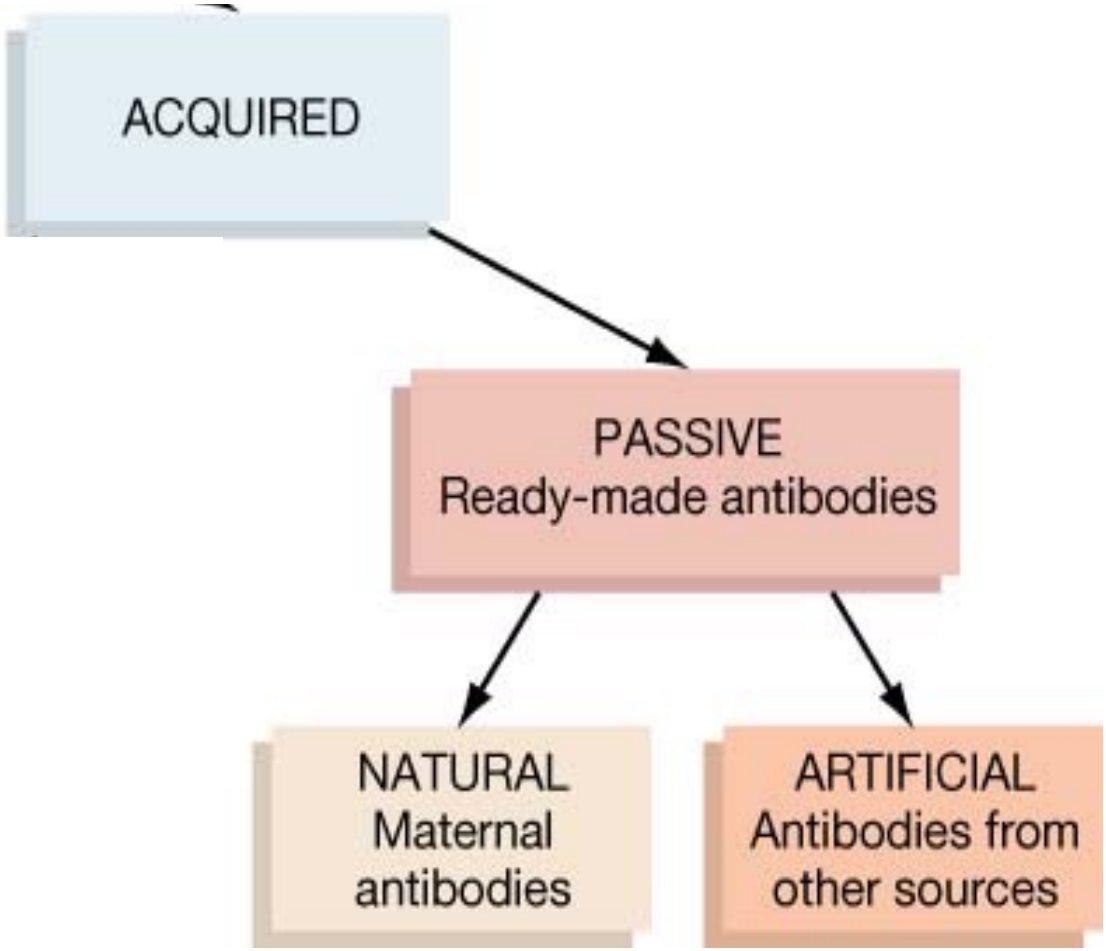
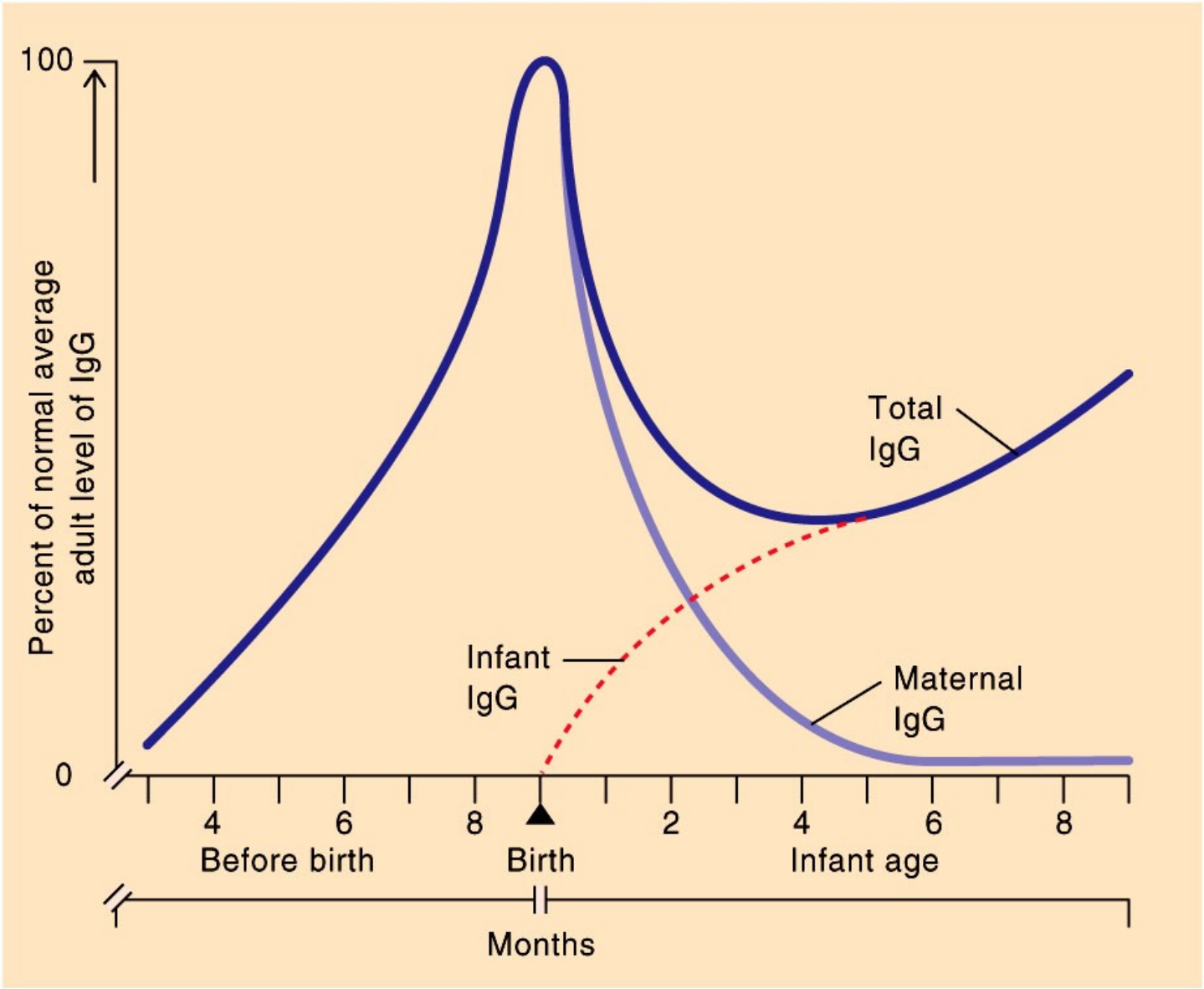
Prevention and Control – passive and active immunization

How do we acquire immunity?



