ADVANCE IMMUNITY :

MSc Microbiology : 2023-2024

Lecture two :

Immunity:

The condition of being resistant to infection.

The first recorded attempts to deliberately induce immunity date back to the 15th century when **people living in China and Turkey** inhaled powder made from smallpox scabs in order to produce protection against this dreaded disease.

late 1700s when an English country doctor by the name of **Edward Jenner** was able to successfully prevent infection with smallpox by injecting a less harmful substance—cowpox—from a disease affecting cows.

Almost a hundred years later when **Louis Pasteur**, often called the "father of immunology," observed by chance that older bacterial cultures accidentally left out on a laboratory bench for the summer would not cause disease when injected into chickens **.** Subsequent injections of more virulent organisms had no effect on the birds that had been previously exposed to the older cultures. In contrast, chickens that were not exposed to the older cultures died after being injected with the new fresh cultures.

In this manner, the first attenuated vaccine was discovered; this event can be considered the birth of immunology. He was thus the first scientist to introduce the concept that vaccination could be applied to any microbial disease.

In the late 1800s, scientists began to identify the actual mechanisms that produce immunity in a host. **Élie Metchnikoff**, a Russian scientist, observed under a microscope that foreign objects introduced into transparent starfish larvae became surrounded by motile amoeboid-like cells that attempted to destroy the penetrating objects. This process was later termed **phagocytosis,** meaning "cells that eat cells." He hypothesized that immunity to disease was based on the action of these scavenger cells and was a natural, or innate, host defense. He was eventually awarded a Nobel Prize for his pioneering work.

ACTIVE & PASSIVE IMMUNITY

Active immunity is a host immune response induced after contact with foreign antigens (e.g., microorganisms). This contact may occur through an infection or an immunization with microbial toxins or antigens. In all these instances, the host actively responds by making antibodies and activated T lymphocytes (i.e., adaptive immunity).

The main advantage of active immunity is that : resistance is long term.

Its major disadvantage is its slow onset, especially the primary response.

Passive immunity is given to a person in the form of immune components that were preformed in another person or animal.

Hospitals have supplies of antibody against toxins produced by bacteria that cause, for example, tetanus and botulism. Administering these to a patient transfers large amounts of antitoxin that is immediately available to neutralize the toxins. Likewise, preformed antibodies to rabies and other viruses can be injected to neutralize viral multiplication.

Other forms of passive immunity are IgG passed from mother to fetus during pregnancy and IgA passed from mother to newborn during breastfeeding.

Passive immunity can even occur between species, as when snakebite victims are given the antibody rich serum from an animal (usually horse or sheep) that was previously inoculated with the venom so that the serum contains high levels of specific antivenom antibodies.

The advantage of passive immunization is the prompt availability of large amounts of antibody. However, in bypassing an active immune response, passive immunization does not confer T cell or B cell memory. Therefore, because antibodies only last a few weeks, the main disadvantage of passive immunization is its short durability. Another disadvantage is the risk of hypersensitivity reactions, if serum from animals is used.

IMMUNOGENS

An immunogen is any molecule that induces an immune response. antigens are immunogens that react with the highly specific receptors on T cells or B cells.

1. Antigens

The features that determine immunogenicity are as follows:

Foreignness

In general, only molecules recognized as "nonself" or foreign are immunogenic (i.e., we are tolerant to our own molecules) .

Molecular Size

The most potent immunogens are large proteins (i.e., molecular weights above 100,000 g/mol), whereas midsized molecules (i.e., molecular weight below 10,000 g/mol) are weakly immunogenic, and very small ones (e.g., amino acids) are nonimmunogenic.

Chemical–Structural Complexity

Some chemical complexity is required for immunogenicity. For example, peptide "homopolymers" that contain a single type of amino acid are less immunogenic than peptides containing diverse amino acids.

Antigenic Determinants (Epitopes)

Epitopes are the chemical features on an antigen that physically bind to antibody or Tcell receptors. Most antigens have more than one epitope (i.e., they are multivalent).

Dosage, Route, and Timing of Antigen Exposure

Vaccine research aims to optimize these factors to find regimens with the best balance of highest immunogenicity, fewest side effects, and most convenient administration.

Host Genetics

The genetic makeup of each individual (especially the genes that form the MHC, can determine that individual's response to a particular immunogen.

2. Haptens

In contrast to an antigen, a hapten is a molecule that is not immunogenic by itself but can react with specific antibody. Haptens can be small molecules, nucleic acids, lipids, or drugs (e.g., penicillins), but because they are not peptides, they cannot activate helper T cells.

Haptens stimulate a primary adaptive response only when covalently bound to a "carrier" protein . In this process, the hapten interacts with the B-cell receptor of a naïve B cell and the entire hapten–carrier protein complex is internalized. The B cell processes this complex and presents a peptide from the carrier protein in association with its MHC protein to helper T cells, and a nearby helper T cell that recognizes that peptide then provides the help that stimulates the B cells to produce antibody to the hapten.

