Course Name	**: Immunology fundamentals**
Course Code	**: APBPH 2202**
Course level	**: Level 4**
Course Credit	**: 4 CU**
Contact Hours	**: 60 Hrs**

IMMUNOLOGY

Course Description

The course deals with understanding the concept of Immunology, branches of immunology, the importance of immunology, immune system, studying various disorders of the human immunity, organs of the immune system, cells in the innate immune system, Immunological Biomolecules and pathogenesis.

Course Objectives

- To help students access a more firm understanding on the wider concept of immunology.
- To enable them learn measures to protect and increase their own immunity by eating balanced diets.
- To increase the students' capacity to identify illnesses that affect the human immunity.

Course Content

Introduction

- Definition of Immunology
- Who is an Immunologist
- Histological examination of the Immune System
- Branches of Immunology
- Essence of Immunology

Immune System

- Meaning of Immune System
- Components of the immune system
- Surface barriers
- Humoral and chemical barriers
- Adaptive immune system

Disorders of Human Immunity

- Immunodeficiencies
- Autoimmunity
- Hypersensitivity
- Other mechanisms

Organs of the Immune System

- Thymus
- Bone-White blood cells
- Spleen-Rich in B and T lymphocytes

Cells in the Innate Immune System

- Mast Cells
- Phagocytes
- Macrophages

Immunological Biomolecules

- Antibodies
- Antigen
- Superantigen
- Histamines
- Cytolysins

Immunity

- Definition of Immunity
- Different types of Immunity

Pathogenesis

- Definition of Pathogens
- Types of Pathogens
- Other Parasites

IMMUNOLOGY MODULE

Course Work

Define immunology and explain the importances of immunology to the medical fraternity

Discuss different immunisable diseases and their respective impact on the population

Introduction

Immunology is a broad branch of biomedical science that covers the study of all aspects of the immune system in all organisms. It deals with the physiological functioning of the immune system in states of both health and diseases; malfunctions of the immune system in immunological disorders (autoimmune diseases, hypersensitivities, immune deficiency, transplant rejection); the physical, chemical and physiological characteristics of the components of the immune system in vitro, in situ, and in vivo. Immunology has applications in several disciplines of science, and as such is further divided.

Immunology is a science that examines the structure and function of the immune system. It originates from medicine and early studies on the causes of immunity to disease. The earliest known reference to immunity was during the plague of Athens in 430 BC. Thucydides noted that people who had recovered from a previous bout of the disease could nurse the sick without contracting

the illness a second time. In the 18th century, Pierre-Louis Moreau de Maupertuis made experiments with scorpion venom and observed that certain dogs and mice were immune to this venomThis and other observations of acquired immunity were later exploited by Louis Pasteur in his development of vaccination and his proposed germ theory of disease. Pasteur's theory was in direct opposition to contemporary theories of disease, such as the miasma theory. It was not until Robert Koch's 1891 proofs, for which he was awarded a Nobel Prize in 1905, that microorganisms were confirmed as the cause of infectious diseaseViruses were confirmed as human pathogens in 1901, with the discovery of the yellow fever virus by Walter Reed.

Immunology made a great advance towards the end of the 19th century, through rapid developments, in the study of humoral immunity and cellular immunity Particularly important was the work of Paul Ehrlich, who proposed the side-chain theory to explain the specificity of the antigen-antibody reaction; his contributions to the understanding of humoral immunity were recognized by the award of a Nobel Prize in 1908, which was jointly awarded to the founder of cellular immunology, Elie Metchnikoff.

Immunologist

According to the American Academy of Allergy, Asthma, and Immunology (AAAAI), "an immunologist is a research scientist who investigates the immune system of vertebrates (including the human immune system). Immunologists include research scientists (Ph.D.) who work in laboratories. Immunologists also include physicians who, for example, treat patients with immune system disorders. Some immunologists are physician-scientists who combine laboratory research with patient care." Imunnologist basically carry out their activities in various sectors which includes science as a whole, laboratories and medicine as a profession, the level of education is rather looked at as doctrate of philosphy, Doctor of Medicine, Doctor of Osteopathic Medicine

Histological examination of the immune system

Even before the concept of immunity (from *immunis*, Latin for "exempt") was developed, numerous early physicians characterised organs that would later prove to be part of the immune system. The key primary lymphoid organs of the immune system are the thymus and bone marrow, and secondary lymphatic tissues such as spleen, tonsils, lymph vessels, lymph nodes, adenoids, and skin and liver. When health conditions warrant, immune system organs including the thymus, spleen, portions of bone marrow, lymph nodes and secondary lymphatic tissues can be surgically excised for examination while patients are still alive.

Many components of the immune system are actually cellular in nature and not associated with any specific organ but rather are embedded or circulating in various tissues located throughout the body.They are several categorise of immunology and they include

Branches of immunology

They are several branches of immunology which include

- Classical immunology
- Clinical immunology
- Computational immunology
- Diagnostic immunology
- Evolutionary immunology
- Immunotherapy
- Systems immunology
- Cancer immunology
- Testicular immunology

Classical immunology

Classical immunology ties in with the fields of epidemiology and medicine. It studies the relationship between the body systems, pathogens, and immunity. The earliest written mention of immunity can be traced back to the plague of Athens in 430 BCE. Thucydides noted that people who had recovered from a previous bout of the disease could nurse the sick without contracting the illness a second time. Many other ancient societies have references to this phenomenon, but it was not until the 19th and 20th centuries before the concept developed into scientific theory.

The study of the molecular and cellular components that comprise the immune system, including their function and interaction, is the central science of immunology. The immune system has been divided into a more primitive innate immune system, and acquired or adaptive immune system of vertebrates, the latter of which is further divided into humoral and cellular components.

The humoral (antibody) response is defined as the interaction between antibodies and antigens. Antibodies are specific proteins released from a certain class of immune cells (B lymphocytes). Antigens are defined as anything that elicits generation of antibodies, hence they are **Anti**body **Gen**erators. Immunology itself rests on an understanding of the properties of these two biological entities. However, equally important is the cellular response, which can not only kill infected cells in its own right, but is also crucial in controlling the antibody response. Put simply, both systems are highly interdependent.

Clinical immunology

Clinical immunology is the study of diseases caused by disorders of the immune system (failure, aberrant action, and malignant growth of the cellular elements of the system). It also involves diseases of other systems, where immune reactions play a part in the pathology and clinical features.

The diseases caused by disorders of the immune system fall into two broad categories: immunodeficiency, in which parts of the immune system fail to provide an adequate response (examples include chronic granulomatous disease), and autoimmunity, in which the immune system attacks its own host's body (examples include systemic lupus erythematosus, rheumatoid arthritis, Hashimoto's disease and myasthenia gravis). Other immune system disorders include different hypersensitivities, in which

the system responds inappropriately to harmless compounds (asthma and other allergies) or responds too intensely.

The most well-known disease that affects the immune system itself is AIDS, caused by HIV. AIDS is an immunodeficiency characterized by the lack of CD4+ ("helper") T cells and macrophages, which are destroyed by HIV.

Clinical immunologists also study ways to prevent transplant rejection, in which the immune system attempts to destroy allografts os

Developmental immunology

The body's capability to react to antigen depends on a person's age, antigen type, maternal factors and the area where the antigen is presented. Neonates are said to be in a state of physiological immunodeficiency, because both their innate and adaptive immunological responses are greatly suppressed. Once born, a child's immune system responds favorably to protein antigens while not as well to glycoproteins and polysaccharides. In fact, many of the infections acquired by neonates are caused by low virulence organisms like Staphylococcus and Pseudomonas. In neonates, opsonic activity and the ability to activate the complement cascade is very limited. For example, the mean level of C3 in a newborn is approximately 65% of that found in the adult. Phagocytic activity is also greatly impaired in newborns. This is due to lower opsonic activity, as well as diminished up-regulation of integrin and selectin receptors, which limit the ability of neutrophils to interact with adhesion molecules in the endothelium. Their monocytes are slow and have a reduced ATP production, which also limits the newborns phagocytic activity. Although, the number of total lymphocytes is significantly higher than in adults, the cellular and humoral immunity is also impaired. Antigen presenting cells in newborns have a reduced capability to activate T cells. Also, T cells of a newborn proliferate poorly and produce very small amounts of cytokines like IL-2, IL-4, IL-5, IL-12, and IFN-g which limits their capacity to activate the humoral response as well as the phagocitic activity of macrophage. B cells develop early in gestation but are not fully active.