Passive Immunity in Infants



Artificial Passive Immunity

- Gamma globulin
  - Ig's from pooled blood of at least 1,000 human donors
    - variable content
    - non-specific
- Specific immune globulin
  - higher titers of specific antibodies

Artificial Passive Immunity

- Gamma globulin
  - Ig's from pooled blood of at least 1,000 human donors
    - variable content
    - non-specific
- Specific immune globulin
  - higher titers of specific antibodies
- Antisera and antitoxins of animal origin

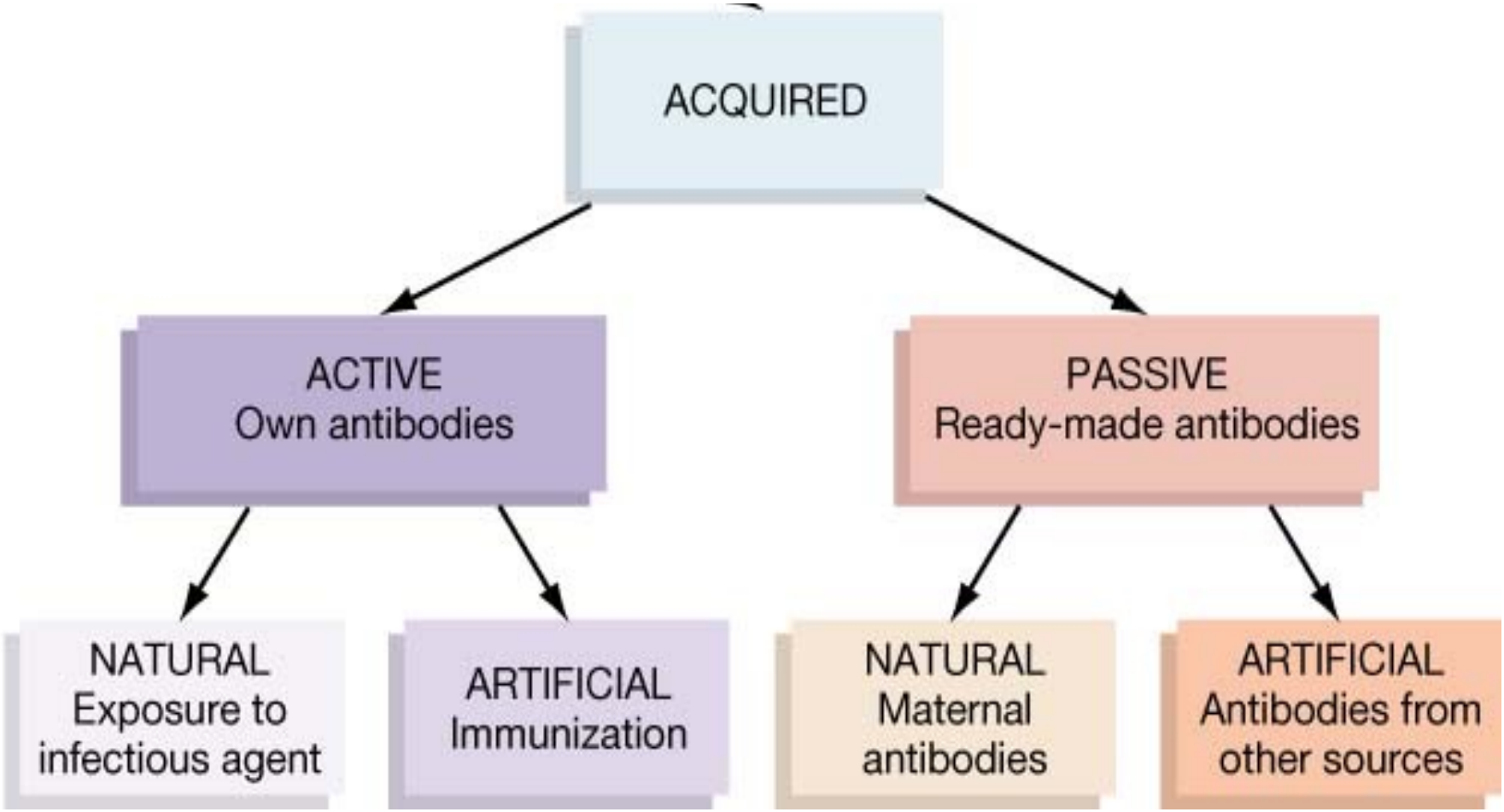
Risks of Passive Immunization

If Antibody is produced in another species, the human recipient can produce an Immune Response against it

In some patients: IgE production against isotypic Ab -> systemic mast cell activation -> type I hypersensitivity

In others → IgM or IgG vs isotype -> complement activation -> Type III hypersensitivity

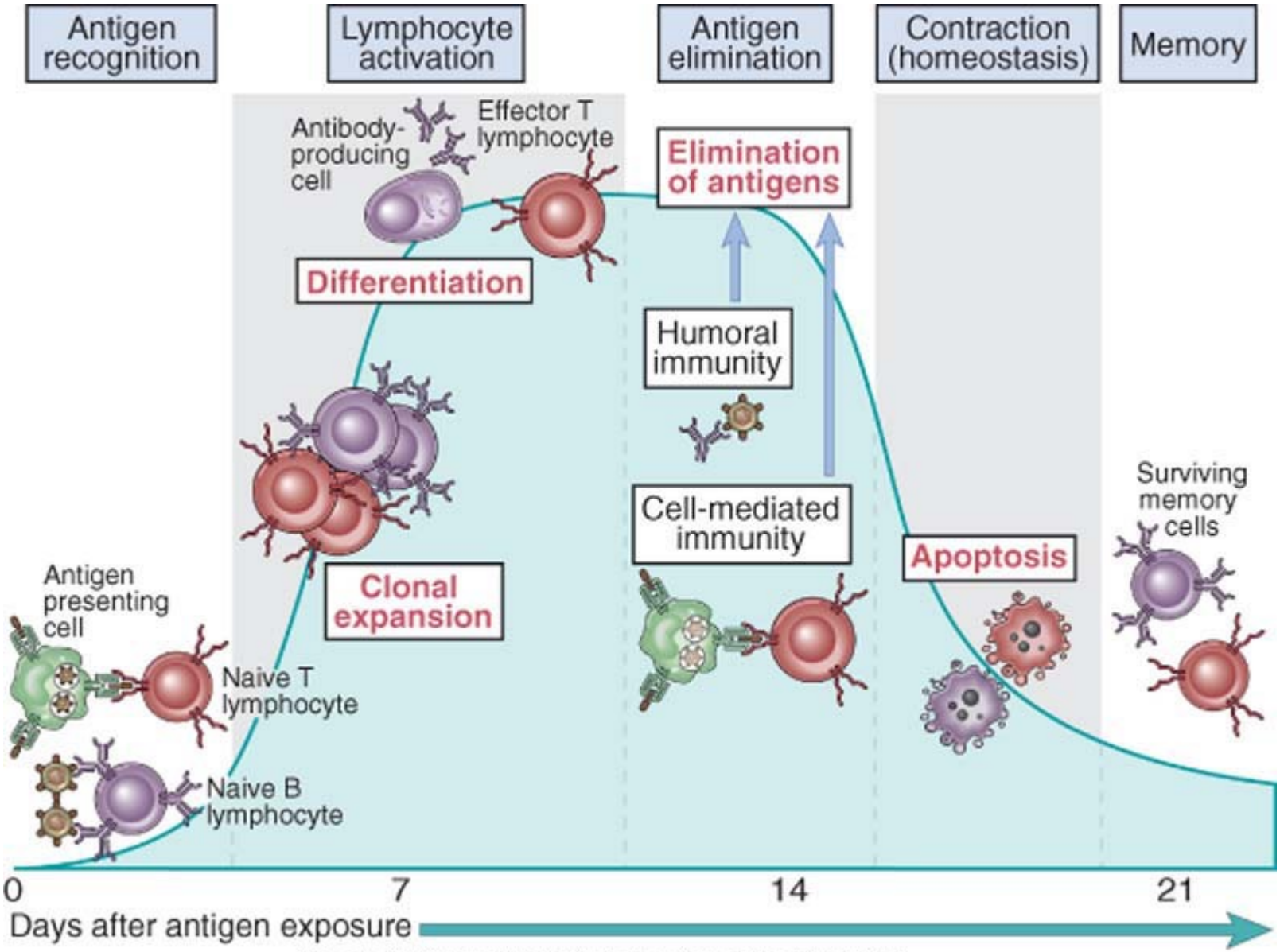
How do we acquire immunity?