This is how conjugate vaccines work; a weak immunogen is "conjugated" to a strong peptide antigen such that T cells (recognizing the peptide) can help B cells (recognizing the weaker immunogen) to produce protective antibody.

Hapten–carrier conjugate induces antibody against the hapten. A hapten bound to a carrier protein can induce antibody to a hapten by the mechanism:

(1) A hapten can bind the surface immunoglobulin receptor on the B cell specific for the hapten.

(2) The hapten–carrier conjugate is taken up by the B cell, which processes the carrier protein into peptides.

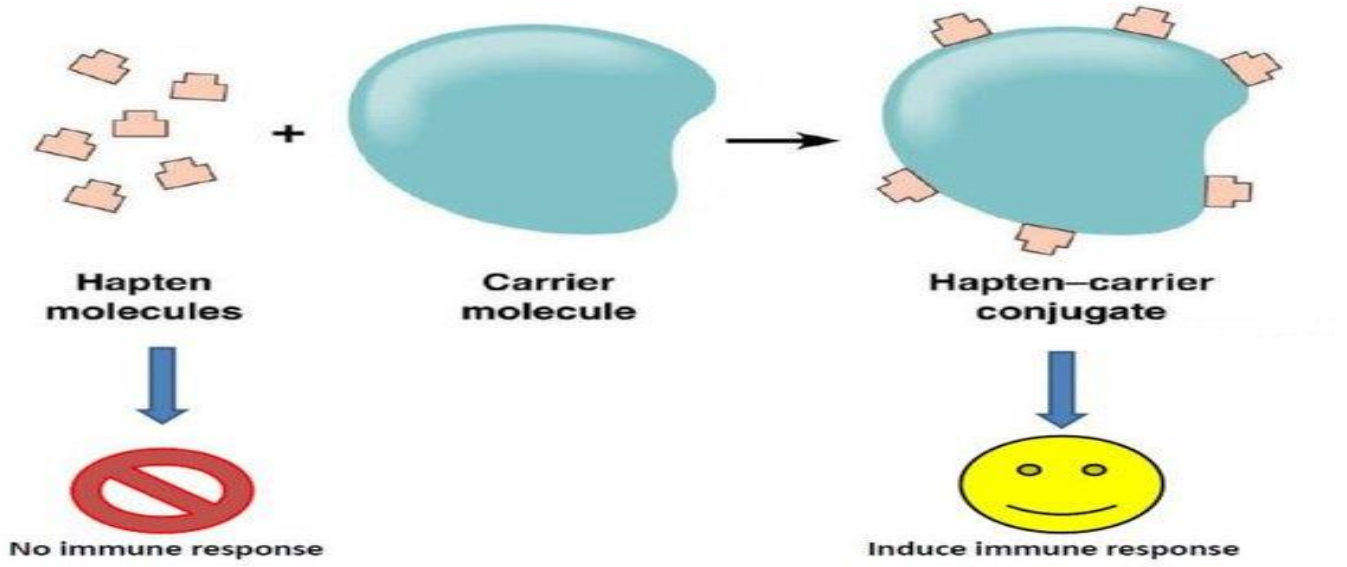
(3) But a hapten alone cannot induce antibody, because only peptides (not haptens) can be loaded onto major histocompatibility complex (MHC) proteins to present to CD4positiveT helper cells.

(4) Tcell recognition of carrier protein epitope by the Tcell receptor prompts production of T helper cytokines that are necessary to stimulate the B cell to differentiate.

Two additional ideas are needed to understand how haptens interact with our immune system. The first is that many haptens bind to our normal proteins and modify these proteins. Some examples of haptens that do this are drugs (e.g., penicillin) and poison oak oil. The hapten–protein combination now becomes immunogenic (i.e., the hapten modifies the protein sufficiently such that when the hapten–peptide combination is presented by the MHC protein, it is recognized as foreign).

The second idea is that a nonimmunogenic hapten can active cells if many hapten molecules bound to a carrier protein bind and cluster antibodies together. The best example of this occurs in mast cells, which are innate cells that become activated when a large number of antibodies are gathered together on the cell surface, a process called receptor crosslinking.

When many molecules of a hapten bind to a host protein, they can cause crosslinking of many penicillin specific IgE molecules on the mast cell surface. This activates the mast cell, which releases the mediators that cause hives (mast cells in the skin), bronchoconstriction (mast cells in the lungs), and anaphylaxis (mast cells in the systemic vasculature).