Monocytes: An Artist's Impression

Maternal factors also play a role in the body's immune response. At birth most of the immunoglobulin is present is maternal IgG. Because IgM, IgD, IgE and IgA don't cross the placenta, they are almost undetectable at birth. Although some IgA is provided in breast milk. These passively acquired antibodies can protect the newborn up to 18 months, but their response is usually short-lived and of low affinity. These antibodies can also produce a negative response. If a child is exposed to the antibody for a particular antigen before being exposed to the antigen itself then the child will produce a dampened response. Passively acquired maternal antibodies can suppress the antibody response to active immunization. Similarly the response of T-cells to vaccination differs in children compared to adults, and vaccines that induce Th1 responses in adults do not readily elicit these same responses in neonates.By 6-9 months after birth, a child's immune system begins to respond more strongly to glycoproteins. Not until 12-24 months of age is there a marked improvement in the

body's response to polysaccharides. This can be the reason for the specific time frames found in vaccination schedules.

During adolescence the human body undergoes several physical, physiological and immunological changes. These changes are started and mediated by different hormones. Depending on the sex either testosterone or 17-β-oestradiol, act on male and female bodies accordingly, start acting at ages of 12 and 10 years.

There is evidence that these steroids act directly not only on the primary and secondary sexual characteristics, but also have an effect on the development and regulation of the immune system.

There is an increased risk in developing autoimmunity for pubescent and post pubescent females and males. There is also some evidence that cell surface receptors on B cells and macrophages may detect sex hormones in the system.

The female sex hormone 17-β-oestradiol has been shown to regulate the level of immunological response. Similarly, some male androgens, like testosterone, seem to suppress the stress response to infection; but other androgens like DHEA have the opposite effect, as it increases the immune response instead of down playing it As in females, the male sex hormones seem to have more control of the immune system during puberty and the time right after than in fully developed adults. Other than hormonal changes physical changes like the involution of the Thymus during puberty will also affect the immunological response of the subject or patient.

Immunotherapy

The use of immune system components to treat a disease or disorder is known as immunotherapy. Immunotherapy is most commonly used in the context of the treatment of cancers together with chemotherapy (drugs) and radiotherapy (radiation). However, immunotherapy is also often used in the immunosuppressed (such as HIV patients) and people suffering from other immune deficiencies or autoimmune diseases.

Diagnostic immunology

The specificity of the bond between antibody and antigen has made it an excellent tool in the detection of substances in a variety of diagnostic techniques. Antibodies specific for a desired antigen can be conjugated with a radiolabel, fluorescent label, or color-forming enzyme and are used as a "probe" to detect it. However, the similarity between some antigens can lead to false positives and other errors in such tests by antibodies cross-reacting with antigens that aren't exact matches.

Evolutionary immunology

Study of the immune system in extant species is capable of giving us a key understanding of the evolution of species and the immune system.

A development of complexity of the immune system can be seen from simple phagocytotic protection of single celled organisms, to circulating antimicrobial

peptides in insects to lymphoid organs in vertebrates. However, it is important to recognize that every organism living today has an immune system that has evolved to be absolutely capable of protecting it from most forms of harm; those organisms that did not adapt their immune systems to external threats are no longer around to be observed.

Insects and other arthropods, while not possessing true adaptive immunity, show highly evolved systems of innate immunity, and are additionally protected from external injury (and exposure to pathogens) by their chitinous shells.

Reproductive immunology

This area of the immunology is devoted to the study of immunological aspects of the reproductive process including fetus acceptance. The term has also been used by fertility clinics to address fertility problems, recurrent miscarriages, premature deliveries, and dangerous complications such as pre-eclampsia.

Essence of immunology

- Branch of Biomedical science
- Immune system
- Immunity
- Viral immunology

Immune system

An **immune system** is a system of biological structures and processes within an organism that protects against disease. In order to function properly, an immune system must detect a wide variety of agents, from viruses to parasitic worms, and distinguish them from the organism's own healthy tissue.

Pathogens can rapidly evolve and adapt to avoid detection and destruction by the immune system. As a result, multiple defense mechanisms have also evolved to recognize and neutralize pathogens. Even simple unicellular organisms such as bacteria possess a rudimentary immune system, in the form of enzymes which protect against bacteriophage infections. Other basic immune mechanisms evolved in ancient eukaryotes and remain in their modern descendants, such as plants and insects. These mechanisms include phagocytosis, antimicrobial peptides called defensins, and the complement system. Jawed vertebrates, including humans, have even more sophisticated defense mechanisms including the ability to adapt over time to recognize specific pathogens more efficiently. Adaptive (or acquired) immunity creates immunological memory after an initial response to a specific pathogen, leading to an enhanced response to subsequent encounters with that same pathogen. This process of acquired immunity is the basis of vaccination.

Disorders of the immune system can result in autoimmune diseases, inflammatory diseases and cancer. Immunodeficiency occur when the immune

system is less active than normal, resulting in recurring and life-threatening infections. In humans, immunodeficiency can either be the result of a genetic disease, such as severe combined immunodeficiency, or acquired conditions such as HIV/AIDS or the use of immunosuppressive medication. In contrast, autoimmunityresult from a hyperactive immune system attacking normal tissues as if they were foreign organisms. Common autoimmune diseases include Hashimoto's thyroiditis, rheumatoid arthritis, diabetes mellitus type 1, and systemic lupus erythematosus. Immunology covers the study of all aspects of the immune system.

Layered defense

The immune system protects organisms from infection with layered defenses of increasing specificity. In simple terms, physical barriers prevent pathogens such as bacteria and viruses from entering the organism. If a pathogen breaches these barriers, the innate immune system provides an immediate, but non-specific response. Innate immune systems are found in all plants and animalsIf pathogens successfully evade the innate response, vertebrates possess a second layer of protection, the adaptive immune system, which is activated by the innate response. Here, the immune system adapts its response during an infection to improve its recognition of the pathogen. This improved response is then retained after the pathogen has been eliminated, in the form of an immunological memory, and allows the adaptive immune system to mount faster and stronger attacks each time this pathogen is encountered

Components of the immune system	
Innate immune system	**Adaptive immune system**
Response is non-specific	Pathogen and antigen specific response
Exposure leads to immediate maximal response	Lag time between exposure and maximal response
Cell-mediated and humoral components	Cell-mediated and humoral components
No immunological memory	Exposure leads to immunological memory
Found in nearly all forms of life	Found only in jawed vertebrates

Both innate and adaptive immunity depend on the ability of the immune system to distinguish between self and non-self molecules. In immunology, *self* molecules are those components of an organism's body that can be distinguished from foreign substances by the immune system Conversely, *non-self* molecules are those recognized as foreign molecules. One class of non-self moleculesare called antigens (short for *anti*body *gen*erators) and are defined as substances that bind to specific immune receptors and elicit an immune response.

Surface barriers

Several barriers protect organisms from infection, including mechanical, chemical, and biological barriers. The waxy cuticle of many leaves, the exoskeleton of insects, the shells and membranes of externally deposited eggs, and skin are examples of mechanical barriers that are the first line of defense against infection However, as organisms cannot be completely sealed against their environments, other systems act to protect body openings such as the lungs, intestines, and the genitourinary tract. In the lungs, coughing and sneezing mechanically eject pathogens and other irritants from the respiratory tract. The flushing action of tears and urine also mechanically expels pathogens, while mucus secreted by the respiratory and gastrointestinal tract serves to trap and entangle microorganisms

Chemical barriers also protect against infection. The skin and respiratory tract secrete antimicrobial peptides such as the β-defensins. Enzymes such as lysozyme and phospholipase A2 in saliva, tears, and breast milk are also antibacterials. Vaginal secretions serve as a chemical barrier following menarche, when they become slightly acidic, while semen contains defensins and zinc to kill pathogens. In the stomach, gastric acid and proteases serve as powerful chemical defenses against ingested pathogens.