Artificial Active Immunity

- Vaccination (Immunization)
  - exposing a person to material that is an antigen but NOT pathogenic.

Phases of immune response



Designing vaccines

Important questions to consider:

1- Which part of the immune system should be activated?

2- Is immunologic memory sufficiently stimulated?

This depends on the disease..

- Influenza has a short incubation (1-2 d); effective immunity against flu depends on maintaining high levels of Ig through repeat immunizations

- Polio virus has a longer incubation (>3d) and gives memory cells time to produce ↑serum Ig and activate immune cell effectors

Childhood vaccines

- 7 major vaccines:
  - **HepB**
  - **DTaP (**Diphtheria, Tetanus, Pertussis)
  - **IPV** (smallpox /vaiolo)
  - **MMR (**measles, mumps, and rubella / morbillo, parotite, rosolia)
  - **Hib (**Haemophilus influenzae type B)
  - **Var** (Varicella)
  - **PCV (**Pneumococcal Conjugate Vaccine)

  *children require booster shots for most…
  (American Academy of Pediatrics, 2002)

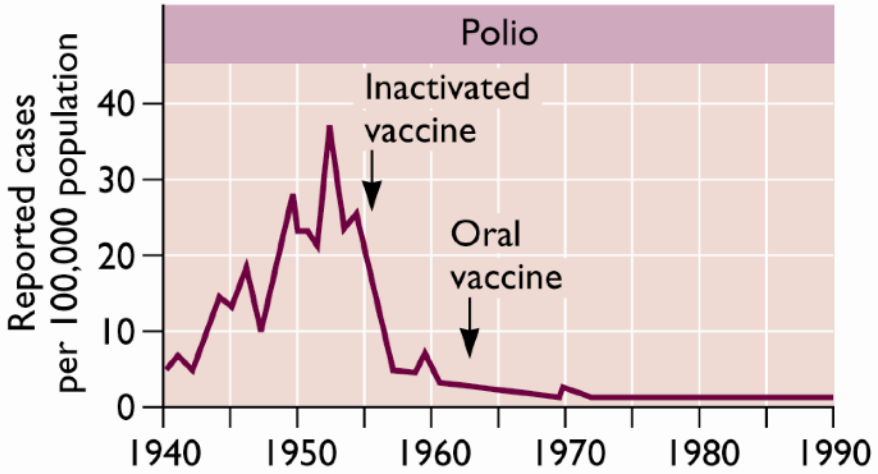
Adult vaccines (dependent on risk group)

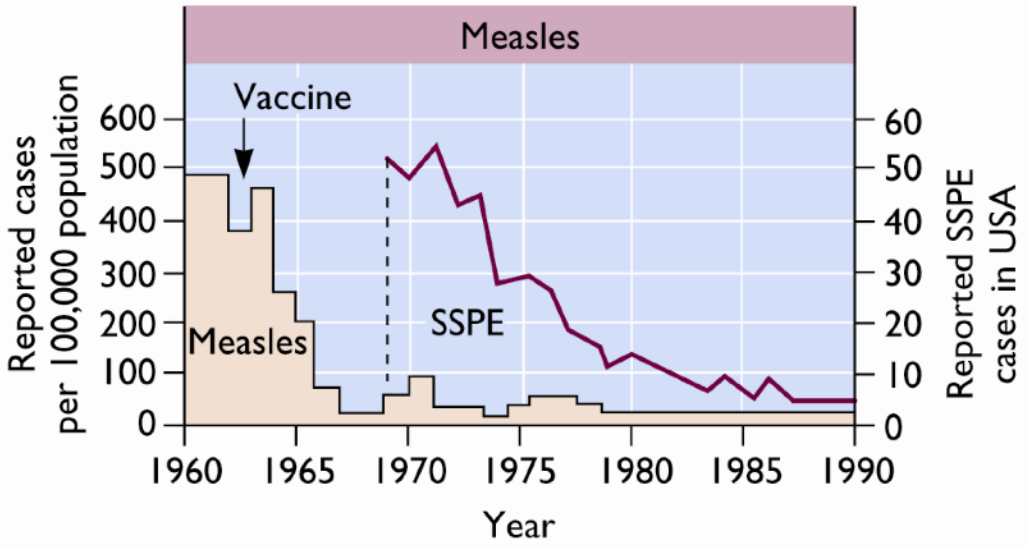
- For those living in close quarters
  - Meningitis (Hib)
  - Pneumonia (PCV)
  - Influenza

- For travelers to endemic areas:
  - Cholera
  - Typhus
  - Typhoid
  - Hepatitis
  - Meningits
  - Yellow fever
  - Polio

Large scale vaccination programs

- Dramatic improvements in public health.
- Nobody in this room has had…
  - Smallpox, Polio, Measles, Chickenpox
  - Mumps, Rubella
- …Because of vaccination
- Smallpox is the only human disease to ever be eradicated





Characteristics of a good vaccine

- **Safe / Few side effects**
- Give long lasting, appropriate protection
- Low in cost
- Stable with long shelf life (no special storage requirements)
- Easy to administer

