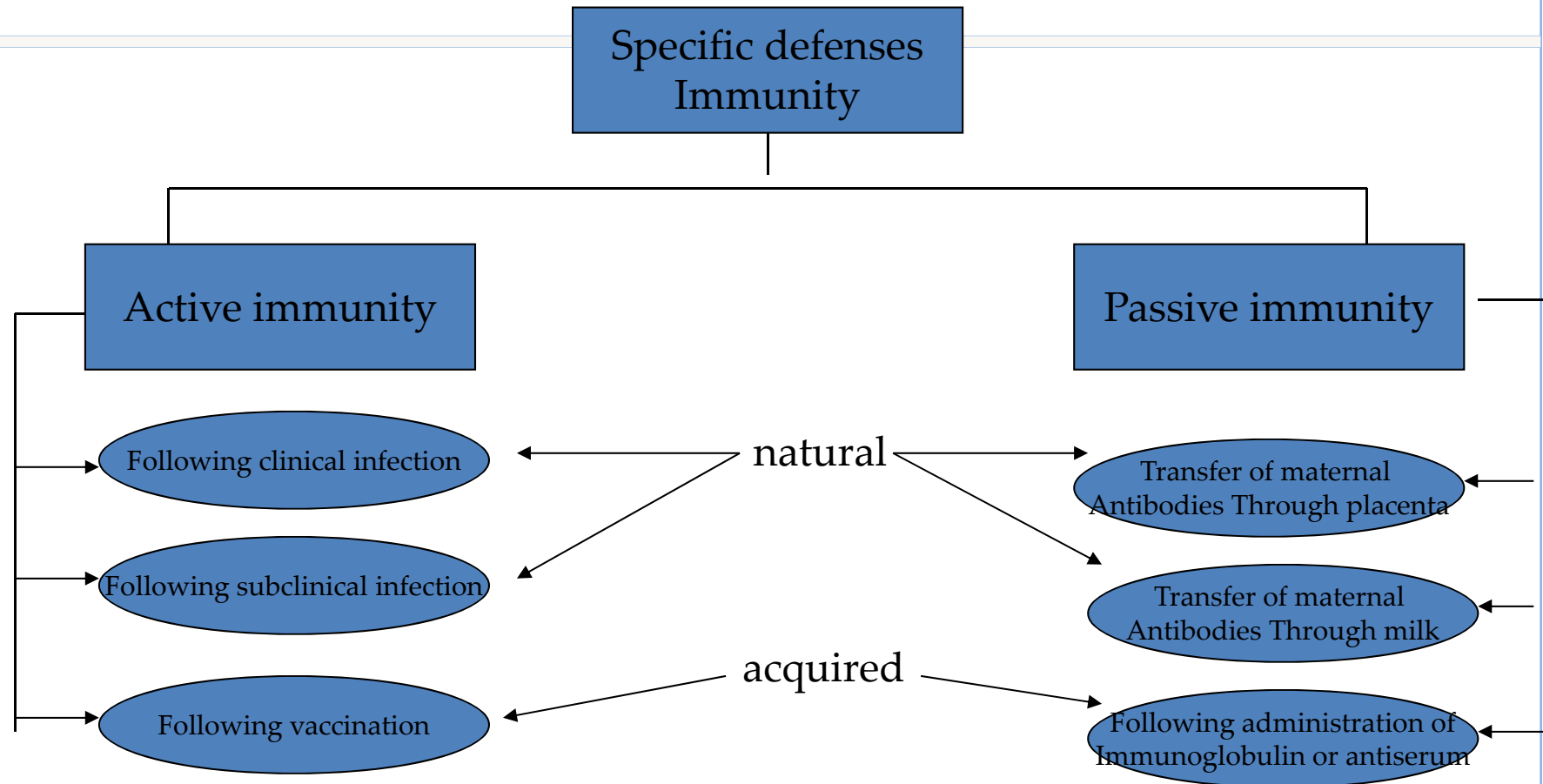