Within the genitourinary and gastrointestinal tracts, commensalflora serve as biological barriers by competing with pathogenic bacteria for food and space and, in some cases, by changing the conditions in their environment, such as pH or available iron This reduces the probability that pathogens will be able to reach sufficient numbers to cause illness. However, since most antibiotics non-specifically target bacteria and do not affect fungi, oral antibiotics can lead to an “overgrowth” of fungi and cause conditions such as a vaginal candidiasis (a yeast infection). There is good evidence that re-introduction of probiotic flora, such as pure cultures of the lactobacilli normally found in unpasteurized yogurt, helps restore a healthy balance of microbial populations in intestinal infections in children and encouraging preliminary data in studies on bacterial gastroenteritis, inflammatory bowel diseases, urinary tract infection and post-surgical infections.

Innate immune system

Microorganisms or toxins that successfully enter an organism will encounter the cells and mechanisms of the innate immune system. The innate response is usually triggered when microbes are identified by pattern recognition receptors, which recognize components that are conserved among broad groups of microorganisms, or when damaged, injured or stressed cells send out alarm signals, many of which (but not all) are recognized by the same receptors as those that recognize pathogens. Innate immune defenses are non-specific, meaning these systems respond to pathogens in a generic way. This system

does not confer long-lasting immunity against a pathogen. The innate immune system is the dominant system of host defense in most organisms.

Humoral and chemical barriers

Inflammation

Inflammation is one of the first responses of the immune system to infection. The symptoms of inflammation are redness, swelling, heat, and pain which are caused by increased blood flow into a tissue. Inflammation is produced by eicosanoids and cytokines, which are released by injured or infected cells. Eicosanoids include prostaglandins that produce fever and the dilation of blood vessels associated with inflammation, and leukotrienes that attract certain white blood cells (leukocytes). Common cytokines include interleukins that are responsible for communication between white blood cells; chemokines that promote chemotaxis; and interferons that have anti-viral effects, such as shutting down protein synthesis in the host cell Growth factors and cytotoxic factors may also be released. These cytokines and other chemicals recruit immune cells to the site of infection and promote healing of any damaged tissue following the removal of pathogens.

Complement system

The complement system is a biochemical cascade that attacks the surfaces of foreign cells. It contains over 20 different proteins and is named for its ability to "complement" the killing of pathogens by antibodies. Complement is the major humoral component of the innate immune response. Many species have complement systems, including non-mammals like plants, fish, and some invertebrates.

In humans, this response is activated by complement binding to antibodies that have attached to these microbes or the binding of complement proteins to carbohydrates on the surfaces of microbes. This recognition signal triggers a rapid killing response The speed of the response is a result of signal amplification that occurs following sequential proteolytic activation of complement molecules, which are also proteases. After complement proteins initially bind to the microbe, they activate their protease activity, which in turn activates other complement proteases, and so on. This produces a catalytic cascade that amplifies the initial signal by controlled positive feedback The cascade results in the production of peptides that attract immune cells, increase vascular permeability, and opsonize (coat) the surface of a pathogen, marking it for destruction. This deposition of complement can also kill cells directly by disrupting their plasma membrane.[33]

Cellular barriers

scanning electron microscope image of normal circulating human blood. One can see red blood cells, several knobby white blood cells including lymphocytes, a monocyte, a neutrophil, and many small disc-shaped platelets.

Leukocytes (white blood cells) act like independent, single-celled organisms and are the second arm of the innate immune system. The innate leukocytes include the phagocytes (macrophages, neutrophils, and dendritic cells), mast cells, eosinophils, basophils, and natural killer cells. These cells identify and eliminate pathogens, either by attacking larger pathogens through contact or by engulfing and then killing microorganisms. Innate cells are also important mediators in the activation of the adaptive immune system

Phagocytosis is an important feature of cellular innate immunity performed by cells called 'phagocytes' that engulf, or eat, pathogens or particles. Phagocytes generally patrol the body searching for pathogens, but can be called to specific locations by cytokines. Once a pathogen has been engulfed by a phagocyte, it becomes trapped in an intracellular vesicle called a phagosome, which subsequently fuses with another vesicle called a lysosome to form a phagolysosome. The pathogen is killed by the activity of digestive enzymes or following a respiratory burst that releases free radicals into the phagolysosome. Phagocytosis evolved as a means of acquiring nutrients, but this role was extended in phagocytes to include engulfment of pathogens as a defense mechanism. Phagocytosis probably represents the oldest form of host defense, as phagocytes have been identified in both vertebrate and invertebrate animals

Neutrophils and macrophages are phagocytes that travel throughout the body in pursuit of invading pathogens. Neutrophils are normally found in the bloodstream and are the most abundant type of phagocyte, normally representing 50% to 60% of the total circulating leukocytes. During the acute phase of inflammation, particularly as a result of bacterial infection, neutrophils migrate toward the site of inflammation in a process called chemotaxis, and are usually the first cells to arrive at the scene of infection. Macrophages are versatile cells that reside within tissues and produce a wide array of chemicals including enzymes, complement proteins, and regulatory factors such as interleukin 1. Macrophages also act as scavengers, ridding the body of worn-out cells and other debris, and as antigen-presenting cells that activate the adaptive immune system.

Dendritic cells (DC) are phagocytes in tissues that are in contact with the external environment; therefore, they are located mainly in the skin, nose, lungs, stomach, and intestines. They are named for their resemblance to neuronaldendrites, as both have many spine-like projections, but dendritic cells are in no way connected to the nervous system. Dendritic cells serve as a link between the bodily tissues and the innate and adaptive immune systems, as they present antigen to T cells, one of the key cell types of the adaptive immune system.

Mast cells reside in connective tissues and mucous membranes, and regulate the inflammatory response. They are most often associated with allergy and anaphylaxis Basophils and eosinophils are related to neutrophils. They secrete chemical mediators that are involved in defending against parasites and play a role in allergic reactions, such as asthma Natural killer (NK cells) cells are leukocytes that attack and destroy tumor cells, or cells that have been infected by viruses.

Adaptive immune system

The adaptive immune system evolved in early vertebrates and allows for a stronger immune response as well as immunological memory, where each pathogen is "remembered" by a signature antigen. The adaptive immune response is antigen-specific and requires the recognition of specific “non-self” antigens during a process called antigen presentation. Antigen specificity allows for the generation of responses that are tailored to specific pathogens or pathogen-infected cells. The ability to mount these tailored responses is maintained in the body by "memory cells". Should a pathogen infect the body more than once, these specific memory cells are used to quickly eliminate it.

Lymphocytes

The cells of the adaptive immune system are special types of leukocytes, called lymphocytes. B cells and T cells are the major types of lymphocytes and are derived from hematopoietic stem cells in the bone marrow. B cells are involved in the humoral immune response, whereas T cells are involved in cell-mediated immune response.

Both B cells and T cells carry receptor molecules that recognize specific targets. T cells recognize a “non-self” target, such as a pathogen, only after antigens (small fragments of the pathogen) have been processed and presented in combination with a “self” receptor called a major histocompatibility complex (MHC) molecule. There are two major subtypes of T cells: the killer T cell and the helper T cell. Killer T cells only recognize antigens coupled to Class I MHC molecules, while helper T cells only recognize antigens coupled to Class II MHC molecules. These two mechanisms of antigen presentation reflect the different roles of the two types of T cell. A third, minor subtype are the γδ T cells that recognize intact antigens that are not bound to MHC receptors.

In contrast, the B cell antigen-specific receptor is an antibody molecule on the B cell surface, and recognizes whole pathogens without any need for antigen processing. Each lineage of B cell expresses a different antibody, so the complete set of B cell antigen receptors represent all the antibodies that the body can manufacture.

Killer T cells

Killer T cells directly attack other cells carrying foreign or abnormal antigens on their surfaces.

Killer T cell are a sub-group of T cells that kill cells that are infected with viruses (and other pathogens), or are otherwise damaged or dysfunctional. As with B cells, each type of T cell recognises a different antigen. Killer T cells are activated when their T cell receptor (TCR) binds to this specific antigen in a complex with the MHC Class I receptor of another cell. Recognition of this MHC:antigen complex is aided by a co-receptor on the T cell, called CD8. The T cell then travels throughout the body in search of cells where the MHC I receptors bear this antigen. When an activated T cell contacts such cells, it releases cytotoxins, such as perforin, which form pores in the target cell's plasma membrane, allowing ions, water and toxins to enter. The entry of another toxin called granulysin (a protease) induces the target cell to undergo apoptosis. T cell killing of host cells is particularly important in preventing the replication of viruses. T cell activation is tightly controlled and generally requires a very strong MHC/antigen activation signal, or additional activation signals provided by "helper" T cells (see below).

