M.Sc. (Third Semester) Examination, 2014
Zoology
Paper: LZT- 301
(Development Biology and Immunology)
Model answer

Section A

1.

(i) (b)
(ii) (b)
(iii) (d)
(iv) (b)
(v) (d)
(vi) (c)
(vii) (d)
(viii) (c)
(ix) (c)
(x) (b)

Section B

Answer No. 2.

Polyspermy is the condition occurs in an egg that has been fertilized by more than one sperm. Diploid organisms normally contain two copies of each chromosome, one from each parent. The cell resulting from polyspermy, on the other hand, contains three or more copies of each chromosome—one from the egg and one each from multiple sperm. Usually, the result is an inviable zygote.

Prevention to polyspermy:

Although many sperm attach to the coats surrounding the egg, it is important that **only one sperm** fuses with the egg plasma membrane and delivers its nucleus into the egg. Two mechanisms are used by animals to ensure that only one sperm fertilizes a given egg: the fast block to polyspermy and the slow block to polyspermy.

Fast block to polyspermy:
In the sea urchin, a fast block to polyspermy occurs within a tenth of a second of fusion. The fast block to polyspermy involves the opening of Na+ channels in the egg plasma membrane. Na+

flows into the egg cell, **depolarizing** the membrane. This depolarization prevents additional sperm from fusing to the egg plasma membrane. The egg plasma membrane is restored to its normal -70mV potential within minutes of fusion as the Na+ channels close, other + ions flow out of the cell, and Na+ is pumped out. If depolarization is prevented, polyspermy occurs.

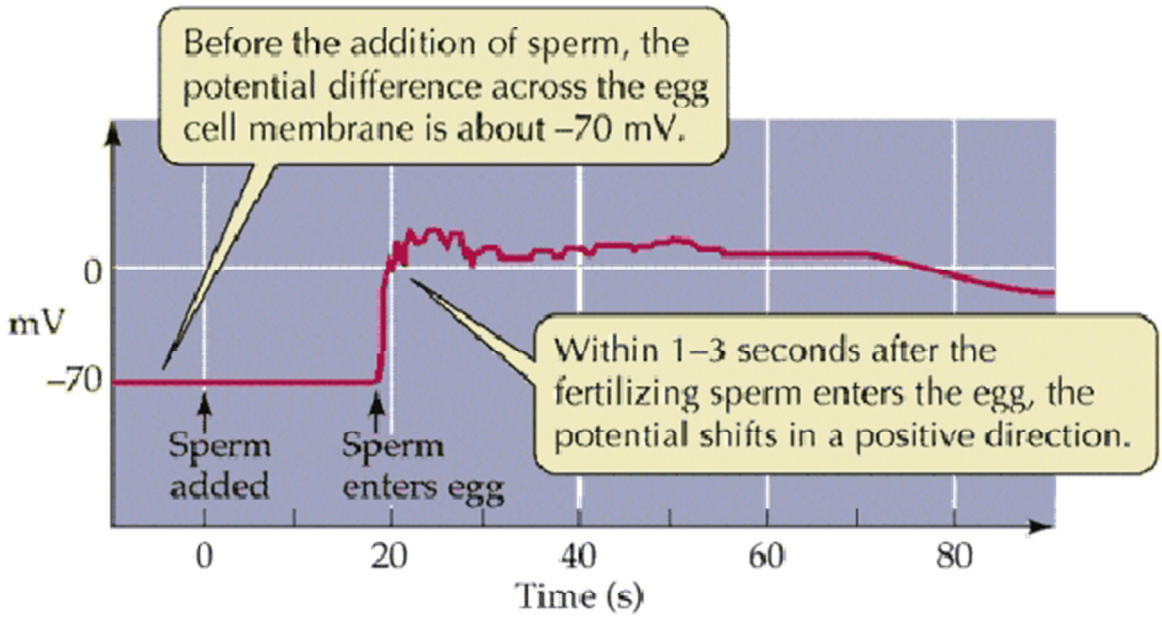


Fig. *Fast block to polyspermy (Purves et al, 1998)*

Slow block to polyspermy:

The slow block to polyspermy begins within 10 seconds of fusion of the sperm and egg plasma membranes. A compound called inositol triphosphate (IP3) causes the release of **Ca++** from intracellular stores in the egg endoplasmic reticulum. Ca++ is first released at the site of sperm entry, and during the next minute, a wave of free Ca++ passes through the egg. This Ca++ results in the fusion of **cortical vesicles** with the egg plasma membrane, releasing their contents into the space surrounding the egg, called the perivitelline space. This raises the vitelline membrane, and inactivates bindin receptors on the vitelline membrane. Thus, any additional sperm are released from the vitelline membrane and no more bind.

