aetiology;
- family contacts.

### Temporary contraindications for OPV:

- acute febrile disease;
- medium and severe clinical forms of diarrheal disease.







## II. Anti-polio vaccination

**Post-vaccination adverse reactions (in the case of OPV) :**

- Minor: discreet pharyngitis, 1-2 low consistency stool;
- Postvaccinal acute FAP (paralysis): within 4-30 days of the vaccinated person and 4-75 days on the contact of the vaccinated.







## II. Anti-polio vaccination

**Live virus**

**Intestinal reproduction**

**1 case / 750,000 doses (first dose administered)**

**Vaccinated**

**contacts**

**immunosuppressed**



# III. Vaccination with DTPa / dT



## Types of preparations:

- Diftero-tetano-pertussis trivacin - DTPa (Infanrix);
- Diphtheria-tetanus dT - in the vaccination of individuals over 14 years of age;
- Tetravalent / pentavalent / hexavalent preparations:
  - Tetraxim (DTPa + VPI),
  - Pentaxim (DTPa + VPI + anti *Haemophilus influenzae* tip *b*).
  - Hexavalent (DTPa + VPI + anti *Haemophilus influenzae* tip *b* + anti Hepatită B).





### III. Vaccination with DTPa / dT



#### Presentation form:

- dT - vials with 0.5 ml / 1 white-milky liquid dose;
- commercially available preparations - pre-filled syringes;

#### Administration :

- i.m., deep - in the infant in the thigh(ham) region, at the 1/3 higher than the medial joint, 2-3 cm lateral to the median line
- or in deltoid in adolescents and adults.



## III. Vaccination with DTPa / dT

### Vaccination schedule with DTPa / dT:

- **Priming:** 3 doses of 0.5 ml DTPa im., at 2,4,11 months concomitantly with IPV, anti-*Haemophilus influenzae type b* and anti-Hepatitis B (hexavalent vaccine);
- **Booster** - at 6 years, with a dose of 0.5 ml DTPa i.m. (tetraivalent vaccine);
- **Booster** - at 14 years, at a dose of 0.5 ml dT;
- Subsequently, from 10 to 10 years, 0.5 ml dT im boosters to maintain the level of protective antibodies;
- If a booster is delayed for various reasons, the vaccination schedule continues, without resuming from the beginning!



# III. Vaccination with DTPa / dT

## Temporary contraindications:

- febrile condition,
- acute infectious diseases,
- TB in evolution.

## Definitive contraindications:

- Encephalopathy pre-existing or onset within the first 7 days after the first dose;

## Precautions for the pertussis component :

- hyperpyrexia greater than or equal to 40°C
- collapse / shock, hypotonic / hypoactive status,
- persistent crying (over 3 hours) within the first 48 hours after vaccination,
- seizures within the first 3 days after immunization.

## Post-vaccination adverse reactions:

- **Local:** erythema, nodule, pain at the site of inoculation;
- **General:** Transient febrile condition,
- **Diphtheria anatoxin** - in adults, delayed type hypersensitivity (Arthus phenomenon);
- **Tetanus anatoxin** - brachial plexus neuropathy (1 case / 100,000 doses), algodistrofic syndrome, guillain-barre syndrome (0.4 cases / 1 million doses); anaphylactic shock - rarissim;
- **Antipertussis component** - persistent crying, convulsions (1/1750 vaccinated persons), hypotonic-hyporesponsive syndrome, postvaccinal encephalopathy (1 case / 2.4 million vaccinations).

# Vaccination with ATPA



## Presentation form:

- ampoules of 0.5, 1, 5 or 10 ml
- aspect of a milky white liquid,
- im. in adult deltoid muscle
- in the absence of ATPA – vaccination with dT.