[Helper T cells

Function of T helper cells: Antigen-presenting cells (APCs) present antigen on their Class II MHC molecules (MHC2). Helper T cells recognize these, with the help of their expression of CD4 co-receptor (CD4+). The activation of a resting helper T cell causes it to release cytokines and other stimulatory signals (green arrows) that stimulate the activity of macrophages, killer T cells and B cells, the latter producing antibodies. The stimulation of B cells and macrophages succeeds a proliferation of T helper cells.

Helper T cells regulate both the innate and adaptive immune responses and help determine which types of immune responses the body will make to a particular pathogen These cells have no cytotoxic activity and do not kill infected cells or clear pathogens directly. They instead control the immune response by directing other cells to perform these tasks.

Helper T cells express T cell receptors (TCR) that recognize antigen bound to Class II MHC molecules. The MHC:antigen complex is also recognized by the helper cell's CD4 co-receptor, which recruits molecules inside the T cell (e.g., Lck) that are responsible for the T cell's activation. Helper T cells have a weaker association with the MHC:antigen complex than observed for killer T cells, meaning many receptors (around 200–300) on the helper T cell must be bound by an MHC:antigen in order to activate the helper cell, while killer T cells can be activated by engagement of a single MHC:antigen molecule. Helper T cell activation also requires longer duration of engagement with an antigen-presenting cell. The activation of a resting helper T cell causes it to release cytokines that influence the activity of many cell types. Cytokine signals produced by helper T cells enhance the microbicidal function of macrophages

and the activity of killer T cells. In addition, helper T cell activation causes an upregulation of molecules expressed on the T cell's surface, such as CD40 ligand (also called CD154), which provide extra stimulatory signals typically required to activate antibody-producing B cells.

γδ T cells

γδ T cells possess an alternative T cell receptor (TCR) as opposed to CD4+ and CD8+ (αβ) T cells and share the characteristics of helper T cells, cytotoxic T cells and NK cells. The conditions that produce responses from γδ T cells are not fully understood. Like other 'unconventional' T cell subsets bearing invariant TCRs, such as CD1d-restricted Natural Killer T cells, γδ T cells straddle the border between innate and adaptive immunity. On one hand, γδ T cells are a component of adaptive immunity as they rearrange TCR genes to produce receptor diversity and can also develop a memory phenotype. On the other hand, the various subsets are also part of the innate immune system, as restricted TCR or NK receptors may be used as pattern recognition receptors. For example, large numbers of human Vγ9/Vδ2 T cells respond within hours to common molecules produced by microbes, and highly restricted Vδ1+ T cells in epithelia will respond to stressed epithelial cells.

An antibody is made up of two heavy chains and two light chains. The unique variable region allows an antibody to recognize its matching antigen

B lymphocytes and antibodies

A B cell identifies pathogens when antibodies on its surface bind to a specific foreign antigen. This antigen/antibody complex is taken up by the B cell and processed by proteolysis into peptides. The B cell then displays these antigenic peptides on its surface MHC class II molecules. This combination of MHC and antigen attracts a matching helper T cell, which releases lymphokines and activates the B cell. As the activated B cell then begins to divide, its offspring (plasma cells) secrete millions of copies of the antibody that recognizes this antigen. These antibodies circulate in blood plasma and lymph, bind to pathogens expressing the antigen and mark them for destruction by complement activation or for uptake and destruction by phagocytes. Antibodies can also neutralize challenges directly, by binding to bacterial toxins or by interfering with the receptors that viruses and bacteria use to infect cells.

Alternative adaptive immune system

Although the classical molecules of the adaptive immune system (e.g., antibodies and T cell receptors) exist only in jawed vertebrates, a distinct lymphocyte-derived molecule has been discovered in primitive jawless vertebrates, such as the lamprey and hagfish. These animals possess a large array of molecules called variable lymphocyte receptors (VLRs) that, like the antigen receptors of jawed vertebrates, are produced from only a small number

(one or two) of genes. These molecules are believed to bind pathogenic antigens in a similar way to antibodies, and with the same degree of specificity.

Immunological memory

When B cells and T cells are activated and begin to replicate, some of their offspring will become long-lived memory cells. Throughout the lifetime of an animal, these memory cells will remember each specific pathogen encountered and can mount a strong response if the pathogen is detected again. This is "adaptive" because it occurs during the lifetime of an individual as an adaptation to infection with that pathogen and prepares the immune system for future challenges. Immunological memory can be in the form of either passive short-term memory or active long-term memory.

Passive memory

Newborn infants have no prior exposure to microbes and are particularly vulnerable to infection. Several layers of passive protection are provided by the mother. During pregnancy, a particular type of antibody, called IgG, is transported from mother to baby directly across the placenta, so human babies have high levels of antibodies even at birth, with the same range of antigen specificities as their mother.[63]Breast milk or colostrum also contains antibodies that are transferred to the gut of the infant and protect against bacterial infections until the newborn can synthesize its own antibodies This is passive immunity because the fetus does not actually make any memory cells or antibodies—it only borrows them. This passive immunity is usually short-term, lasting from a few days up to several months. In medicine, protective passive immunity can also be transferred artificially from one individual to another via antibody-rich serum

The time-course of an immune response begins with the initial pathogen encounter, (or initial vaccination) and leads to the formation and maintenance of active immunological memory.

Active memory and immunization

Long-term *active* memory is acquired following infection by activation of B and T cells. Active immunity can also be generated artificially, through vaccination. The principle behind vaccination (also called immunization) is to introduce an antigen from a pathogen in order to stimulate the immune system and develop specific immunity against that particular pathogen without causing disease associated with that organism. This deliberate induction of an immune response is successful because it exploits the natural specificity of the immune system, as well as its inducibility. With infectious disease remaining one of the leading causes of death in the human population, vaccination represents the most effective manipulation of the immune system mankind has developed.

Most viral vaccines are based on live attenuated viruses, while many bacterial vaccines are based on acellular components of micro-organisms, including harmless toxin components. Since many antigens derived from acellular vaccines do not strongly induce the adaptive response, most bacterial vaccines are provided with additional adjuvants that activate the antigen-presenting cells of the innate immune system and maximize immunogenicity

Disorders of human immunity

The immune system is a remarkably effective structure that incorporates specificity, inducibility and adaptation. Failures of host defense do occur, however, and fall into three broad categories: immunodeficiencies, autoimmunity, and hypersensitivities.

Immunodeficiencies

Immunodeficiencies occur when one or more of the components of the immune system are inactive. The ability of the immune system to respond to pathogens is diminished in both the young and the elderly, with immune responses beginning to decline at around 50 years of age due to immunosenescence. In developed countries, obesity, alcoholism, and drug use are common causes of poor immune function However, malnutrition is the most common cause of immunodeficiency in developing countries. Diets lacking sufficient protein are associated with impaired cell-mediated immunity, complement activity, phagocyte function, IgA antibody concentrations, and cytokine production. Additionally, the loss of the thymus at an early age through genetic mutation or surgical removal results in severe immunodeficiency and a high susceptibility to infection.

Immunodeficiencies can also be inherited or 'acquired'. Chronic granulomatous disease, where phagocytes have a reduced ability to destroy pathogens, is an example of an inherited, or congenital, immunodeficiency. AIDS and some types of cancer cause acquired immunodeficiency.

Autoimmunity

Overactive immune responses comprise the other end of immune dysfunction, particularly the autoimmune disorders. Here, the immune system fails to properly distinguish between self and non-self, and attacks part of the body. Under normal circumstances, many T cells and antibodies react with “self” peptides. One of the functions of specialized cells (located in the thymus and bone marrow) is to present young lymphocytes with self antigens produced throughout the body and to eliminate those cells that recognize self-antigens, preventing autoimmunity.