- Public must see more benefit than risk

Table 19.1 Features of smallpox that enabled its eradication

Virology and disease aspects
No secondary hosts: this is a human-only virus
Long incubation period
Infectious only after incubation period
Low communicability
No persistent infection
Subclinical infections are not a source of spread
Easily diagnosed

Types of vaccines

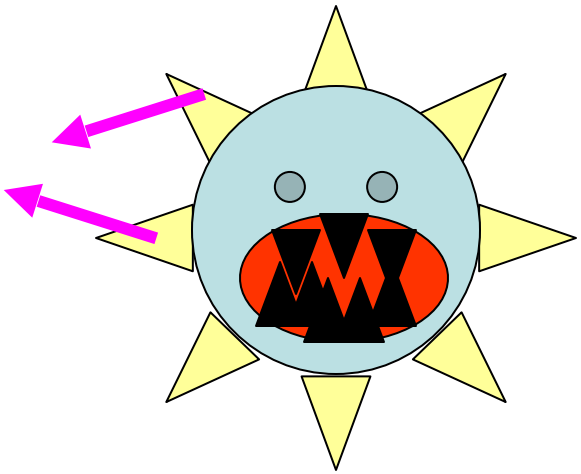
- whole agent

- subunit of the agent
  - recombinant
  - individual parts alone

Whole agent vaccines
Killed using heat or formaldehyde

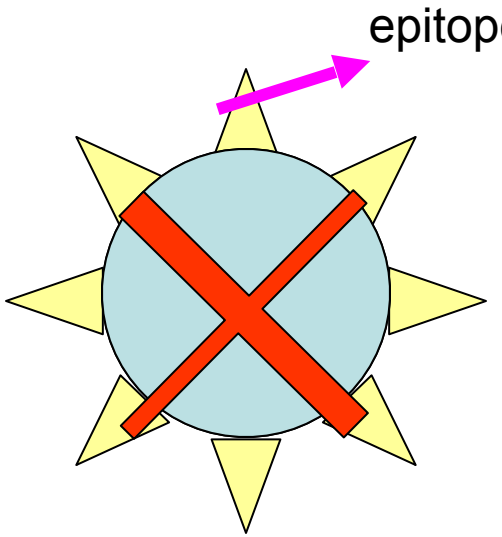
Live virus

epitopes



Killed virus

epitopes

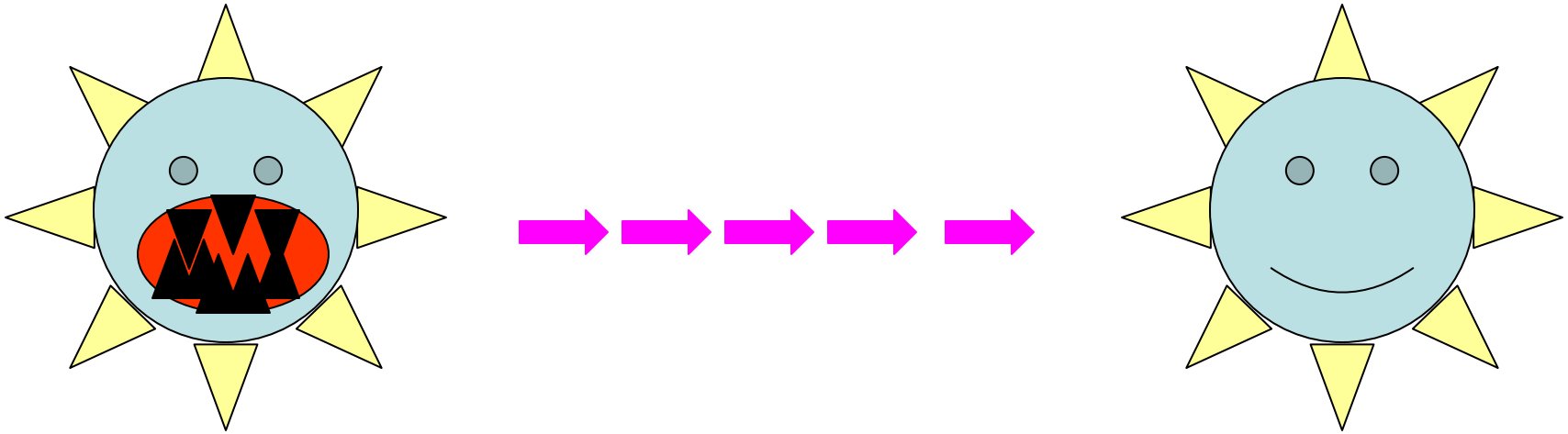


Inactivated polio vaccine (Salk)

Influenza (Classic)