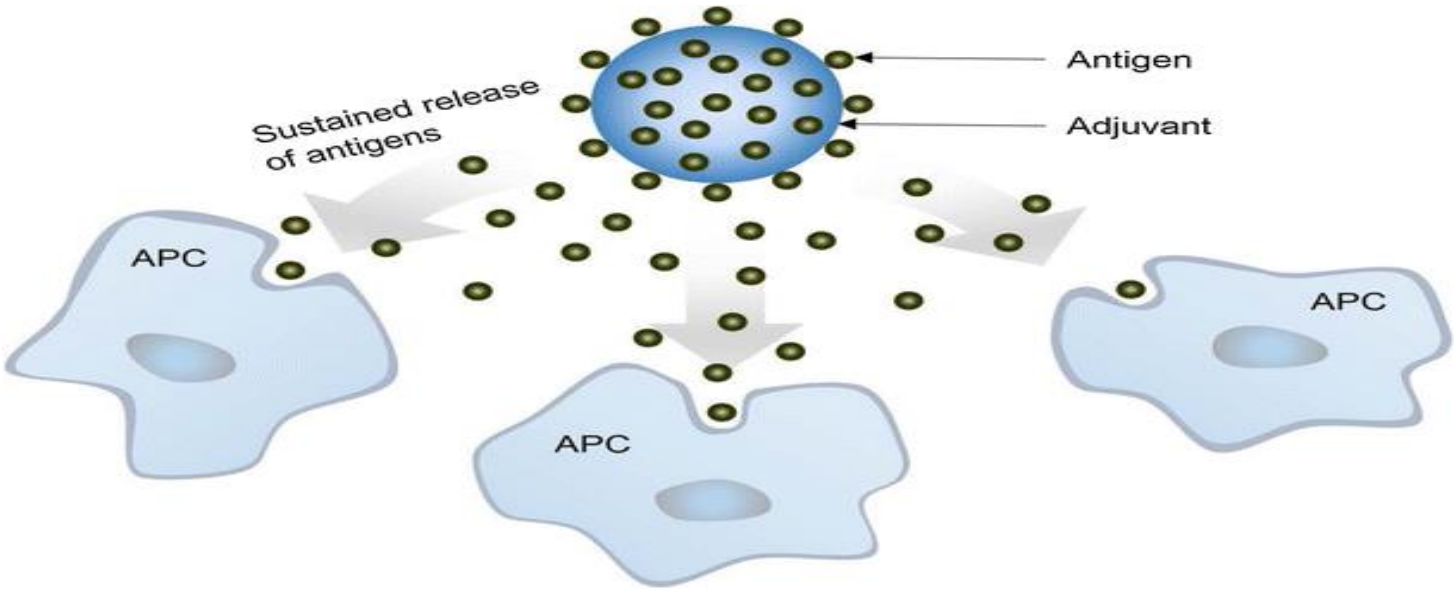


3. Adjuvants

Adjuvants enhance the immune response to an immunogen, but they do so without binding to antibody or to the immunogen.

Adjuvants can act by causing slow release of immunogen, thereby prolonging the stimulus; they can enhance uptake of immunogen by antigen presenting cells; they can speed up the migration of antigen presenting cells into the lymphoid tissues; and they can induce costimulatory molecules.

Another way adjuvants can work is by binding Toll like receptors on the surface of macrophages and B cells, which results in cytokine production that enhances T cell and B cell responses to the immunogen.



Immunity is less than optimal at both ends of life (i.e., in the newborn and the elderly). In newborns, natural barriers, such as the intestine, are not fully developed until 3 to 4 weeks of life, and innate cells, such as phagocytes, are less sensitive to cytokines and chemokines. Newborns have more circulating lymphocytes than adults, but the newborn's lymphocytes are individually less effective.

IgG and IgA production begins after birth and only reaches protective levels at around 1 year. As a consequence, until around 6 months, most of the circulating IgG is, in fact, maternal derived antibody that crossed the placenta before birth, and the mucosal surface of the gastrointestinal tract is similarly protected by maternal IgA that is secreted into breast milk.

However, as we become elderly, immunity declines. The thymus, which is the source of all new T cells , begins to atrophy during puberty, and by the time we reach age 60, we mostly rely on memory T cells for immunity because our ability to generate T cells that recognize new antigens is greatly decreased. B cells similarly trend toward a more experienced and "exhausted" state later in life.

As a result, the immune responses to certain vaccines and infections are blunted.

As in the very young, the elderly experience a somewhat increased frequency and severity of infections, such as influenza.

In addition, the elderly can develop "reactivation" of a latent infection, caused by, for example, Mycobacterium tuberculosis or varicellazoster virus, which was previously held in check by their "young" immune system.

This phenomenon, known as immunosenescence, might explain why older age groups are so hard hit by COVID19.

And there is another troubling implication: vaccines, which activate the immune system to fight off invaders, often perform poorly in older people. The best strategy for quelling the pandemic might fail in exactly the group that needs it most.