Hypersensitivity

Hypersensitivity is an immune response that damages the body's own tissues. They are divided into four classes (Type I – IV) based on the mechanisms involved and the time course of the hypersensitive reaction. Type I hypersensitivity is an immediate or anaphylactic reaction, often associated with allergy. Symptoms can range from mild discomfort to death. Type I hypersensitivity is mediated by IgE, which triggers degranulation of mast cells and basophils when cross-linked by antigen. Type II hypersensitivity occurs when antibodies bind to antigens on the patient's own cells, marking them for destruction. This is also called antibody-dependent (or cytotoxic) hypersensitivity, and is mediated by IgG and IgM antibodies.[Immune complexes (aggregations of antigens, complement proteins, and IgG and IgM antibodies) deposited in various tissues trigger Type III hypersensitivity reactions. Type IV hypersensitivity (also known as cell-mediated or *delayed type hypersensitivity*) usually takes between two and three days to develop. Type IV reactions are involved in many autoimmune and infectious diseases, but may also involve *contact dermatitis* (poison ivy). These reactions are mediated by T cells, monocytes, and macrophages.

Other mechanisms

It is likely that a multicomponent, adaptive immune system arose with the first vertebrates, as invertebrates do not generate lymphocytes or an antibody-based humoral response. Many species, however, utilize mechanisms that appear to be precursors of these aspects of vertebrate immunity. Immune systems appear even in the structurally most simple forms of life, with bacteria using a unique defense mechanism, called the restriction modification system to protect themselves from viral pathogens, called bacteriophages. Prokaryotes also possess acquired immunity, through a system that uses CRISPR sequences to retain fragments of the genomes of phage that they have come into contact with in the past, which allows them to block virus replication through a form of RNA interference.

Pattern recognition receptors are proteins used by nearly all organisms to identify molecules associated with pathogens. Antimicrobial peptides called defensins are an evolutionarily conserved component of the innate immune response found in all animals and plants, and represent the main form of invertebrate systemic immunity The complement system and phagocytic cells are also used by most forms of invertebrate life. Ribonucleases and the RNA interference pathway are conserved across all eukaryotes, and are thought to play a role in the immune response to viruses.

Unlike animals, plants lack phagocytic cells, but many plant immune responses involve systemic chemical signals that are sent through a plant. Individual plant cells respond to molecules associated with pathogens known as Pathogen-associated molecular patterns or PAMPs. When a part of a plant becomes infected, the plant produces a localized hypersensitive response, whereby cells at the site of infection undergo rapid apoptosis to prevent the

spread of the disease to other parts of the plant. Systemic acquired resistance (SAR) is a type of defensive response used by plants that renders the entire plant resistant to a particular infectious agent. RNA silencing mechanisms are particularly important in this systemic response as they can block virus replication.

Tumor immunology

Macrophages have identified a cancer cell (the large, spiky mass). Upon fusing with the cancer cell, the macrophages (smaller white cells) will inject toxins that kill the tumor cell. Immunotherapy for the treatment of cancer is an active area of medical research.

Another important role of the immune system is to identify and eliminate tumors. The *transformed cells* of tumors express antigens that are not found on normal cells. To the immune system, these antigens appear foreign, and their presence causes immune cells to attack the transformed tumor cells. The antigens expressed by tumors have several sources; some are derived from oncogenic viruses like human papillomavirus, which causes cervical cancer, while others are the organism's own proteins that occur at low levels in normal cells but reach high levels in tumor cells. One example is an enzyme called tyrosinase that, when expressed at high levels, transforms certain skin cells (e.g. melanocytes) into tumors called melanomas. A third possible source of tumor antigens are proteins normally important for regulating cell growth and survival, that commonly mutate into cancer inducing molecules called oncogenes.

The main response of the immune system to tumors is to destroy the abnormal cells using killer T cells, sometimes with the assistance of helper T cells. Tumor antigens are presented on MHC class I molecules in a similar way to viral antigens. This allows killer T cells to recognize the tumor cell as abnormal. NK cells also kill tumorous cells in a similar way, especially if the tumor cells have fewer MHC class I molecules on their surface than normal; this is a common phenomenon with tumors. Sometimes antibodies are generated against tumor cells allowing for their destruction by the complement system.

Clearly, some tumors evade the immune system and go on to become cancers. Tumor cells often have a reduced number of MHC class I molecules on their surface, thus avoiding detection by killer T cells. Some tumor cells also release products that inhibit the immune response; for example by secreting the cytokine TGF-β, which suppresses the activity of macrophages and lymphocytes. In addition, immunological tolerance may develop against tumor antigens, so the immune system no longer attacks the tumor cells.

Paradoxically, macrophages can promote tumor growth when tumor cells send out cytokines that attract macrophages, which then generate cytokines and

growth factors that nurture tumor development. In addition, a combination of hypoxia in the tumor and a cytokine produced by macrophages induces tumor cells to decrease production of a protein that blocks metastasis and thereby assists spread of cancer cells.

Physiological regulation

Hormones can act as immunomodulators, altering the sensitivity of the immune system. For example, female sex hormones are known immunostimulators of both adaptiveand innate immune responses Some autoimmune diseases such as lupus erythematosus strike women preferentially, and their onset often coincides with puberty. By contrast, male sex hormones such as testosterone seem to be immunosuppressive Other hormones appear to regulate the immune system as well, most notably prolactin, growth hormone and vitamin D.

When a T-cell encounters a foreign pathogen, it extends a vitamin D receptor. This is essentially a signaling device that allows the T-cell to bind to the active form of vitamin D, the steroid hormone calcitriol. T-cells have a symbiotic relationship with vitamin D. Not only does the T-cell extend a vitamin D receptor, in essence asking to bind to the steroid hormone version of vitamin D, calcitriol, but the T-cell expresses the gene CYP27B1, which is the gene responsible for converting the pre-hormone version of vitamin D, calcidiol into the steroid hormone version, calcitriol. Only after binding to calcitriol can T-cells perform their intended function. Other immune system cells that are known to express CYP27B1 and thus activate vitamin D calcidiol, are dendritic cells, keratinocytes and macrophages.

It is conjectured that a progressive decline in hormone levels with age is partially responsible for weakened immune responses in aging individuals. Conversely, some hormones are regulated by the immune system, notably thyroid hormone activity. The age-related decline in immune function is also related to dropping vitamin D levels in the elderly. As people age, two things happen that negatively affect their vitamin D levels. First, they stay indoors more due to decreased activity levels. This means that they get less sun and therefore produce less cholecalciferol via UVB radiation. Second, as a person ages the skin becomes less adept at producing vitamin D.

The immune system is affected by sleep and rest, and sleep deprivation is detrimental to immune function. Complex feedback loops involving cytokines, such as interleukin-1 and tumor necrosis factor-α produced in response to infection, appear to also play a role in the regulation of non-rapid eye movement (REM) sleep. Thus the immune response to infection may result in changes to the sleep cycle, including an increase in slow-wave sleep relative to REM sleep.

Nutrition and diet

The function of the immune system, like most systems in the body, is dependent on proper nutrition. It has been long known that severe malnutrition leads to immunodeficiency. Overnutrition is also associated with diseases such as diabetes and obesity, which are known to affect immune function. More moderate malnutrition, as well as certain specific trace mineral and nutrient deficiencies, can also compromise the immune response.

Specific foods may also affect the immune system; for example, fresh fruits, vegetables, and foods rich in certain fatty acids may foster a healthy immune system while an excess of pro-inflammatory fatty acids can cause an imbalance in the immune system. Likewise, fetal undernourishment can cause a lifelong impairment of the immune system. In traditional medicine, some herbs are believed to stimulate the immune system, such as echinacea, licorice, ginseng, astragalus, sage, garlic, elderberry, and hyssop, as well as honey.

Manipulation in medicine

The immune response can be manipulated to suppress unwanted responses resulting from autoimmunity, allergy, and transplant rejection, and to stimulate protective responses against pathogens that largely elude the immune system (see immunization). Immunosuppressive drugs are used to control autoimmune disorders or inflammation when excessive tissue damage occurs, and to prevent transplant rejection after an organ transplant.