# Vaccination with ATPA

- I. Primary prophylactic immunization of un-vaccination persons or below the protective level with anti-tetanus antibodies:**
  - 2 doses of 0.5 ml ATPA im. at 30 days + a booster with a dose of 0.5 ml ATPA one year after primo-vaccination and another identical booster 5 years after first boosters;
- II. Vaccination of pregnant women in the 33 weeks of pregnancy with 0.5 ml im. ATPA – of a new pregnancy is revaccination with ATPA only if it has been over 10 years since the last administration;**





# Preventive conduct in case of tetanus wounds

## III. Anti-tetanus prophylaxis post-exposure :

- Correctly vaccinated individuals: 1 dose of 0.5 ml ATPA, im. in the deltoid region;
  - Politraumatism with massive blood loss - 3,000-20,000 IU anti-tetanus serum or 200-500 U anti-tetanus Ig;
  - Unvaccinated or with unknown vaccine history - Anti-Tetanus serum 3.000-20.000 IU (after desensitization) or 200-500 U anti-Tetanus Ig + Accelerated vaccination with 3 doses of 0.5 ml ATPA im, at 14 days + 1 booster at 1 year;
  - In the case of superficial plagues, only anti-tetanus vaccination is administered;
- Surgical wound removal with wide debridement, removal of foreign bodies, excision of devitalized tissues, realization of hemostasis;
  - Aseptization of wound with hydrogen peroxide 3%;
  - Antibioprophylaxis: Penicillin or Erythromycin 2 g / 10 days.



# Vaccination with ATPA

- **There are no contraindications for ATPA emergency vaccination in the presence of tetanus potential wound!**
- Efficiency: 10 years after a complete scheme.





# IV. MMR Vaccination



## Types of vaccine used in Romania

### Monovalent:

- Anti-measles – **Rouvax**;
- Anti-rubella – **Rudivax**, Ervevax, Cendevax;

■ **Bivalent:** MR – **Eolarix**;

■ **Trivalente:** Trimovax, Priorix, MMR

### Presentation form:

- pre-filled syringe with 0.5 ml solvent, with white - yellowish lyophilized vaccine vial.

### The inoculation pathway

- i.m. / sc. for MMR and anti-rubella;  
s.c. in deltoid, for anti-measles.



## IV. MMR Vaccination

### Vaccination table in Romania :

- First vaccination with 0.5 ml ROR, im / cm. at the age of 12 months;
- A booster of 0.5 ml ROR, i.m./ s.c. at 5 years;

### Temporary contraindications :

- febrile condition;
- florid tuberculosis;
- severe malnutrition,
- chronic diseases of the respiratory system during activation period; treatment with immunoglobulins or blood derivatives;
- chemo / radio / cortico-therapeutic treatment.

### Definitive contraindications:

- Anaphylactic antecedents to egg protein or neomycin;
- congenital or acquired immunodeficiencies (leukemias, neoplasms);
- pregnancy.

- **Administration of the anti-measles vaccine after 72 hours of an infected contact can no longer counteract the infection but causes mild measles!**



## IV. MMR Vaccination

### Adverse reactions – 5 to 25 days after vaccination

#### Minore:

- fever;
- rhinopharyngeal catarrh;
- respiratory / ocular symptomatology, rapid transient;
- digestive disorders: nausea, vomiting;
- transient exanthema;
- arthralgia, transient arthritis.



#### Major reactions:

- convulsions;
- postvaccinal encephalopathy;
- meningoencephalitis;
- parotidities or unilateral deafness (due to anti-mumps component);
- rarely thrombocytopenia;
- MMR – Infantile autism ???





# V. Anti-hepatitis B vaccination

## Hepatitis B risk groups:

- Medium, superior and auxiliary medical and sanitary personnel;
- Military personnel;
- Patients with hematologic disorders, neoplasia, multiply blood transfused or organ transplants;
- Staff/residents of childcare facilities, prisons or mental health institutions;
- People from areas with high endemicity;
- People with risk-generating sexual behaviors: homosexuals, bisexuals, prostitutes, people with multiple partners, patients with other sexually transmitted diseases;
- Persons using intravenous narcotics,
- persons who accept tattoo techniques or piercing;
- Newborns with mothers carrying HBV (markers in blood);
- Family members or entourage of HBV-infected persons.