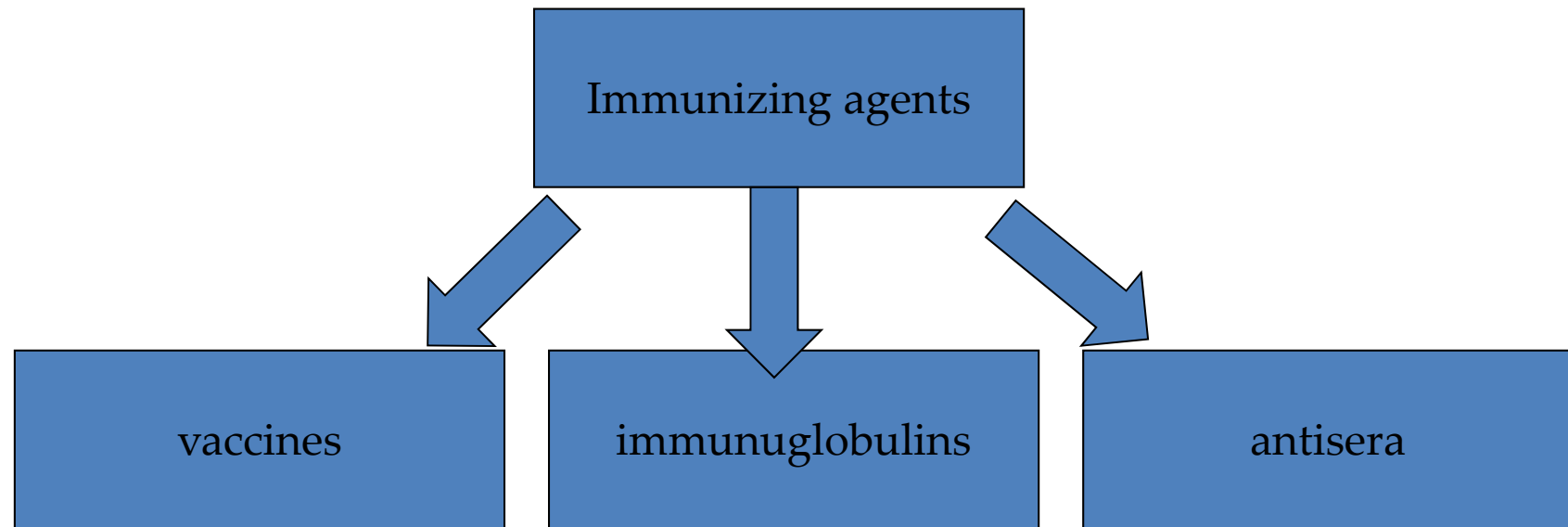