Anti-inflammatory drugs are often used to control the effects of inflammation. Glucocorticoids are the most powerful of these drugs; however, these drugs can have many undesirable side effects, such as central obesity, hyperglycemia, osteoporosis, and their use must be tightly controlled. Lower doses of anti-inflammatory drugs are often used in conjunction with cytotoxic or immunosuppressive drugs such as methotrexate or azathioprine. Cytotoxic drugs inhibit the immune response by killing dividing cells such as activated T cells. However, the killing is indiscriminate and other constantly dividing cells and their organs are affected, which causes toxic side effects. Immunosuppressive drugs such as ciclosporin prevent T cells from responding to signals correctly by inhibiting signal transduction pathways.

Larger drugs (>500 Da) can provoke a neutralizing immune response, particularly if the drugs are administered repeatedly, or in larger doses. This limits the effectiveness of drugs based on larger peptides and proteins (which are typically larger than 6000 Da). In some cases, the drug itself is not immunogenic, but may be co-administered with an immunogenic compound, as is sometimes the case for Taxol. Computational methods have been developed to predict the immunogenicity of peptides and proteins, which are particularly useful in designing therapeutic antibodies, assessing likely virulence of mutations in viral coat particles, and validation of proposed peptide-based drug treatments. Early techniques relied mainly on the

observation that hydrophilicamino acids are overrepresented in epitope regions than hydrophobic amino acids; however, more recent developments rely on machine learning techniques using databases of existing known epitopes, usually on well-studied virus proteins, as a training set. A publicly accessible database has been established for the cataloguing of epitopes from pathogens known to be recognizable by B cells. The emerging field of bioinformatics-based studies of immunogenicity is referred to as *immunoinformatics*. Immunoproteomics is a term used to describe the study of large sets of proteins (proteomics) involved in the immune response.

Manipulation by pathogens

The success of any pathogen depends on its ability to elude host immune responses. Therefore, pathogens evolved several methods that allow them to successfully infect a host, while evading detection or destruction by the immune system. Bacteria often overcome physical barriers by secreting enzymes that digest the barrier, for example, by using a type II secretion system. Alternatively, using a type III secretion system, they may insert a hollow tube into the host cell, providing a direct route for proteins to move from the pathogen to the host. These proteins are often used to shut down host defenses.

An evasion strategy used by several pathogens to avoid the innate immune system is to hide within the cells of their host (also called intracellularpathogenesis). Here, a pathogen spends most of its life-cycle inside host cells, where it is shielded from direct contact with immune cells, antibodies and complement. Some examples of intracellular pathogens include viruses, the food poisoningbacterium*Salmonella* and the eukaryotic parasites that cause malaria (*Plasmodium falciparum*) and leishmaniasis (*Leishmania spp.*). Other bacteria, such as *Mycobacterium tuberculosis*, live inside a protective capsule that prevents lysis by complement. Many pathogens secrete compounds that diminish or misdirect the host's immune response. Some bacteria form biofilms to protect themselves from the cells and proteins of the immune system. Such biofilms are present in many successful infections, e.g., the chronic *Pseudomonas aeruginosa* and *Burkholderiacenocepacia* infections characteristic of cystic fibrosis. Other bacteria generate surface proteins that bind to antibodies, rendering them ineffective; examples include *Streptococcus* (protein G), *Staphylococcus aureus* (protein A), and *Peptostreptococcusmagnus* (protein L)

The mechanisms used to evade the adaptive immune system are more complicated. The simplest approach is to rapidly change non-essential epitopes (amino acids and/or sugars) on the surface of the pathogen, while keeping essential epitopes concealed. This is called antigenic variation. An example is HIV, which mutates rapidly, so the proteins on its viral envelope that are essential for entry into its host target cell are constantly changing. These frequent changes in antigens may explain the failures of vaccines directed at

this virus. The parasite *Trypanosomabrucei* uses a similar strategy, constantly switching one type of surface protein for another, allowing it to stay one step ahead of the antibody response. Masking antigens with host molecules is another common strategy for avoiding detection by the immune system. In HIV, the envelope that covers the viron is formed from the outermost membrane of the host cell; such "self-cloaked" viruses make it difficult for the immune system to identify them as "non-self" structures.

Organs of the immune system

- Thymus
- Bones - White blood cells (leukocytes) are produced in bone marrow
- Spleen - Rich in B and T lymphocytes.

Tissues of the immune system

- Bone marrow

Cells of the immune system

- White blood cells (leukocytes)
  - *Granulocytes ,Neutrophil granulocytes (neutrophils), Eosinophil granulocytes (eosinophils), Basophil granulocytes, Lymphocytes*

· B cells

Plasma B cells, Memory B cells, B-1 cells, B-2 cells

· Natural killer cells (NK cells)

· T cells

Helper T cells, Cytotoxic T cells, Memory T cells, Regulatory T cells Natural Killer T cells, γδ T cells

- Cells of the innate immune system
  - Mast cells
  - Phagocytes
  - Macrophages

Immunological biomolecules

- Antibodies
- Antigen
- Superantigen
- Histamines

- Cytolysins

Immune system disorders

- Hypersensitivity, Allergy (immune system disorder) .Allergen

Autoimmunity, Immunodeficiency, Transplant rejection

Immunological treatments

- Immunosuppressive drug
- Vaccine
- Vaccination

Immunity (medical)

Immunity is a biological term that describes a state of having sufficient biological defenses to avoid infection, disease, or other unwanted biological invasion. In other words, it is nothing but the capability of the body to resist harmful microbes from entering the body. Immunity involves both specific and non-specific components. The non-specific components act either as barriers or as eliminators of wide range of pathogens irrespective of antigenic specificity. Other components of the immune system adapt themselves to each new disease encountered and are able to generate pathogen-specific immunity.

Innate immunity, or nonspecific, immunity is the natural resistance with which a person is born. It provides resistance through several physical, chemical, and cellular approaches. Microbes first encounter the epithelial layers, physical barriers that line our skin and mucous membranes. Subsequent general defenses include secreted chemical signals (cytokines), antimicrobial substances, fever, and phagocytic activity associated with the inflammatory response. The phagocytes express cell surface receptors that can bind and respond to common molecular patterns expressed on the surface of invading microbes. Through these approaches, innate immunity can prevent the colonization, entry, and spread of microbes.

Adaptive immunity is often sub-divided into two major types depending on how the immunity was introduced. **Naturally acquired immunity** occurs through contact with a disease causing agent, when the contact was not deliberate, whereas **artificially acquired immunity** develops only through deliberate actions such as vaccination. Both naturally and artificially acquired immunity can be further subdivided depending on whether immunity is induced in the host or passively transferred from a immune host. **Passive immunity** is acquired through transfer of antibodies or activated T-cells from an immune host, and is short lived -- usually lasting only a few months -- whereas **active immunity** is induced in the host itself by antigen, and lasts much longer, sometimes life-long. The diagram below summarizes these divisions of immunity.

A further subdivision of adaptive immunity is characterized by the cells involved; humoral immunity is the aspect of immunity that is mediated by secreted antibodies,

whereas the protection provided by cell mediated immunity involves T-lymphocytes alone. Humoral immunity is active when the organism generates its own antibodies, and passive when antibodies are transferred between individuals. Similarly, cell mediated immunity is active when the organisms' own T-cells are stimulated and passive when T cells come from another organism.

The modern word "immunity" derives from the Latin *immunis*, meaning exemption from military service, tax payments or other public services.] The first written descriptions of the concept of immunity may have been made by the Athenian Thucydides who, in 430 BC, described that when the plague hit Athens *"the sick and the dying were tended by the pitying care of those who had recovered, because they knew the course of the disease and were themselves free from apprehensions.* ***For no one was ever attacked a second time, or not with a fatal result****"*.The term "immunes", is also found in the epic poem "Pharsalia" written around 60 B.C. by the poet Marcus AnnaeusLucanus to describe a North African tribe's resistance to snake venom.

The first clinical description of immunity which arose from a specific disease causing organism is probably *Kitab fi al-jadariwa-al-hasbah* (*A Treatise on Smallpox and Measles*, translated 1848) written by the Islamic physician Al-Razi in the 9th century. In the treatise, Al Razi describes the clinical presentation of smallpox and measles and goes on to indicate that that exposure to these specific agents confers lasting immunity (although he does not use this term). However, it was with Louis Pasteur's Germ theory of disease that the fledgling science of immunology began to explain how bacteria caused disease, and how, following infection, the human body gained the ability to resist further infections.