# V. Anti-hepatitis B vaccination

## Types of vaccine :



- **1st generation vaccines:** plasma preparations of AgHBs - disused;
- **Generation II vaccines** - obtained by genetic recombination - **Engerix B, Euvax B, Recombivax;**
- **Third Generation Vaccines** - Gen Hevac B, Gen HBvax;
- **Associated vaccines:**
  - **Twinrix** – inactivated anti-hepatitis A v. + anti-hepatitis B recombinant DNA v.;
  - hexavalent combinations DTPa + VPI + anti-Haemophilus influenzae type b + AgHBs recombinant DNA vaccine.





# V. Anti-hepatitis B vaccination

## Presentation form:

- vials, ampoules or pre-filled syringes with 1 dose for pediatric use (10 g / 0.5 ml) or adult (20 g / 1 ml);

## Administration:

- im. in the antero-external region of the thigh (ham) (in neonates, infants and young children);
- intradermal injection in children over 3 years of age and adults.

## I. Newborns vaccination:

- first dose of 0.5 ml. in the first 24 hours after birth;
- the following 3 doses - at 2, 4 and 11 months in hexavalent vaccine;
- Newborns from mothers carrying HBV (+ markers) :
  - vaccination 0, 1 or 2 and 6 months;
  - in the same time with - 0.5 ml anti-hepatitis B specific IgM in the first few hours after birth.

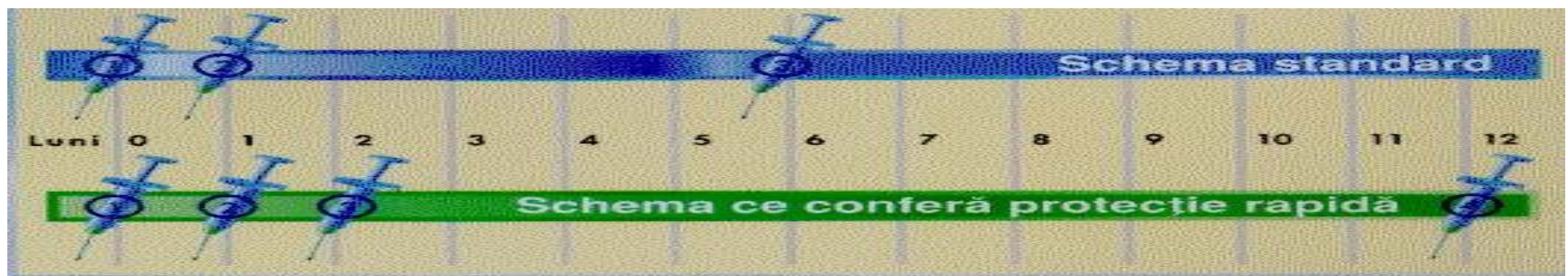


# V. Anti-hepatitis B vaccination

## II. Pre-exposure prophylactic vaccination

- students previously unvaccinated;
- medical students previously unvaccinated;
- adults at risk for hepatitis B.

- im. 3 doses of 0.5 ml (for children up to 15 years of age) or 1 ml (over 15 years of age) - 0, 1 month and 6 months after the first dose;
- Ab antiHBs - 1-3 months after vaccination, in 90% of immunocompetent adults and over 95% of infants;
- postvaccinal protective titre - above 10 mUI / ml.





# New anti-HBV vaccination strategy

## **First vaccination (3 doses) < 25 years:**

- ✓ Preferably in the first year of life;
- ✓ Long-lasting immunity (all life);
- ✓ No boosters required;
- ✓ **Exception: risk groups;**
- ✓ Verification anti-HBs titre at 10 years;
- ✓ Non-protective titre: 1 booster.