Viral Vaccines

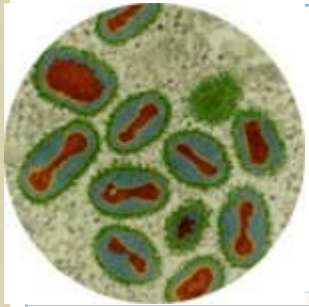
Immunity



Immunizing agents



- Even 2,500 Years Ago, People Knew Immunity Worked
- Greek physicians noticed that people who survived smallpox never got it again
- Becoming infected by certain diseases gives immunity



Origin of Vaccines

- Smallpox-first disease people tried to prevent by purposely inoculating themselves with other infections
- Inoculation-started in India or China before 200 BC
- Physicians immunized patients by picking off pieces from drying pustules of a person suffering from a mild case of smallpox, grinding the scales to a powdery substance, and then inserting the powder into the person's nose
- In 1718, **Lady Mary Montague** reported that the Turks have a habit of deliberately inoculating themselves with fluid taken from mild cases of smallpox
- Lady Montague inoculated her own children in this manner

- In 1796, **Edward Jenner**, observed that milkmaids get infected with cowpox-a mild relative of the deadly smallpox virus
- Jenner took infectious fluid from hand of **milkmaid Sarah Nelmes**
 - Inserted this fluid, by scratching or injection, into the arm of a healthy local eight year old boy, **James Phipps**
 - Phipps then showed symptoms of cowpox infection and recovered after 48 days
 - Jenner injected some smallpox-infected matter into Phipps- did not later show signs of smallpox infection



Vaccination

- Vaccination is a method of giving antigen to stimulate the immune response through active immunization
- A vaccine is an immuno-biological substance designed to produce specific protection against a given disease
 - Viable or nonviable pathogens or purified products
- A vaccine is “antigenic” but not “pathogenic”

- **Smallpox presented many advantages that made this possible**

- No animal reservoir
- Lifelong immunity
- Subclinical cases rare
- One serotype
- Infectivity does not precede overt symptoms

**As a result, after a world-wide effort
Smallpox was eliminated as a human disease in 1978**

Types of vaccines

- Live vaccines-Attenuated live vaccines
- Inactivated (killed vaccines)
- Surface antigen (recombinant) vaccines
- Toxoids
- Polysaccharide and polypeptide (cellular fraction) vaccines

Live attenuated vaccines

- Virulent pathogenic organisms are treated to become attenuated
- Retain their immunogenicity
- Attenuated microbes reproduce in the recipients –more robust and long lasting immune response
- Should not be administered to persons with suppressed immune response
 - Risk of reverting to an active pathogen
- Sabin Polio Vaccine, Measles, Mumps Rubella, Varicella

Temperature-sensitive mutants

- Unique form of live, attenuated viral vaccine
- Temperature sensitive mutants as the immunogen
- Mutant replicates in cooler air passages of the nose-IgA induced
- Does not replicate in the warmer lung tissue –no disease caused
- Influenza virus vaccines

Advantages of Live Attenuated Vaccines

- Attenuated (weakened) form of the "wild" virus or bacterium
- **Herd Immunity/ community immunity**
- Can replicate themselves so the immune response is more similar to natural infection
- Usually effective with one dose

Concerns of live vaccines

1. Revert to virulence
2. A second virus could contaminate the vaccine if it was present in the cell cultures –in 1960 inactivated polio and SV40 “passenger” virus in monkey kidney cells- sarcomas

Inactivated (killed) vaccines

- Organisms are killed/inactivated by heat or chemicals
- Remain antigenic
- Usually safe but less effective
- No risk of vaccine associated infection
- More heat stable
- Only absolute contraindication: severe local or general reaction to a previous dose

Inactivated Vaccines

- Cannot replicate and thus generally not as effective as live vaccines
- Usually require 3-5 doses
- Immune response mostly antibody based
- No chance of recreating live pathogen

Microbial extracts

- Instead of whole organism, its composed of antigen molecules
- Extracted from the pathogen or prepared by recombinant DNA techniques
- Efficacy of these vaccines varies

Surface antigen (recombinant) vaccines

- It is prepared by cloning HBsAg gene in yeast cells where it is expressed
- HBsAg produced is then used for vaccine preparations
- Their efficacy and safety also appear to be high

Cloned protein antigens have pluses and minuses

Advantages

- Easily manufactured and often relatively stable
- Cannot “revert” to recreate pathogen

Disadvantages

- **Poorly immunogenic**
- **Post-translational modifications**
- **Poor CTL response**

Toxoids

- Prepared by detoxifying the exotoxins of some bacteria rendering them antigenic but not pathogenic
- Adjuvant (e.g. alum precipitation) is used to increase the potency of vaccine

Non-infectious vaccines

- Inactivated or killed pathogen:
 - Salk Polio Vaccine, rabies vaccine
- Recombinant vaccines:
 - Hepatitis B
- Toxoid vaccines:
 - diphtheria, tetanus and pertussis