Whole agent vaccines Attenuated

- attenuated - a process that lessens the virulence of a microbe

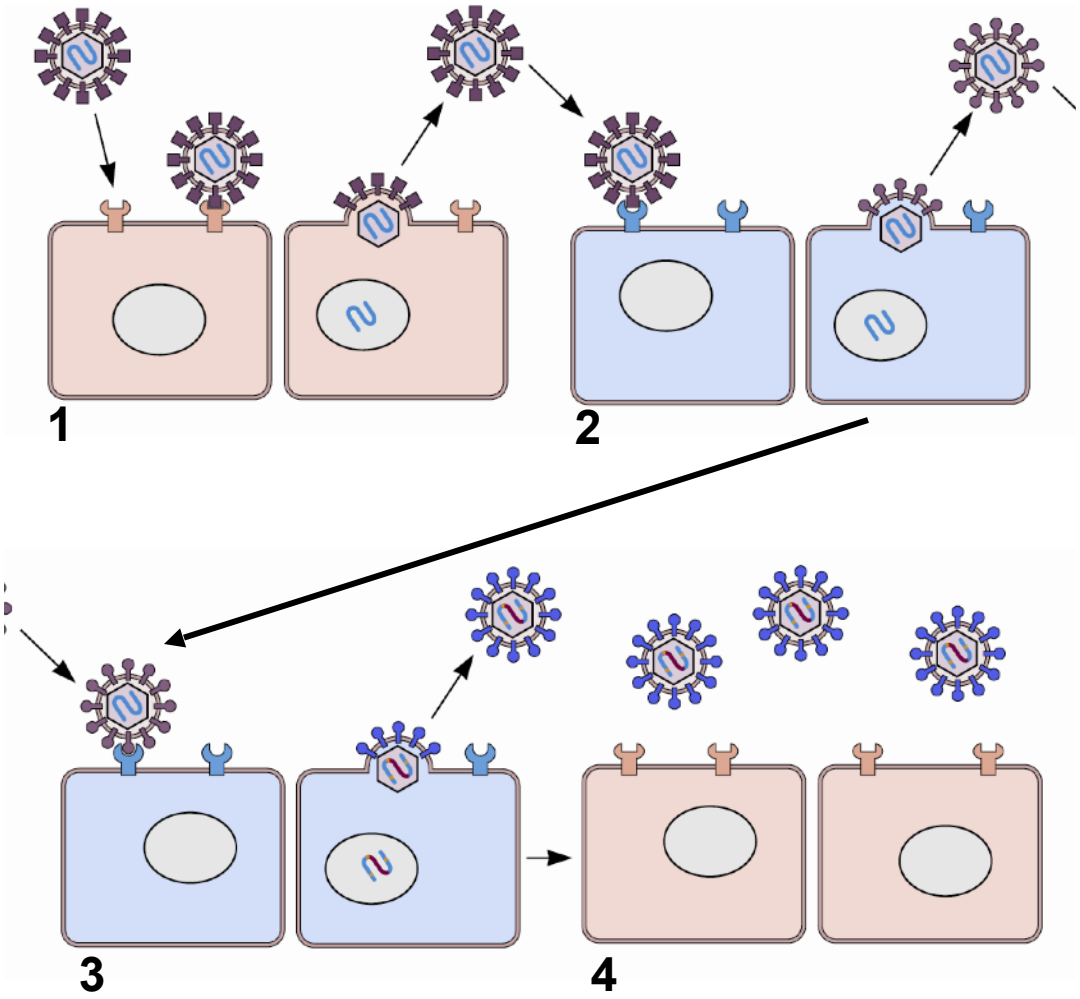


oral polio vaccine (Sabin),

MMR (measles, mumps, rubella)

Influenza -- Flumist

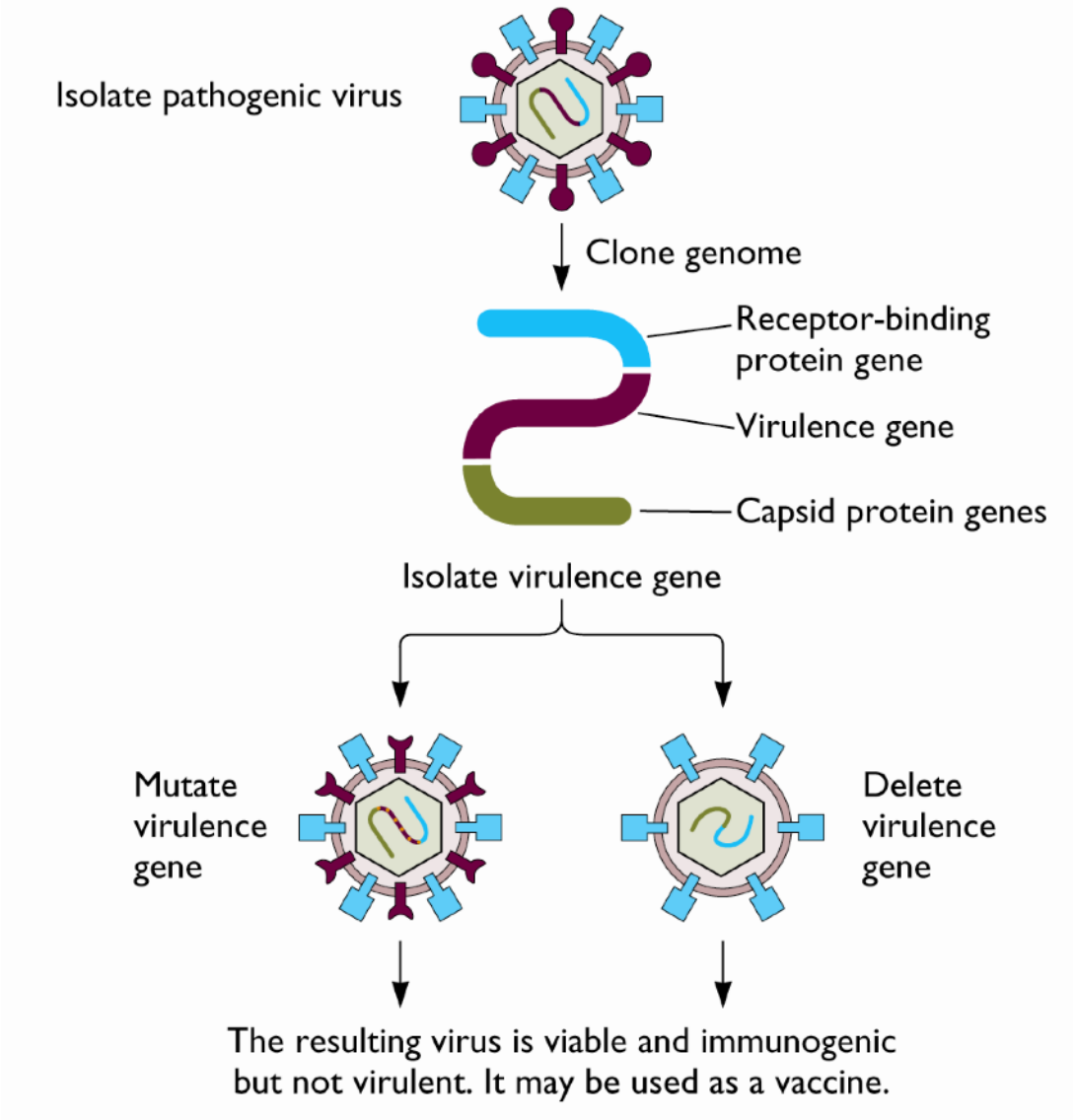
Attenuation of viruses by passage through non-human cells



1. Pathogenic virus isolated from patient, grown in human cells
2. Infect monkey cells with cultured virus
3. Virus acquires many mutations that allow it to grow well in monkey cells
4. Mutations make the virus unable to grow well in human cells

