Describe Antigens & Concepts involved in vaccine development

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What is antigen?

- ✓ An antigen is any substance that can trigger an immune response in the body.
- ✓ Immune system recognizes the substance as foreign or dangerous and takes action to neutralize or destroy it.
- ✓ Antigens can be found on the surface of bacteria, viruses, fungi, parasites, and other microorganisms.
- ✓ Antigens can also be found on the surface of cells from other people or animals, and even on the surface of some non-living substances like pollen and dust mites.

Types of antigen

1. Carbohydrate Antigens: Sugar molecules (polysaccharides). Found on the surface of bacteria, fungi, and some viruses. Primarily activate the humoral immune response, leading to the production of antibodies. **Examples: Bacterial capsules:** polysaccharide capsule, **Blood group antigens:** The ABO blood group system, **Lipopolysaccharide (LPS):** A component of the outer membrane of Gram-negative bacteria, LPS is a powerful stimulator of the immune system.

2. Protein Antigens: Amino acids linked together in a specific sequence. The most common type of antigen. Protein antigens can activate both the humoral and cell-mediated immune responses. **Examples:** The spike protein of SARS-CoV-2 virus is a protein antigen that is recognized by the immune system.

3. Lipid Antigens: Composed of fatty acids and other lipid molecules. Less common than protein and carbohydrate antigens and are often found in combination with other molecules, such as proteins or carbohydrates. **Examples: Mycolic acids:** Lipids found in the cell wall of Mycobacterium tuberculosis, the bacterium that causes tuberculosis.

Antigen Vs Immunogen

Feature	Antigen	Immunogen
Molecular Size	Can be small or large	Usually large
Complexity	Can be simple or complex	Usually complex
Ability to induce immune response	May or may not induce	Always induces
Examples	Haptens, small peptides, simple sugars	Proteins, polysaccharides, vaccines

All immunogens are antigens, but not all antigens are immunogens.

Steps of antigen preparation for vaccines

Antigen preparation is a crucial step in vaccine development. It involves selecting, isolating, and processing the specific components of a pathogen that will trigger a protective immune response without causing disease.

1. Antigen Selection to induce a strong and effective immune response. These are typically proteins or polysaccharides found on the surface of the pathogen. Factors – Immunogenicity, Safety, Stability, Ease of production

2. Antigen Isolation and Purification: Grow the pathogen and isolate the antigen. The isolated antigen is purified to remove any contaminants.

3. Antigen Processing: Inactivation or attenuation/Fragmenting the antigen/Conjugating the antigen/Adding adjuvants.

4. Characterization and Quality Control.

5. Formulation and Storage.

Vaccine formulation

1. Choose adjuvants: Add substances to boost the immune response to the antigen.
2. Add stabilizers: Include ingredients to protect the antigen and maintain its potency.
3. Include preservatives: Prevent contamination in multi-dose vials.
4. Determine the optimal formulation: Balance the ingredients for maximum efficacy and safety.
5. Ensure sterility and purity.
6. Fill and package.
7. Quality control and testing: Conduct rigorous tests to ensure safety, purity, and potency.

Vaccine adjuvants are like boosters that make vaccines work better.

Types of Adjuvants and Vaccine Examples:

- Aluminum Salts: These are the most common adjuvants, found in vaccines like:
  - DTaP (diphtheria, tetanus, and pertussis), Hepatitis A, Hepatitis B, HPV (human papillomavirus), Pneumococcal vaccines
- Emulsions: MF59, an oil-in-water emulsion, is used in some flu vaccines to make them more effective.
- Toll-like Receptor Agonists: Monophosphoryl lipid A (MPL) in the HPV vaccine Cervarix and the shingles vaccine Shingrix. CpG oligodeoxynucleotides are used in the Hepatitis B vaccine Heplisav-B.
- Saponins: QS-21, a saponin-based adjuvant, is included in the shingles vaccine Shingrix.
- Virosomes: Inflexal V, a flu vaccine, uses virosomes to improve its effectiveness.

How Adjuvants Help Vaccines:

- Stronger Response
- Targeted Defense
- Adjuvents allow for lower doses of the antigen.
- New Vaccines

Development of immunity

When a vaccine is injected, the body's immune system recognizes the vaccine antigen as foreign and initiates a series of steps to process and eliminate it, ultimately leading to the development of immunity.

1. Uptake and Processing by Antigen-Presenting Cells (APCs):
2. Antigen Presentation: MHC Binding: Some of these peptides bind to Major Histocompatibility Complex (MHC) molecules.
3. T Cell Activation and Differentiation
4. B Cell Activation and Antibody Production
5. Immune Memory Cells: Some of the activated T and B cells become long-lived memory cells.