Polio

- Vaccination is the only effective method of preventing poliomyelitis
-

Attenuated live poliovirus (Sabin)Vaccine

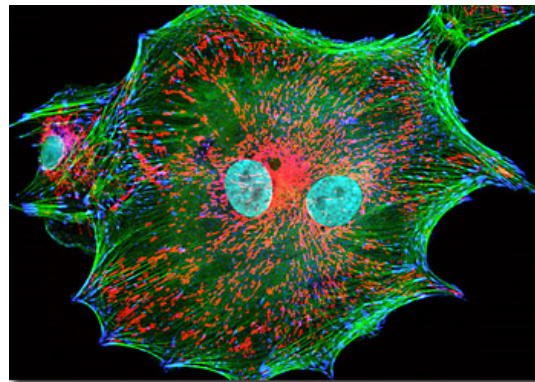
Attenuated by **passage in foreign host** (monkey kidney cells)

Selection to grow in new host makes virus less suited to original host

Can be administered orally

Provides life long protection for > 95% of recipients after the primary 3 doses series

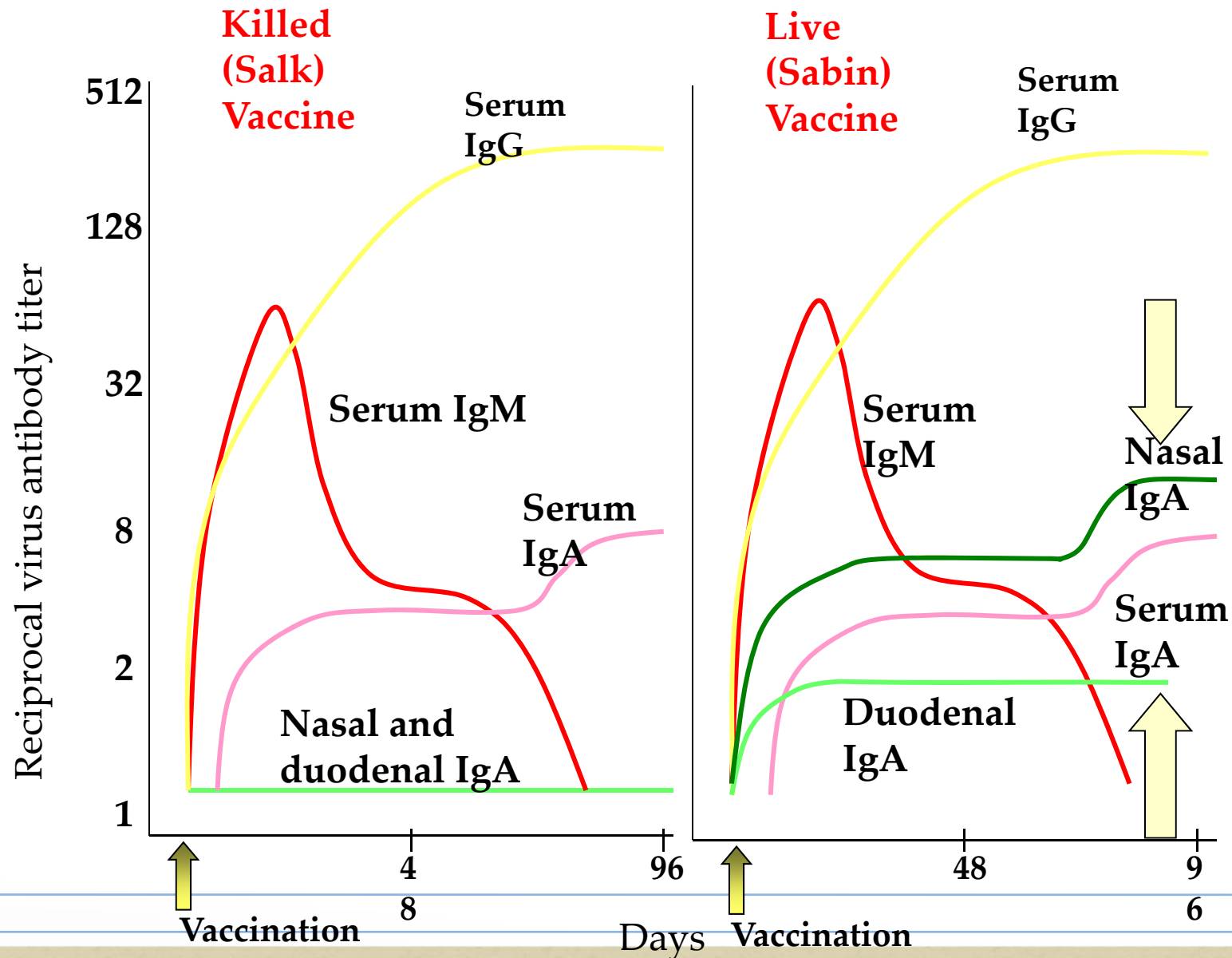
Provides early GIT immunity-Local gut immunity (IgA)