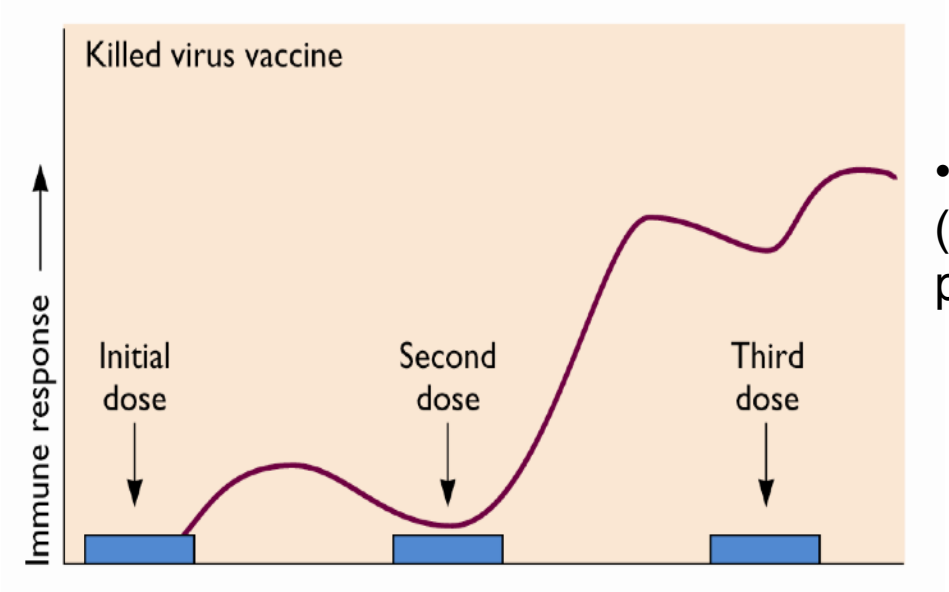
→ Vaccine candidate

Construction of recombinant attenuated virus

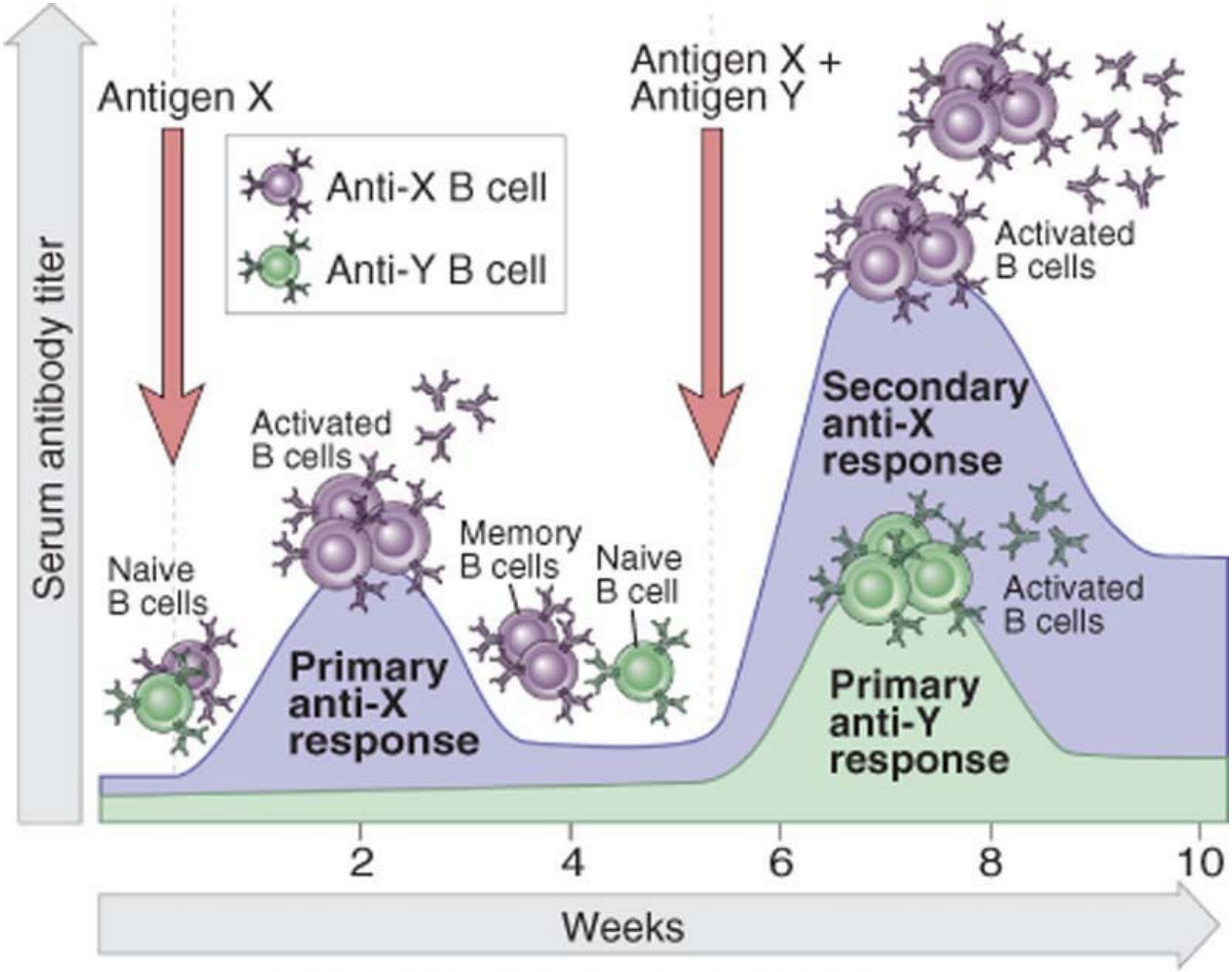


1. **Isolate virus**
2. **Clone genome**
3. **Isolate virulence gene**
4. **Mutate or delete virulence gene**
5. **Resulting virus is**
   - **Viable**
   - **Immunogenic**
   - **Not virulent**
   - **Can be used as a vaccine**

Vaccines stimulate immune memory



•Killed virus vaccine requires multiple doses (booster shots) to adequately stimulate a protective immune response



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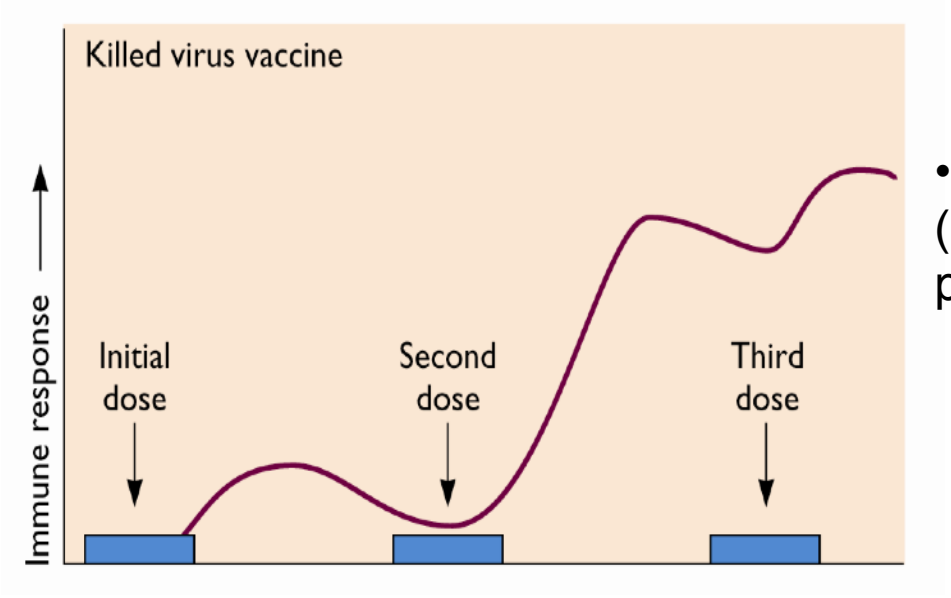