## **First vaccination (3 doses) at > 25 years :**

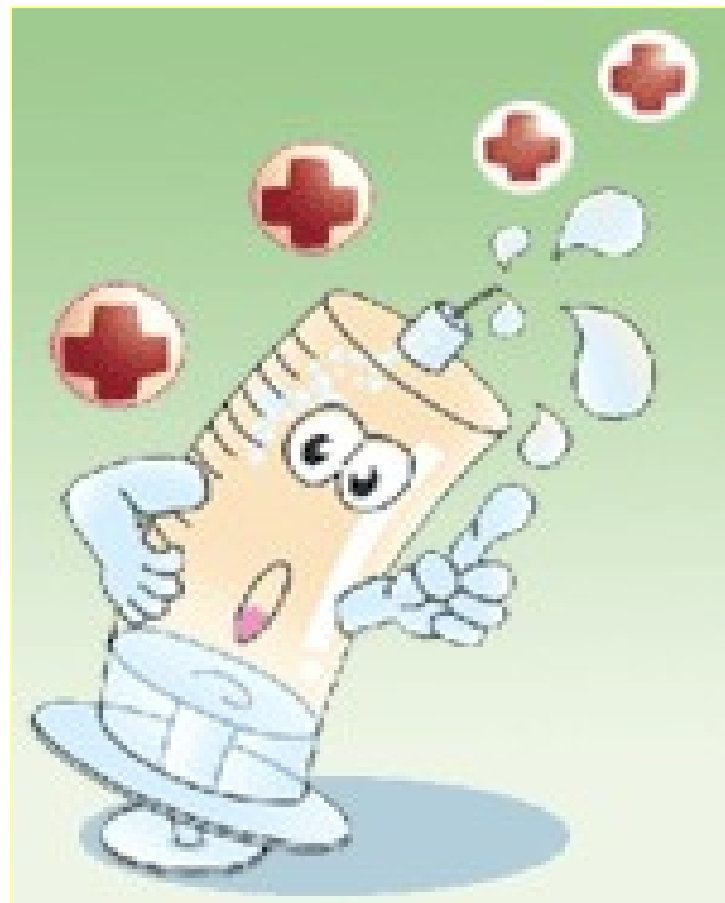
- ✓ Immunity at least 15 years;
- ✓ Dosage of anti-HBs titre at 10-15 years;
- ✓ Non-protective titre: 1 booster;
- ✓ Maximum 6 doses/life.



# V. Anti-hepatitis B vaccination

## III. Prophylactic vaccination post-exposure

- medical staff with major professional risk or sexual contact of persons with acute or chronic type B hepatitis;
- Dosage of AgHBs, Ab antiHBs,
- If the negative, Ab antiHBs previously unvaccinated: rapid 4-dose vaccination at 0,1,2 and 12 months + anti-hepatitis B specific Ig - 0.06 ml / kg, i.m. in the first 24 hours;
- In previously vaccinated: booster if Ab antiHBs <10 mUI / ml.





# V. Anti-hepatitis B vaccination

## Contraindications:

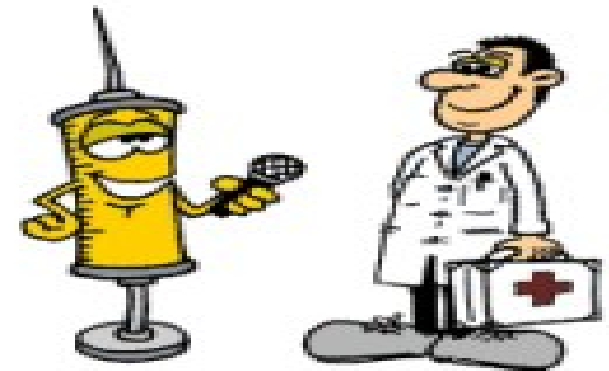
- **Temporary:** severe acute febrile illness;
- **Definitive:**
  - Anaphylactic antecedents to beer yeast;
  - people with plaques sclerosis or with heredo-collateral for demyelinating diseases.