Passive immunity

Passive immunity is the transfer of active immunity, in the form of readymade antibodies, from one individual to another. Passive immunity can occur naturally, when maternal antibodies are transferred to the fetus through the placenta, and can also be induced artificially, when high levels of human (or horse) antibodies specific for a pathogen or toxin are transferred to non-immune individuals. Passive immunization is used when there is a high risk of infection and insufficient time for the body to develop its own immune response, or to reduce the symptoms of ongoing or immunosuppressive diseases. Passive immunity provides immediate protection, but the body does not develop memory, therefore the patient is at risk of being infected by the same pathogen later.

Naturally acquired passive immunity

Maternal passive immunity is a type of naturally acquired passive immunity, and refers to antibody-mediated immunity conveyed to a fetus by its mother during pregnancy. Maternal antibodies (MatAb) are passed through the placenta to the fetus by an FcRn receptor on placental cells. This occurs around the third month of gestation IgG is the only antibody isotype that can pass through the placenta. Passive immunity is also provided through the transfer of IgA antibodies found in breast milk that are transferred to the gut of the infant, protecting against bacterial infections, until the newborn can synthesize its own antibodies.

Artificially acquired passive immunity

Artificially acquired passive immunity is a short-term immunization induced by the transfer of antibodies, which can be administered in several forms; as human or animal blood plasma, as pooled human immunoglobulin for intravenous (IVIG) or intramuscular (IG) use, and in the form of monoclonal antibodies (MAb). Passive transfer is used prophylactically in the case of immunodeficiency diseases, such as hypogammaglobulinemia. It is also used in the treatment of several types of acute infection, and to treat poisoning.Immunity derived from passive immunization lasts for only a short period of time, and there is also a potential risk for hypersensitivity reactions, and serum sickness, especially from gamma globulin of non-human origin.

The artificial induction of passive immunity has been used for over a century to treat infectious disease, and prior to the advent of antibiotics, was often the only specific treatment for certain infections. Immunoglobulin therapy continued to be a first line therapy in the treatment of severe respiratory diseases until the 1930's, even after sulfonamide lot antibiotics were introduced.

Passive transfer of cell-mediated immunity

Passive or "adoptive transfer" of cell-mediated immunity, is conferred by the transfer of "sensitized" or activated T-cells from one individual into another. It is rarely used in humans because it requires histocompatible (matched) donors, which are often difficult to find. In unmatched donors this type of transfer carries severe risks of graft versus host disease.[7] It has, however, been used to treat certain diseases including some types of cancer and immunodeficiency. This type of transfer differs from a bone marrow transplant, in which (undifferentiated) hematopoietic stem cells are transferred.

Active immunity

The time course of an immune response. Due to the formation of immunological memory, reinfection at later time points leads to a rapid increase in antibody production and effector T cell activity. These later infections can be mild or even inapparent.

When B cells and T cells are activated by a pathogen, memory B-cells and T- cells develop. Throughout the lifetime of an animal these memory cells will "remember" each specific pathogen encountered, and are able to mount a strong response if the pathogen is detected again. This type of immunity is both *active* and *adaptive* because the body's immune system prepares itself for future challenges. Active immunity often involves both the cell-mediated and humoral aspects of immunity as well as input from the innate immune system. The *innate system* is present from birth and protects an individual from pathogens regardless of experiences, whereas adaptive immunity arises only after an infection or immunization and hence is "acquired" during life.

Naturally acquired active immunity

Naturally acquired active immunity occurs when a person is exposed to a live pathogen, and develops a primary immune response, which leads to immunological

memory. This type of immunity is “natural” because it is not induced by deliberate exposure. Many disorders of immune system function can affect the formation of active immunity such as immunodeficiency (both acquired and congenital forms) and immunosuppression.

Artificially acquired active immunity

Artificially acquired active immunity can be induced by a vaccine, a substance that contains antigen. A vaccine stimulates a primary response against the antigen without causing symptoms of the disease.The term vaccination was coined by Edward Jenner and adapted by Louis Pasteur for his pioneering work in vaccination. The method Pasteur used entailed treating the infectious agents for those diseases so they lost the ability to cause serious disease. Pasteur adopted the name vaccine as a generic term in honor of Jenner's discovery, which Pasteur's work built upon.

In 1807, the Bavarians became the first group to require that their military recruits be vaccinated against smallpox, as the spread of smallpox was linked to combat. the practice of vaccination would increase with the spread of war.

There are four types of traditional vaccines:

- Inactivated vaccines are composed of micro-organisms that have been killed with chemicals and/or heat and are no longer infectious. Examples are vaccines against flu, cholera, plague, and hepatitis A. Most vaccines of this type are likely to require booster shots.
- Live, attenuated vaccines are composed of micro-organisms that have been cultivated under conditions which disable their ability to induce disease. These responses are more durable and do not generally require booster shots. Examples include yellow fever, measles, rubella, and mumps.
- Toxoids are inactivated toxic compounds from micro-organisms in cases where these (rather than the micro-organism itself) cause illness, used prior to an encounter with the toxin of the micro-organism. Examples of toxoid-based vaccines include tetanus and diphtheria.
- Subunit -vaccines are composed of small fragments of disease causing organisms. A characteristic example is the subunit vaccine against Hepatitis B virus.

Most vaccines are given by hypodermic injection as they are not absorbed reliably through the gut. Live attenuated polio and some typhoid and cholera vaccines are given orally in order to produce immunity based in the bowel.

PATHOGENESIS

A pathogen (Greek: πάθος*pathos*, "suffering, passion" and γενής*genēs* (-gen) "producer of") or **infectious agent** - in colloquial terms, a **germ** — is a microbe or microorganism such as a virus, bacterium, prion, or fungus that causes disease in its animal or planthost.[1][2] There are several substrates including *pathways* whereby pathogens

can invade a host; the principal pathways have different episodic time frames, but soil contamination has the longest or most persistent potential for harboring a pathogen.

The body contains many natural orders of defense against some of the common pathogens (such as *Pneumocystis*) in the form of the human immune system and by some "helpful" bacteria present in the human body's normal flora. However, if the immune system or "good" bacteria is damaged in any way (such as by chemotherapy, human immunodeficiency virus (HIV), or antibiotics being taken to kill other pathogens), pathogenic bacteria that were being held at bay can proliferate and cause harm to the host. Such cases are called opportunistic infection.

Some pathogens (such as the bacterium *Yersinia pestis*, which may have caused the Black Plague, the *Variola* virus, and the Malaria protozoa) have been responsible for massive numbers of casualties and have had numerous effects on afflicted groups. Of particular note in modern times is HIV, which is known to have infected several million humans globally, along with the Influenza virus. Today, while many medical advances have been made to safeguard against infection by pathogens, through the use of vaccination, antibiotics, and fungicide, pathogens continue to threaten human life. Social advances such as food safety, hygiene, and water treatment have reduced the threat from some pathogens. Not all pathogens are negative. In entomology, pathogens are one of the "Three P's" (predators, pathogens, and parasitoids) that serve as natural or introduced biological controls to suppress arthropodpest populations.

Types of pathogen

Viral

Pathogenic viruses are mainly those of the families of: Adenoviridae, bacteria Picornaviridae, Herpesviridae, Hepadnaviridae, Flaviviridae, Retroviridae, Orthomyxoviridae, Paramyxoviridae, Papovaviridae, Polyomavirus, Rhabdoviridae, Togaviridae. Some notable pathogenic viruses cause smallpox, influenza, mumps, measles, chickenpox, ebola, and rubella. Viruses typically range between 20-300 nanometers in length.

Bacterial

Although the vast majority of bacteria are harmless or beneficial to ones body, a few pathogenic bacteria can cause infectious diseases. The most common bacterial disease is tuberculosis, caused by the bacterium *Mycobacterium tuberculosis*, which affects just about 2 million people mostly in sub-Saharan Africa. Pathogenic bacteria contribute to other globally important diseases, such as pneumonia, which can be caused by bacteria such as *Streptococcus* and *Pseudomonas*, and foodborne illnesses, which can be caused by bacteria such as *Shigella*, *Campylobacter* and *Salmonella*. Pathogenic bacteria also cause infections such as tetanus, typhoid fever, diphtheria, syphilis and Hansen's disease. Bacteria can often be killed by antibiotics because the cell wall in the outside is destroyed and then the DNA. They typically range between 1 and 5 micrometers in length.