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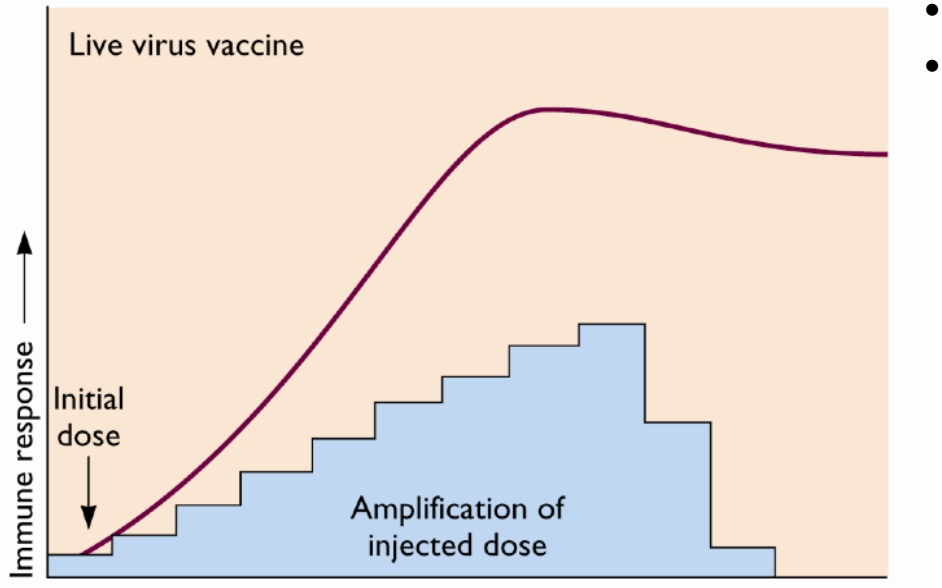


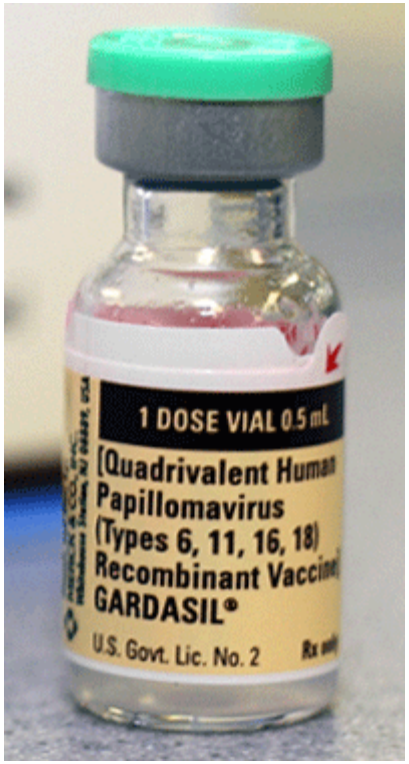
•Live virus vaccines replicate in the host.
•No requirement for boosters.

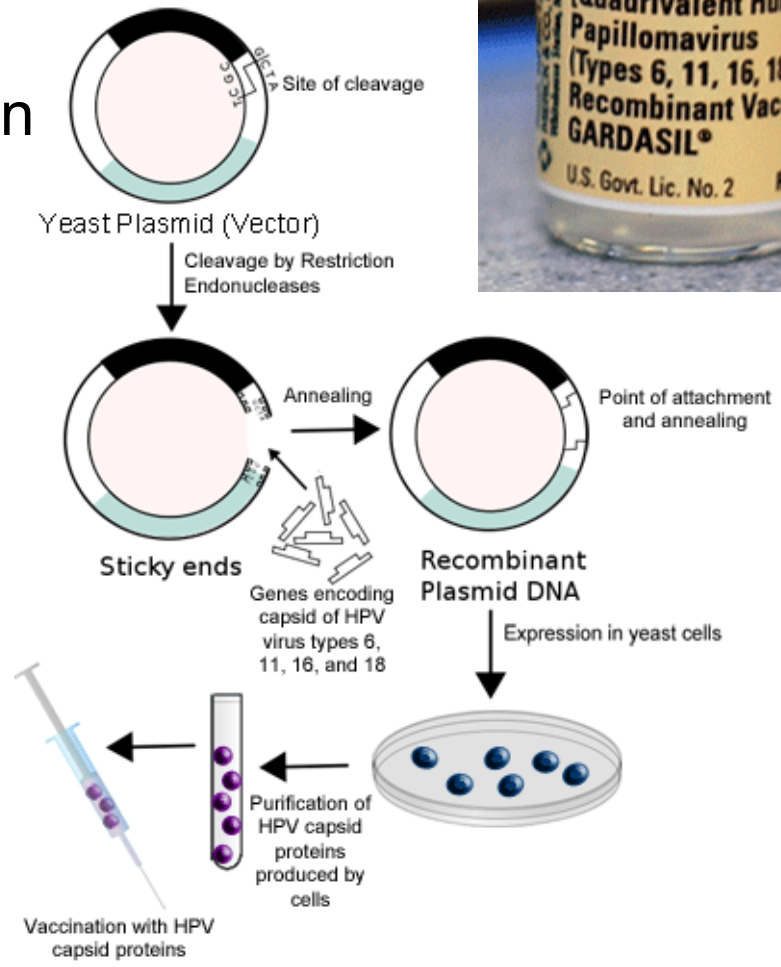
- Advantages for live vaccines
  - multiply like natural organism
  - require fewer doses and boosters
  - long-lasting

- Disadvantages for live vaccines
  - special storage
  - back mutation
  - side effects

Subunit vaccines

- Single antigen or mixture of antigens
- Safer (cannot reproduce)
- However, often less effective than whole agent vaccines
- Can be costly
- Always require boosters





Overcoming Subunit vaccine problems

1. Multiple doses
2. Use adjuvants
   - prolongs stimulation of immune response
   - works by trapping the antigens in a chemical complex and releases them slowly

Types of vaccines

Live vaccines	Live Attenuated vaccines	Killed Inactivated vaccines	Toxoids	Cellular fraction vaccines	Recombinant vaccines
•Small pox variola vaccine	•BCG •Typhoid oral •Plague •Oral polio •Yellow fever •Measles •Mumps •Rubella •Intranasal Influenza •Typhus	•Typhoid •Cholera •Pertussis •Plague •Rabies •Salk polio •Intra-muscular influenza •Japanise encephalitis	•Diphtheria •Tetanus	•Meningococcal polysaccharide vaccine •Pneumococcal polysaccharide vaccine •Hepatitis B polypeptide vaccine	•Hepatitis B vaccine