## Side effects:

- **Local reactions** – erythema, induration, pain at the site of inoculation;
- **General** - subfebrility, headache, myalgia, arthralgia, fatigue; digestive disorders - nausea, abdominal pain; allergic manifestations - pruritus, urticaria, erythema multiforme - mild and self-limiting;
- Rarely - encephalitis, paralysis, neuritis.

***MA Hernan et al. - Recombinant hepatitis B vaccine and risk of multiple sclerosis. Neurology sept 2004;63:838-842.***

✓ MS risk in the adult > 18 years - 3 times higher in anti-HBV vaccinated individuals <3 years prior to the onset of neurological signs; In the newborn and small child - zero risk. There was no cause-effect relationship!



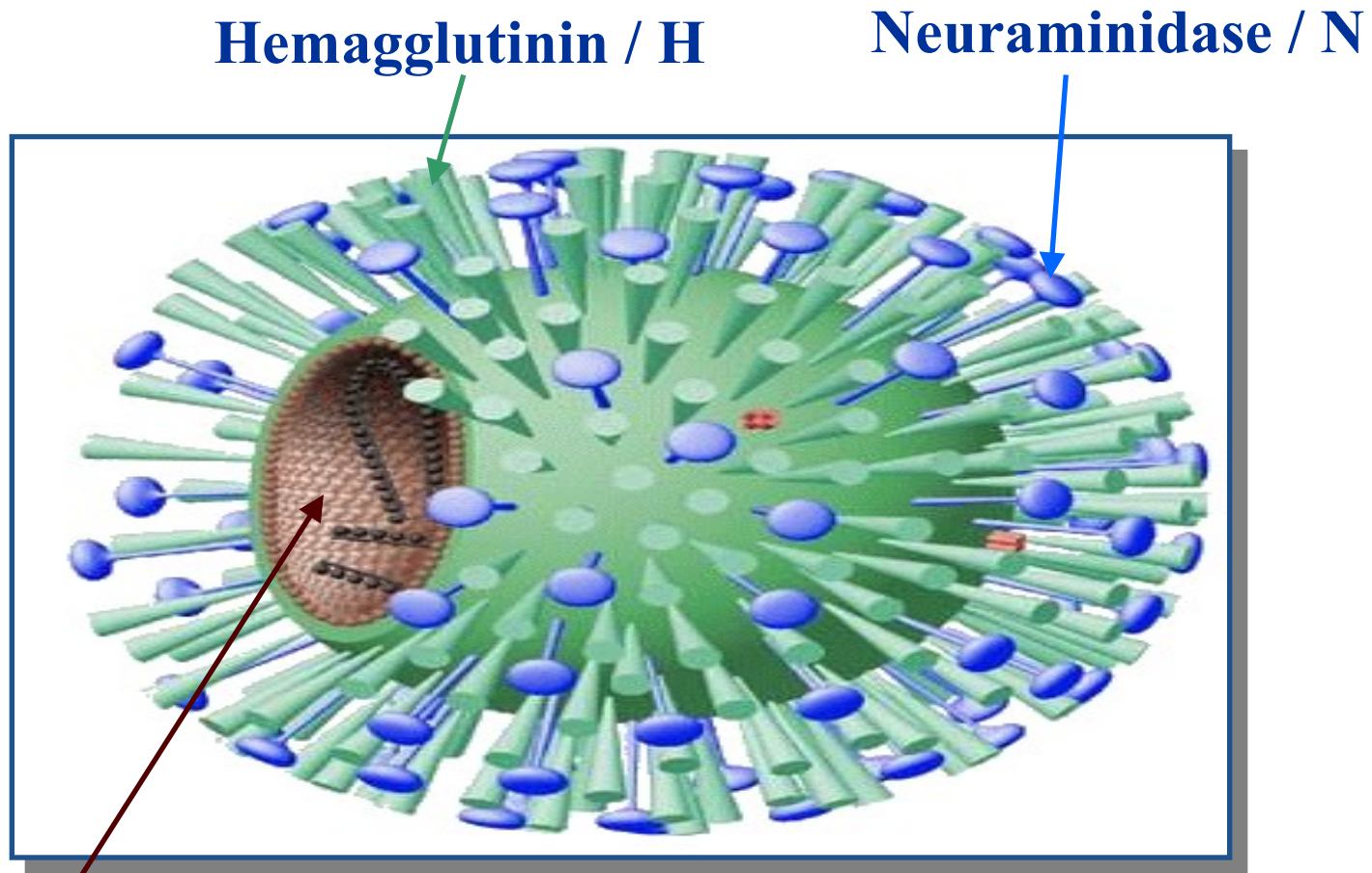
# **National Immunization Programme Romania**