Inactivated poliovirus (Salk) Vaccine

- Formaldehyde-fixed
- No reversion
- Safe for use in immunocompromised persons and their contacts
- Disadvantages:
 - Administration by injection only
 - Provides less GI immunity-possibility of asymptomatic infection of GI tract with wild poliovirus-risk of transmission

Live virus generates a more complete immune response



Passive –active immunity

- Induced by giving both-
 - immune globulins to provide immediate protection
 - a vaccine to provide long-term protection
-

Post-exposure prophylaxis

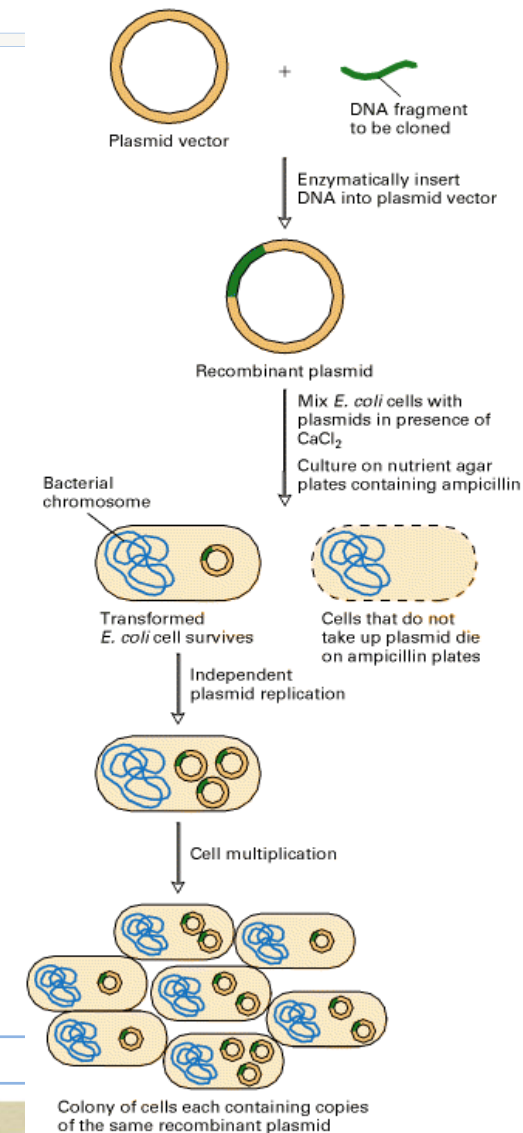
- 2 vaccines are effective when given PEP:
 - Rabies
 - Hepatitis B
- ◆ Have long incubation period
- ◆ Vaccine –induced immunity can prevent the disease