Fungal: Pathogenic fungi

Fungi comprise a eukaryotic kingdom of microbes that are usually saprophytes but can cause diseases in humans, animals and plants. Fungi are the most common cause of diseases in crops and other plants. Life threatening fungal infections in humans most often occur in immunocompromised patients or vulnerable people with a weakened immune system, although fungi are common problems in the immunocompetent population as the causative agents of skin, nail or yeast infections. Most antibiotics that function on bacterial pathogens cannot be used to treat fungal infections because fungi and their hosts both have eukaryotic cells. Most clinical fungicides belong to the azole group. The typical fungal spore size is 1-40 micrometer in length.

Other parasites

Human parasites Some eukaryotic organisms, such as protists and helminths, cause disease. One of the best known diseases caused by protists in the genus *Plasmodium* is malaria. These can range from: 3-200 micrometers in length.

Prionic

Prions are infectious pathogens that do not contain nucleic acids. Prions are abnormal proteins whose presence causes some diseases such as scrapie, bovine spongiform encephalopathy (mad cow disease) and Creutzfeldt–Jakob disease.[4] The discovery of prion as a new class of pathogen led Stanley B. Prusiner to receive the Nobel Prize in Physiology or Medicine in 1997.

Potency

Research into the basis of the ability of pathogens to cause disease provides evidence from multiple and diverse species of the existence of pathogenicity or virulence factors, encoded within the pathogens' genetic material, that facilitate the ability of microbes to cause disease. Microbiologists generally agree that it is not in interest of an infectious agent to kill its host because that would limit the organism's ability to multiply and spread to new hosts. Virulence factors usually serve some beneficial function in the microbe's life cycle, such as allowing spread in the body or attachment to host cells, and cause disease and death of the host only accidentally. Long term interaction of a pathogen with a population of hosts over many generations frequently results in adaptation of both the pathogen and host, leading to less disease. Thus especially deadly agents are often assumed to be recently introduced into the host population and have not yet become well adapted.

Transmission

Transmission of pathogens occurs through many different routes, including airborne, direct or indirect contact, sexual contact, through blood, breast milk, or other body fluids, and through the fecal-oral route. One of the primary pathways by which food or water become contaminated is from the release of untreated sewage into a drinking water supply or onto cropland, with the result that people who eat or drink contaminated sources become infected. In developing countries most sewage is

discharged into the environment or on cropland; even in developed countries there are periodic system failures resulting in a sanitary sewer overflow.

Neutrophil Function: From Mechanisms to Disease

Neutrophils are the most abundant white blood cells in circulation, and patients with congenital neutrophil deficiencies suffer from severe infections that are often fatal, underscoring the importance of these cells in immune defense. In spite of neutrophils' relevance in immunity, research on these cells has been hampered by their experimentally intractable nature. Here, we present a survey of basic neutrophil biology, with an emphasis on examples that highlight the function of neutrophils not only as professional killers, but also as instructors of the immune system in the context of infection and inflammatory disease. We focus on emerging issues in the field of neutrophil biology, address questions in this area that remain unanswered, and critically examine the experimental basis for common assumptions found in neutrophil literature.

Reflex Principles of Immunological Homeostasis

The reasoning that neural reflexes maintain homeostasis in other body organs, and that the immune system is innervated, prompted a search for neural circuits that regulate innate and adaptive immunity. This elucidated the inflammatory reflex, a prototypical reflex circuit that maintains immunological homeostasis. Molecular products of infection or injury activate sensory neurons traveling to the brainstem in the vagus nerve. The arrival of these incoming signals generates action potentials that travel from the brainstem to the spleen and other organs. This culminates in T cell release of acetylcholine, which interacts with α7 nicotinic acetylcholine receptors (α7 nAChR) on immunocompetent cells to inhibit cytokine release in macrophages. Herein is reviewed the neurophysiological basis of reflexes that provide stability to the immune system, the neural- and receptor-dependent mechanisms, and the potential opportunities for developing novel therapeutic devices and drugs that target neural pathways to treat inflammatory diseases.

Tolerance of Infections

A host has two methods to defend against pathogens: It can clear the pathogens or reduce their impact on health in other ways. The first, resistance, is well studied. Study of the second, which ecologists call tolerance, is in its infancy. Tolerance measures the dose response curve of a host's health in reaction to a pathogen and can be studied in a simple quantitative manner. Such studies hold promise because they point to methods of treating infections that put evolutionary pressures on microbes different from antibiotics and vaccines. Studies of tolerance will provide an improved foundation to describe our interactions with all microbes: pathogenic, commensal, and mutualistic. One obvious mechanism affecting tolerance is the intensity of an immune response; an overly exuberant immune response can cause collateral damage through immune effectors and because of the energy allocated away from other physiological functions. There are potentially many other tolerance mechanisms, and here we systematically describe tolerance using a variety of animal systems.

Induced $CD4^+Foxp3^+$ Regulatory T Cells in Immune Tolerance

Regulatory T lymphocytes are essential to maintain homeostasis of the immune system, limiting the magnitude of effector responses and allowing the establishment of immunological tolerance. Two main types of regulatory T cells have been identified—natural and induced (or adaptive)—and both play significant roles in tuning down effector immune responses. Adaptive $CD4^+Foxp3^+$ regulatory T (iTreg) cells develop outside the thymus under a variety of conditions. These include not only antigen presentation under subimmunogenic or noninflammatory conditions, but also chronic inflammation and infections. We speculate that the different origin of iTreg cells (noninflammatory versus inflammatory) results in distinct properties, including their stability. iTreg cells are also generated during homeostasis of the gut and in cancer, although some cancers also favor expansion of natural regulatory T (nTreg) cells. Here we review how iTreg cells develop and how they participate in immunological tolerance, contrasting, when possible, iTreg cells with nTreg cells.

VLR-Based Adaptive Immunity

Lampreys and hagfish are primitive jawless vertebrates capable of mounting specific immune responses. Lampreys possess different types of lymphocytes, akin to T and B cells of jawed vertebrates, that clonally express somatically diversified antigen receptors termed variable lymphocyte receptors (VLRs), which are composed of tandem arrays of leucine-rich repeats. The VLRs appear to be diversified by a gene conversion mechanism involving lineage-specific cytosine deaminases. VLRA is expressed on the surface of T-like lymphocytes; B-like lymphocytes express and secrete VLRB as a multivalent protein. VLRC is expressed by a distinct lymphocyte lineage. VLRA-expressing cells appear to develop in a thymus-like tissue at the tip of gill filaments, and VLRB-expressing cells develop in hematopoietic tissues. Reciprocal expression patterns of evolutionarily conserved interleukins and chemokines possibly underlie cell-cell interactions during an immune response. The discovery of VLRs in agnathans illuminates the origins of adaptive immunity in early vertebrates.

REFRENCES

- David K. Male - 2004 - 141 pages – immunology, an illustrasted outline
- David K. Male, Jonathan Brostoff, Ivan Maurice Roitt - 2006 - 552 pages - Immunology
- Richard Coico, Geoffrey Sunshine - 2009 - 391 pages – Short course handbook
- Richard A. Goldsby, Thomas J. Kindt, Barbara A. Osborne - 2006 – Immunology a comprehensive review
- Klaus D. Elgert - 2009 - 726 pages – Understanding immunology
- SulabhaPathak, UrmiPalan - 2005 - 411 pages – Essentials and fundamental of immunology

- Robert A. Meyers - 2007 - 435 pages – Immunology, from cell biology to disease
- J. David M. Edgar - 2006 - 202 pages – A core text with self assessment

1. David K. Male - 2004 - 141 pages – immunology, an illustrasted outline
2. David K. Male, Jonathan Brostoff, Ivan Maurice Roitt - 2006 - 552 pages - Immunology
3. Richard Coico, Geoffrey Sunshine - 2009 - 391 pages – Short course handbook
4. Richard A. Goldsby, Thomas J. Kindt, Barbara A. Osborne - 2006 – Immunology a comprehensive review
5. Klaus D. Elgert - 2009 - 726 pages – Understanding immunology
6. Sulabha Pathak, Urmi Palan - 2005 - 411 pages – Essentials and fundamental of immunology