## **II. Vaccinations in high-risk situations**





# I. Influenza vaccination



**RNP with nucleoprotein and 8 segments of single strand RNA**





# Influenza vaccination



## The central component of the virus :

- ✓ It is the soluble antigen of the influenza virus;
- ✓ It consists of ribonucleoprotein, consisting of nucleoprotein and 8 segments of RNA, each of which is a gene;
- ✓ Associated with ribonucleoprotein, viral transcriptase is found, which makes theoretically possible 256 genetic recombinations between ribonucleoprotein fragments;

## The peripheral shell :

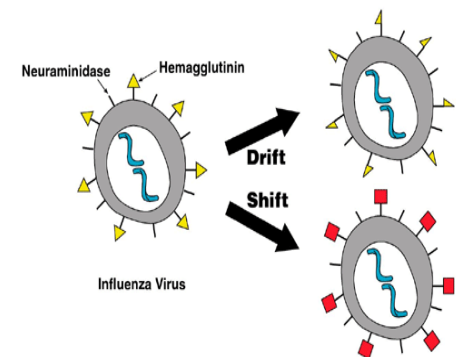
- ✓ Lipoprotein, double layered;
  - ✓ Coated with glycoprotein structures with surface antigens :
    - **Hemagglutinins (H)**, in the form of a stick, at least 16, with a role in attaching the virus to host cell specific receptors and triggering infection;
    - **Neuraminidases (N)**, 9, in the form of a fungus;
- String formula: Ex: A / Hong Kong / 1/68 (H3, N2)

# Influenza vaccination – atg. variability

## Antigenic drifts (minor variability):

- ✓ once every few years the sequence of AAs in the structure of hemagglutinin or neuroaminidase changes and new variants of the same subtype of influenza virus appear;
- ✓ They can cause moderate epidemics;

### Influenza: Antigenic Drift and Shift



## Antigenic shifts (major variability):

- ✓ at a greater interval, 2 different subtypes of influenza virus simultaneously infect the same host cell and may undergo a rearrangement of the 8 gene segments;
- ✓ Generates new subtypes of influenza virus, potentially pandemic, in a naïve immune population.



# I. Influenza vaccination

## Types of flu vaccines:

- Vaccines with live attenuated strains;
- Inactivated influenza virus vaccines;
- Trivalent vaccines with antigenic fragments:
  - only with Surface Atg - Influvac, Fluarix;
  - with surface antigenic fragments but also with the influenza virion - Vaxigrip.





# I. Influenza vaccination

## **Epidemic risk groups:**

- elderly over 65 years;
- long-term residents of the elderly house, other medical-social institutions;
- institutionalized children;
- children and adults with chronic cardio-pulmonary, metabolic, kidney, hemoglobinopathies, congenital or acquired immunodepression;
- children and adolescents treated with Aspirin (Kawasaki disease);
- medical staff, teaching staff, civil servants, etc.

## **Presentation form:**

- pre-filled ampoules / syringes of 0.5 ml / 1 dose;

## **Administration method:**

- 2 doses of 0.5 ml im./deeply sc., at 30 days, for children under 8, previously unvaccinated;
- 1 single dose of 0.5 ml over this age;
- for children between 6 months and 3 years, the dose is 0.25 ml;
- Place of inoculation - in the deltoid or in the anterolateral thigh region (for children under 2 years of age).