DNA vaccines

- These vaccines contain purified DNA encoding the appropriate viral proteins genetically engineered into a viral vector or plasmid
- DNA injections can transduce cells so antigens are expressed and presented
- No danger that it would cause infection

Modern molecular biology has offered new approaches to make vaccines

1. Clone gene from virus or bacteria
and express this protein antigen
in yeast, bacteria or
mammalian cells in culture

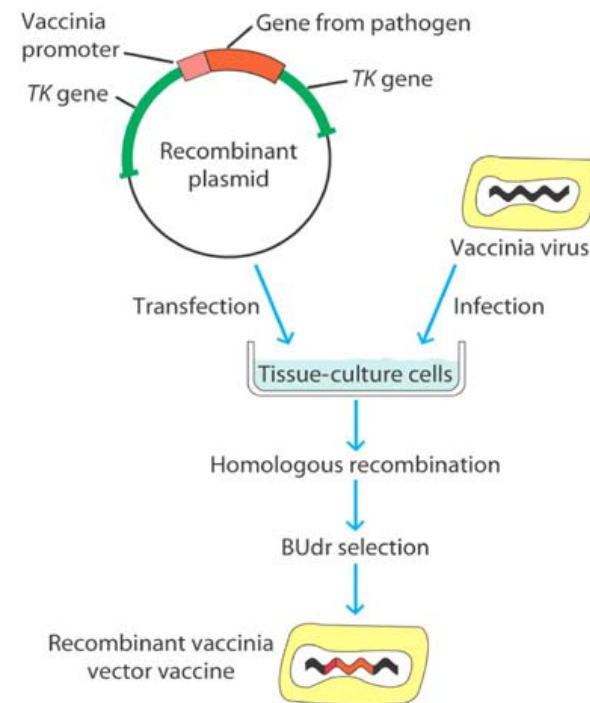


Modern molecular biology has offered new approaches to make vaccines

2. Clone gene from virus or bacteria

Into genome of another virus (adenovirus, canary pox, vaccinia)

And use this live virus as vaccine



Types of vaccines

Live vaccines	Live Attenuated vaccines	Killed Inactivated vaccines	Toxoids	Cellular fraction vaccines	Recombinant vaccines
<ul style="list-style-type: none"> • Small pox variola vaccine 	<ul style="list-style-type: none"> • BCG • Typhoid oral • Plague • Oral polio • Yellow fever • Measles • Mumps • Rubella • Intranasal Influenza • Typhus 	<ul style="list-style-type: none"> • Typhoid • Cholera • Pertussis • Plague • Rabies • Salk polio • Intra-muscular influenza • Japanese encephalitis 	<ul style="list-style-type: none"> • Diphtheria • Tetanus 	<ul style="list-style-type: none"> • Meningococcal polysaccharide vaccine • Pneumococcal polysaccharide vaccine • Hepatitis B polypeptide vaccine 	<ul style="list-style-type: none"> • Hepatitis B vaccine

Routes of administration

- Deep subcutaneous or intramuscular route (most vaccines)
- Oral route (sabine vaccine, oral BCG vaccine)
- Intradermal route (BCG vaccine)
- Scarification (small pox vaccine)
- Intranasal route (live attenuated influenza vaccine)

Scheme of immunization

- Primary vaccination
 - One dose vaccines (BCG, variola, measles, mumps, rubella, yellow fever)
 - Multiple dose vaccines (polio, DPT, hepatitis B)
- Booster vaccination

To maintain immunity level after it declines after some time has elapsed (DT, MMR).

Levels of effectiveness

- Absolutely protective(100%): yellow fever vaccine
- Almost absolutely protective (99%): Variola, measles, mumps, rubella vaccines, and diphtheria and tetanus toxoids.
- Highly protective (80-95%): polio, BCG, Hepatitis B, and pertussis vaccines.
- Moderately protective (40-60%) TAB, cholera vaccine, and influenza killed vaccine.