Universal Immunization Programme (UIP)

- Target beneficiaries: Children aged 0-17 years and pregnant women.
- Coverage: The program targets 26.7 million newborns and 29 million pregnant women annually.
- Focus: Preventing 12 vaccine-preventable diseases:
  - Nationally: Diphtheria, Pertussis, Tetanus, Polio, Measles, Rubella, Tuberculosis, Hepatitis B, Meningitis & Pneumonia (caused by Haemophilus Influenzae type B)
  - Sub-nationally: Rotavirus diarrhea, Pneumococcal Pneumonia, Japanese Encephalitis (in endemic districts)
- Schedule: The program follows a specific immunization schedule, with vaccines administered at different ages and intervals.
- Delivery: Vaccines are provided free of charge at government health facilities and outreach sessions.
- Monitoring: The program is continuously monitored to assess coverage, identify gaps, and improve performance.

Vaccine Name	Type of Vaccine	Dose	Route	Schedule
BCG	Live attenuated	0.1 ml (0.05 ml for infants < 1 month)	Intradermal	At birth or as early as possible till one year of age
Hepatitis B	Recombinant	0.5 ml	Intramuscular	Birth dose within 24 hours, then at 6, 10, and 14 weeks
OPV	Live attenuated	2 drops	Oral	Birth dose within 15 days, then at 6, 10, and 14 weeks, booster at 16-24 months
IPV (Inactivated Polio Vaccine)	Inactivated	0.1 ml	Intramuscular	At 6 and 14 weeks
Pentavalent (DPT-Hib-HepB)	Combination	0.5 ml	Intramuscular	At 6, 10, and 14 weeks, booster at 16-24 months
Rotavirus Vaccine	Live attenuated	5 drops	Oral	At 6, 10, and 14 weeks
PCV (Pneumococcal Conjugate Vaccine)	Conjugate	0.5 ml	Intramuscular	At 6 weeks and 14 weeks, booster at 9 months
MR (Measles-Rubella)	Live attenuated	0.5 ml	Subcutaneous	First dose at 9-12 months, second dose at 16-24 months
Vitamin A	Supplement	1 ml (1 lakh IU) at 9 months, 2 ml (2 lakh IU) at 16 months, then every 6 months up to 5 years	Oral	With MR vaccine and then every 6 months up to 5 years
DPT Booster	Combination	0.5 ml	Intramuscular	At 16-24 months and 5-6 years
Td (Tetanus and adult diphtheria)	Toxoid	0.5 ml	Intramuscular	At 10 years, 16 years, and for pregnant women

DNA vaccines deliver a pathogen's genetic material (DNA) into a person's cells, instructing them to produce a specific antigen. This triggers an immune response, teaching the body to recognize and fight the actual pathogen. They typically consist of a plasmid, a circular piece of DNA, containing the gene encoding the antigen and a promoter to initiate its production in human cells.

Administration: DNA vaccines are often administered through injection.

Advantages:

Stability: More stable than traditional vaccines, making storage and transport easier.

Safety: Do not contain live pathogens, reducing the risk of causing illness.

Versatility: Can be designed to target various pathogens, including viruses, bacteria, and parasites.

Broad Immunity: Can induce both cellular and humoral immune responses, providing comprehensive protection.

Challenges:

Limited Human Efficacy: While promising in animal studies, efficacy in humans has been limited so far.

Delivery Challenges: Efficiently delivering DNA into cells can be challenging.

Potential for Integration: Theoretical risk of DNA integrating into the host's genome, though not observed in trials.

Human Trials: Undergoing trials for various diseases, including HIV, malaria, and cancer.

Example: ZyCoV-D, the world's first plasmid DNA vaccine for human use, against COVID-19.

mRNA vaccines are a new type of vaccine that teach your body how to fight off a disease using messenger RNA (mRNA). The mRNA codes for a harmless piece of a virus or bacteria, called an antigen.

1. Injection: The mRNA vaccine is injected into your body.
2. Delivery: The mRNA enters your cells.
3. Production: Cells read the mRNA instructions and produce the antigen.
4. Presentation: Display the antigen on their surface.
5. Recognition: Immune system recognizes the antigen as foreign and mounts a defense.
6. Immunity: This creates antibodies and memory cells that protect you if you encounter the real virus or bacteria in the future.

Example: The Pfizer-BioNTech and Moderna COVID-19 vaccines are examples of mRNA vaccines. They use mRNA that codes for the spike protein of the SARS-CoV-2 virus.