# I. Influenza vaccination

## Contraindications:

### ■ Definitive:

- anaphylactic reactions to egg;
- children – vaccinated only with antigenic vaccines, **the corpuscular ones being more reactogenic**;

### ■ Temporary:

- acute infectious diseases;
- febrile conditions, etc.

## Adverse reactions:

### ■ Local:

- pain, edema, swelling;

### ■ Systemic:

- moderate fever, headaches, chills, myalgia, arthralgia;

### ■ Exceptional:

- neuritis, convulsions;
- encephalomyelitis;
- Guillain-Barré syndrome;
- transient thrombocytopenia;

■ Corpuscular vaccines have a more obvious reactogenicity.





# Other vaccines



**Anti-hepatitis A vaccine**



**Anti-Haemophilus vaccine  
type B**



# Other vaccines



**Anti- varicella –  
zoster vaccine**



**Antirabic vaccine**





# REVIEW

1. A 12-month-old child, coming for vaccination to a family doctor, will receive : \* (single answer question)
  - Hexavalent vaccin ;
  - Pentavalent vaccin ;
  - IPV;
  - MMR;
  - DTPa – IPV.
  
2. What vaccine is administered in 2016 at 14 years (in Romania):\* (single answer question)
  - DTP;
  - DTPa;
  - dT;
  - dTpa;
  - Anti-rubella v.





# REVIEW

3. What vaccine is given in the younger child in 4 doses: **\*(single answer question)**

- anti-tetanus vaccine;
- anti-hepatitis B vaccine;
- BCG;
- MMR;
- anti-polio vaccine.

4. A 5-year old child, integrated in the community, with a history of asthma, currently compensated, apparently without other pathological symptoms, is called for vaccination. Determine which preparation is being administered: **\*(single answer question)**

- Tetravalent vaccin ;
- DTPa;
- Nothing is administered;
- IPV;
- MMR.



# Passive immunization

```
graph BT; SERUMS((SERUMS)) --> TotalIg((Total Ig)); SpecificIg((Specific Ig)) --> TotalIg;
```

The diagram illustrates the components of passive immunization. At the top, a yellow rounded rectangle contains the title 'Passive immunization'. Below it, a large blue upward-pointing arrow indicates the flow of information. At the base of the arrow, three circles are arranged horizontally. The leftmost circle is dark blue with a light blue border and contains the word 'SERUMS'. The middle circle is yellow with a dark yellow border and contains the text 'Total Ig'. The rightmost circle is dark blue with a light blue border and contains the text 'Specific Ig'.

**SERUMS**

**Total  
Ig**

**Specific  
Ig**

# 1. Specific sera (antitoxins)

- antibody solutions obtained from the serum of animals - especially horses, immunized with specific antigens;
- severe anaphylactic reactions!!

1. Anti-anthrax serum

2. Anti-botulinum serum

3. Anti-diphtheric serum

4. Anti-rabic serum

5. Anti-tetanic serum

# 1. Specific sera (antitoxins)

## Administration rules :

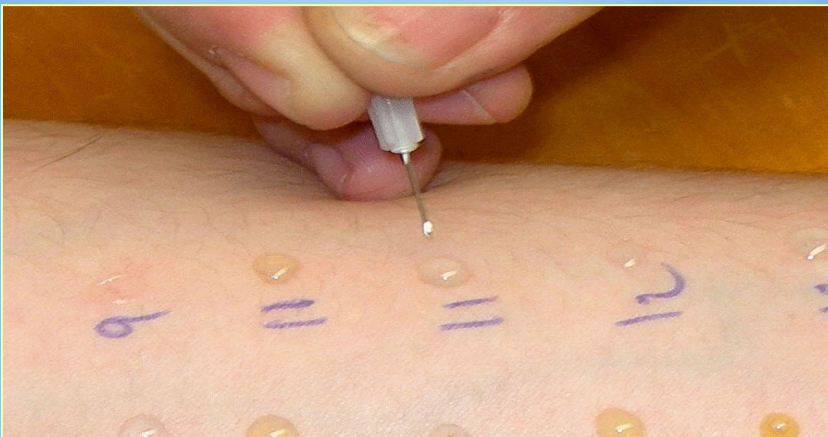
- Dose - calculated according to the intended purpose (curative or prophylactic), age and body weight;
- single dose, in order to increase the effectiveness and decrease the risk of adverse reactions;
- administration as soon as possible because sera can neutralize only circulating toxins, not those fixed on cells;
- administration route - i.m., in thigh region
- careful supervision from the first few minutes (for anaphylactic shock emergency response) and within the next 7 to 10 days for the discovery of possible late reactions.



