Acquisition of Immunity

Passive Immunity

Passive immunization = Transfer of antibodies

→ Antibodies can be transfered between people (and animals)

→ Any immune protection lasts as long as the antibodies are present

Examples:

1. Antitoxins (Antibodies from horses)

   Diptheria

   Tetanus

   Botulinum

2. Antivenoms
3. Human gammaglobulin (IgG from many plasma donors)

Maternal

1. IgG through placenta
2. IgA through breastmilk

Active Immunization

Vaccines are usually **active** immunizations

→ Induce adaptive immune response similar to "natural infection"

→ Establishes memory T and B cells

Most vaccines prevent disease but not infection innoculations → immunizations → vaccines

immunization = any injection to illicit an immune response

Preventive Vaccines

Given to naive individuals in order to provide protection from primary infection or prevent disease

Therapeutic Vaccines

Given to infected individuals to prevent / reduce disease or stimulate anti-tumor response

Smallpox Eradication (Vaccinia)

Why was eradication possible?

1. No animal reservoir

2. Lifelong immunity
3. One serotype → little antigenic variation

   No repeat infections
4. Effective attenuated vaccine provided long-term immunity

Routes for Vaccination

Many vaccines are given intramuscular or subcutaneous

→ Live polio virus and rotavirus vaccine given orally

Immunization site will influece where immune responses are elicited but most vaccines are tested in easy to administer route and assessed for protection

FluMist

Intranasal vaccine for influenza

Replicates only in nasal cavity

Flu Vaccine

100 million doses available each year

Usually trivalent (With 3 different viral strains)

Traditional approach: Identify "new" virulent strains, recombine, and grow in eggs

Subcutaneous or Intradermal

Subcutaneous = under skin

Intradermal = between skin layers (can see bubble under skin)

Ex: Monkeypox

Why this method?

→ Supposedly because of focus on skin

→ Likely just how it was tested

Vaccines need Adjuvants

Adjuvants added in order to enhance immunogenicity

→ Activate macrophages and DCs to increase inflammation

Old adjuvants were inorganic salts such as aluminum hydroxide, aluminum phosphate, or calcium phosphate

→ Newer adjuvants provide ligands to bind TLRs

→ AS01-AS06 are oil in water emulsions with Lipid A, or Saponin (detergent), or CpG (DNA)

→ Contain PAMPS to activate inflammation via TLRs

Dealing with Antigenic Variation

Some viruses have many different antigenic subtypes and high mutation rates

Types of Vaccines

Attenuated Vaccines

Made by growing pathogen in non-human cell culture until pathogen is less virulent

→ Less virulent = Less pathogenic = Less disease-causing

Ex:

1. Oral Polio Vaccine (OPV)
2. Measles
3. Mumps
4. Rubella
5. Varicella Zoster Virus (VZV)

Advantages:

1. Self-replicating (low dose)
2. Real virus

   No adjuvant

   Authentic antigen presentation
3. More effective at eliciting CTLs

Disadvantages

1. If vaccine replicates, it could infect other people and become virulent
2. Does not deal with strain variability / antigenic variation

Inactivated Vaccines

Killed (inactivated) whole organism OR inactivated toxin

→ Done by heat, chemicals, or irradiation

Ex:

1. Influenza
2. Hepatitis A

3. Pertussis
4. Salk inactivated polio vaccines (IPV)
5. Tetanus
6. Diptheria

Advantages: No revirulence (more safe)

Disadvantages: No replication (poor antigen presentation)

Live Vector Vaccines

Insert genes from pathogen into a well characterized vaccine vector

Ex:

1. Vaccinia
2. Adenovirus
3. Salmonella
4. Vesicular stomatitus

Advantages:

1. Self replicating
2. No adjuvant needed

Disadvantages: Live vector could be an issue with potential pathogenesis

Recombinant Protein Vaccines

Identify immunogenic proteins by its envelope or outer membrane

Advantages: Less expensive and very safe

Disadvantages: Need adjuvant and boosters (may not elicit long-term memory)

Ex: Human Papilloma Virus (HPV) Vaccine

→ Mimics structure without containing any HPV viral DNA

Viral Spike Protein

Key target of neutralizing antibodies

Moderna's SARS CoV-2 mRNA Vaccine

1. mRNA for spike protein inside lipid nanoparticles
2. Host cells "uptake" the spike and generate the protein
3. Proteins get released from cell to generate Th antibody response

Advantages:

1. Fast production and ease for inserting new viral strain into same mRNA vector
2. Mimics aspects of infection

    Gets into cells

    Makes proteins

    Activates TLRs
3. Safer than most vaccine types

Disadvantages:

1. Must be encapsulated in lipids or sugars
2. Must be frozen
3. Not very stable once thawed

Johnson and Johnson Adeno/Spike vaccine (66-72% efficacy)

1. Spike gene added to Adenovirus 26
2. Adenoviruses are common viruses

Issues in Vaccine Development

Always tested first in young, healthy people

Efficacy

Most common human vaccines are >90% protective

Influenza vaccine is 20-70% protective

Different efficacy in adults, children, and immunocompromised individuals

Cost

Most original attenuated vaccines were incredibly cheap

The WHO Big Six cost les than $1 per person

1. Diptheria toxoid
2. Tetanus Toxoid
3. Acellular pertussis (DTap)
4. Polio
5. Measles
6. BCG

New vaccines have high development costs

→ Can take years to go down depending on volume of production