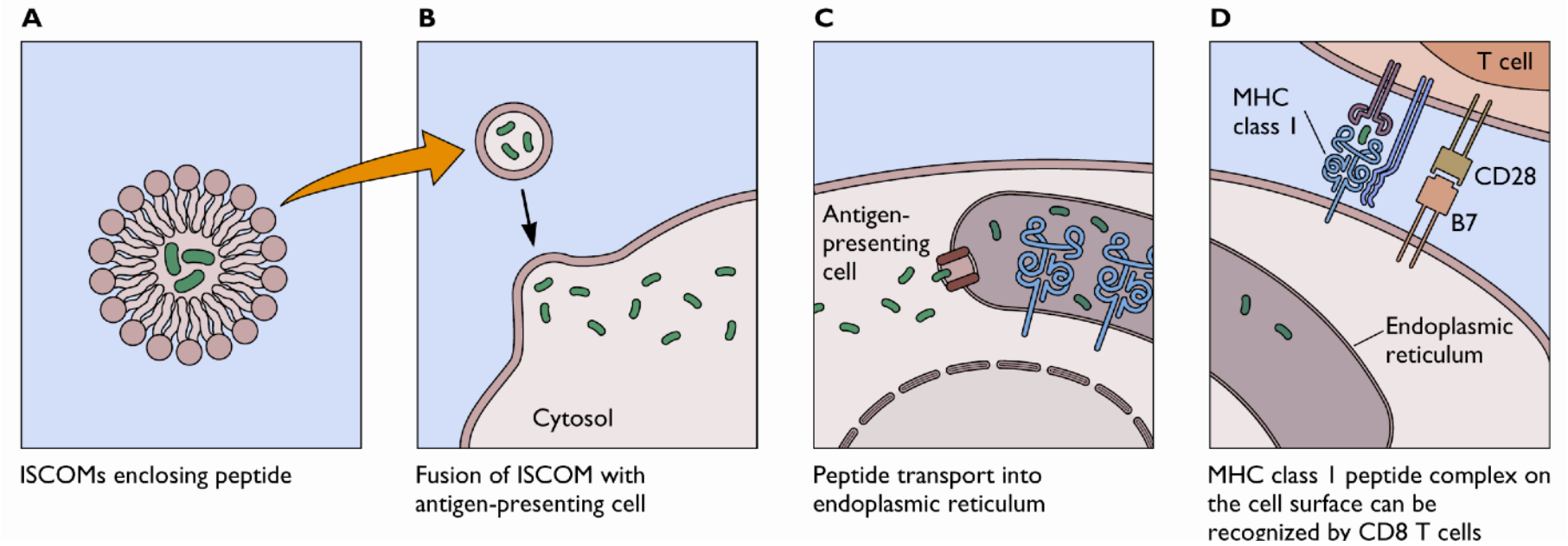
Vaccine delivery systems and adjuvants

Table 19.4 Vaccine delivery systems and adjuvants[a]

Type of system or adjuvant	Characteristics
Aluminum salt	Aluminum hydroxide or phosphate. Forms precipitates with soluble antigen, making the complexes more immunogenic; antigen "depot" at site of injection; complement activation.
Emulsions	Freund's complete adjuvant: antigen suspended in water-mineral oil emulsion with killed *Mycobacterium tuberculosis* bacteria or muramyl di- or tripeptide to stimulate strong T-cell responses. Freund's incomplete adjuvant: antigen suspended in water-in-mineral oil emulsion.
Microspheres	Antigen encapsulated in polymers of lactic and glycolic acids. They are biodegradable and cause slow release of antigen.
ISCOMs	Immune-stimulating complexes composed of glycosides in an adjuvant called QuilA (a purified saponin from the plant *Quillaja saponaria*), cholesterol, phospholipids, and antigens. Form spheres of 30–40 nm in diameter that incorporate antigen.

Vaccine delivery systems and adjuvants

ISCOMS as peptide delivery systems



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Nucleic acid vaccines	Genes encoding antigens expressed from strong promoters are introduced directly to muscle or skin using physical methods or liposomes leading to intracellular protein production and presentation of antigen to the immune system.

Representative results of DNA vaccine trials

Table 19.5 Representative results of DNA vaccine trials[a]

Virus	Proteins	Induction of antibody	Induction of CTL response	Protection against challenge
Bovine herpesvirus	gD	+	ND	+ (cattle)
Hepatitis B virus	Surface and core antigens	+ (chimpanzees); ND (humans)	+ (chimpanzees)	+ (chimpanzees)
Hepatitis C virus	Nucleocapsid	+	+	+ (mice)
Herpes simplex virus type 1	gD, gB	+	+	+ (mice)
HIV type 1	Env, Gag, Rev	+	+	+ (rhesus macaques)
Influenza virus	HA, M1, Np	+	+	+ (chickens, mice)
Lymphocytic choriomeningitis virus	NP	+	+	+ (mice)
Rabies virus	Glycoprotein, NP	+	+	+ (cynomolgus monkeys)
Respiratory syncytial virus	Glycoprotein	+	+	+ (mice)

DNA vaccines Vs Traditional vaccines

DNA vaccines

- Uses only the DNA from infectious organisms.
- Avoid the risk of using actual infectious organism.
- Provide both Humoral & Cell mediated immunity
- Refrigeration is not required

Traditional vaccines

- Uses weakened or killed form of infectious organism.
- Create possible risk of the vaccine being fatal.
- Provide primarily Humoral immunity
- Usually requires Refrigeration.

DISADVANTAGES

- Limited to protein immunogen only
- Extended immunostimulation leads to chronic inflammation
- Some antigen require processing which sometime does not occur

Vaccine delivery systems and adjuvants

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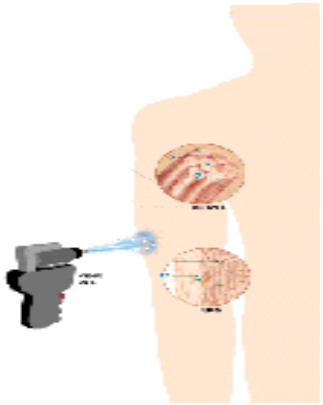
Nucleic acid vaccines	Genes encoding antigens expressed from strong promoters are introduced directly to muscle or skin using physical methods or liposomes leading to intracellular protein production and presentation of antigen to the immune system.
Engineered viruses	Genes encoding foreign antigens are introduced into a viral genome (the vector) such that the new protein is made following infection. Common viral vectors are vaccinia virus, adenovirus, and baculovirus. Many other viruses can also be modified to express foreign genes.

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)

Routes of administration

- ***Gene gun delivery:-***



- Adsorbed plasmid DNA into gold particles
- Ballistically accelerated into body with gene gun.

HOW DNA VACCINE WORKS

BY TWO PATHWAYS

ENDOGENOUS :- Antigenic Protein is presented by cell in which it is produced

EXOGENOUS :- Antigenic Protein is formed in one cell but presented by different cell

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).

Periods of maintained immunity due to vaccines

- Short period (months): cholera vaccine
- Two years: TAB vaccine
- Three to five years: DPT vaccine
- Five or more years: BCG vaccine
- Ten years: yellow fever vaccine
- Solid immunity: measles, mumps, and rubella vaccines.

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.

Vaccination Coverage

- Vaccination coverage is the percent of at risk or susceptible individuals, or population who have been fully immunized against particular diseases by vaccines or toxoids. To be significantly effective in prevention of disease on mass or community level at least a satisfactory proportion (75% or more) of the “at risk” population must be immunized.

New approaches

- Cancer
- HIV/AIDS
- Malaria

Vaccines against bioterrorism

- Anthrax
- Small pox
- plague

Vaccination: It works

REDPEN/
BLACKPEN

Hey guys - I don't even feel any rain. Why are we doing this again? Just put down the stupid umbrellas - they're bad for your arms anyway.