# 1. Specific sera (antitoxins)

## Administration:

- Anamnesis focused on personal allergic antecedents;
- Mandatory testing of serum sensitivity
  - by conjunctival instillation;
  - scarification tegumentary;
  - intradermal injection of a serum dilution (generally 1/100 or 1/10).



# 1. Specific sera (antitoxins)

## The minimum desensitization scheme :

- negative people to test without a history of allergies;
- **S.c. - 0,25 ml** serum dilution 1/10 in physiological saline → 30 min;
- **S.c. - 0,25 ml** undiluted serum → 30 min;
- **S.c. - 1 ml** undiluted serum → 30 min;
- the rest of the calculated serum dose - **im.**



## Slow desensitization (schema Besredka):

- Sequential, subcutaneous administration over a 30-minute interval of increasing doses with decreasing dilutions,
- In allergic reactions - after 30 minutes of the previous dose administered to which the reaction occurred.



# 1. Specific sera (antitoxins)

## Immediate side effects:

- **Nonspecific febrile reaction** - chills, fever, agitation, drowsiness, heat at the injection site within the first hour after administration;
- **Anaphylactic shock** – urticarial eruption, glottis edema, bronchospasm, hypotension and filiform pulse.



## Late side effects

- **The Arthus phenomenon** - local congestion, progressing sometimes to necrosis and gangrene;
- **Accelerated serum reactions** - after 2-5 days of serotherapy;
- **Serum sickness** - after 6-12 days of serum administration, fever, urticaria, face swelling, glottis edema, arthralgia, neuritis.

## 2. Total immunoglobulins

- sterile solutions containing human IgG, comprising the entire spectrum of infections and immunizations by persons who have passed;
- **In measles prophylaxis** – i.m. **0,2 - 0,4 ml/kg body**, în primele 3-4 zile după contactul infectant; evitate în prezent;
- **In the prophylaxis of viral hepatitis A** - i.m. **0,02 - 0,05 ml/kg body**, in the very first week after infected contact;
- **Monomeric IgG-type immunoglobulins:**
  - i.v. in immunodeficiency replacement therapy (congenital hypogammaglobulinaemia, HIV infection);
  - in autoimmune diseases (idiopathic thrombocytopenic purpura);
  - in the treatment of severe infections with intra-infective immunosuppression (septicemia, meningitis, pneumonia)
  - Ex: Octagam.

### 3. Specific immunoglobulins

- They contain specific human antibodies against a particular micro-organism or a specific antigenic determinant;
- routine Ig - **Anti-Tetanus and anti-rabies Ig**;
- **Varicella-zoster antiviral IgG** - prevention of postexposure disease in immunodeprived children (with leukemias, lymphomas, HIV / AIDS);
- **Cytomegalovirus antiviral Ig** – prophylaxis / treatment of cytomegalovirus disease in transplant recipient patient;
- **Antihepatitis B IgA** (in combination with anti-hepatitis B vaccination):
  - post-exposure prophylaxis in newborn babies from mothers with HBV markers;
  - after mucosal / parenteral contact with infective biological fluids (medical staff, sex contacts).

# Passive immunization products



# Thank you!