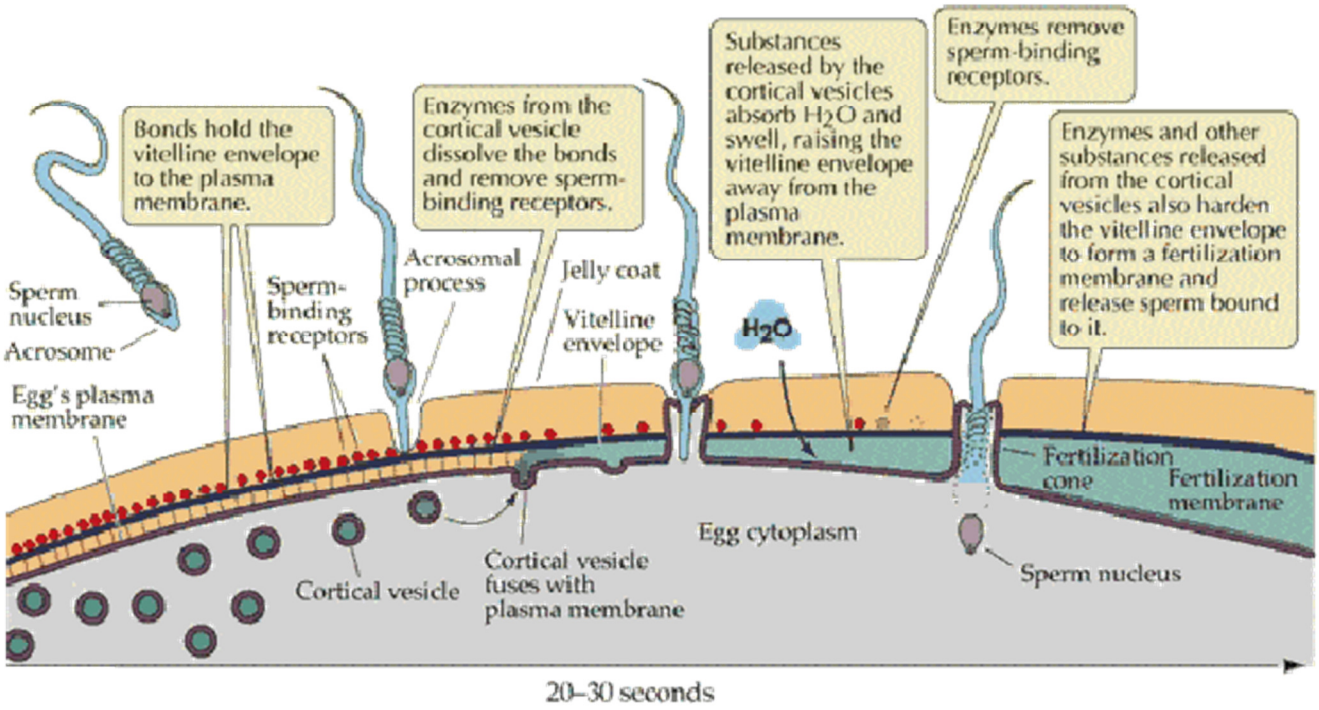


Fig. *Slow block to polyspermy (Purves et al, 1998)*

The slow block to polyspermy in the sea urchin embryo consists of a physical barrier to further sperm penetration into the egg. Cortical granule exocytosis results in the formation of the fertilization envelope (often called the fertilization "membrane", even though the structure is not a true membrane). The fertilization envelope is formed by the lifting of the vitelline envelope away from the egg plasma membrane. The cortical granules contain enzymes that aid in the detachment of the vitelline envelope, as well as other components that aid the osmotic swelling of the fertilization envelope away from the egg. Cortical granules also contain extracellular matrix proteins that are deposited on the egg surface, including the protein hyalin, which is the major component of the hyaline layer.

Answer No. 3.

Primitive Streak

The primitive streak is a structure that forms in the blastula during the early stages of avian, reptilian and mammalian embryonic development. The presence of the primitive streak will establish bilateral symmetry, determine the site of gastrulation and initiate germ layer formation.

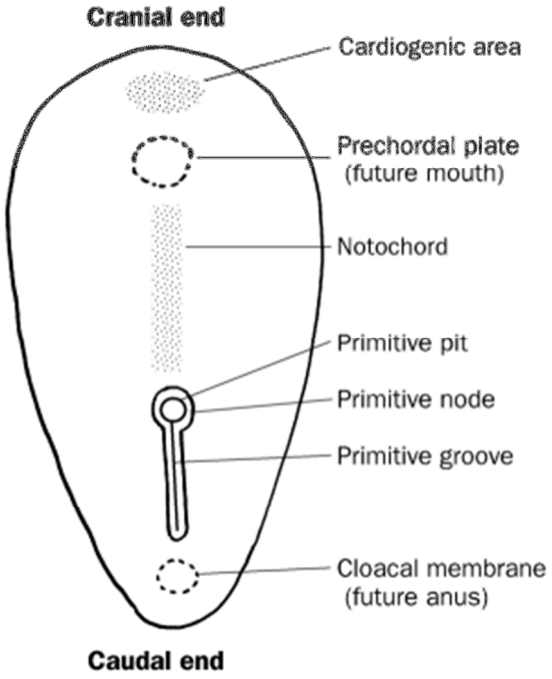


Fig. D*evelopment of primitive streak*

Significance of the primitive streak:

(1) The primitive pit represents the dorsal opening of the blastopore (neurenteric canal).

(2) The primitive node corresponds to the dorsal lip of blastopore (future tail bud).

(3) The primitive groove and folds are comparable to the opposed lateral lips of the blastopore.

(4) The posterior end of primitive streak may be compared with the ventral region of the blastopore (future anal opening).

(5) The first cells which migrate through the primitive streak are those destined to become foregut.

Avian Gastrulation

Avian embryos differ from those of other vertebrates in several respects – among them, they have a large mass of yolk, the cells initially divide from the centre of a disk with cleavage planes that open into the yolk. This process generates the primitive streak which defines bilateral symmetry, and through which cells from the superficial layer (epiblast) ingress to generate two new layers of embryonic cells (mesoderm and endoderm). This period of development starts to define the three axes of the future embryo (head–tail, dorsoventral and left–right) and embryo fates start to be fixed.

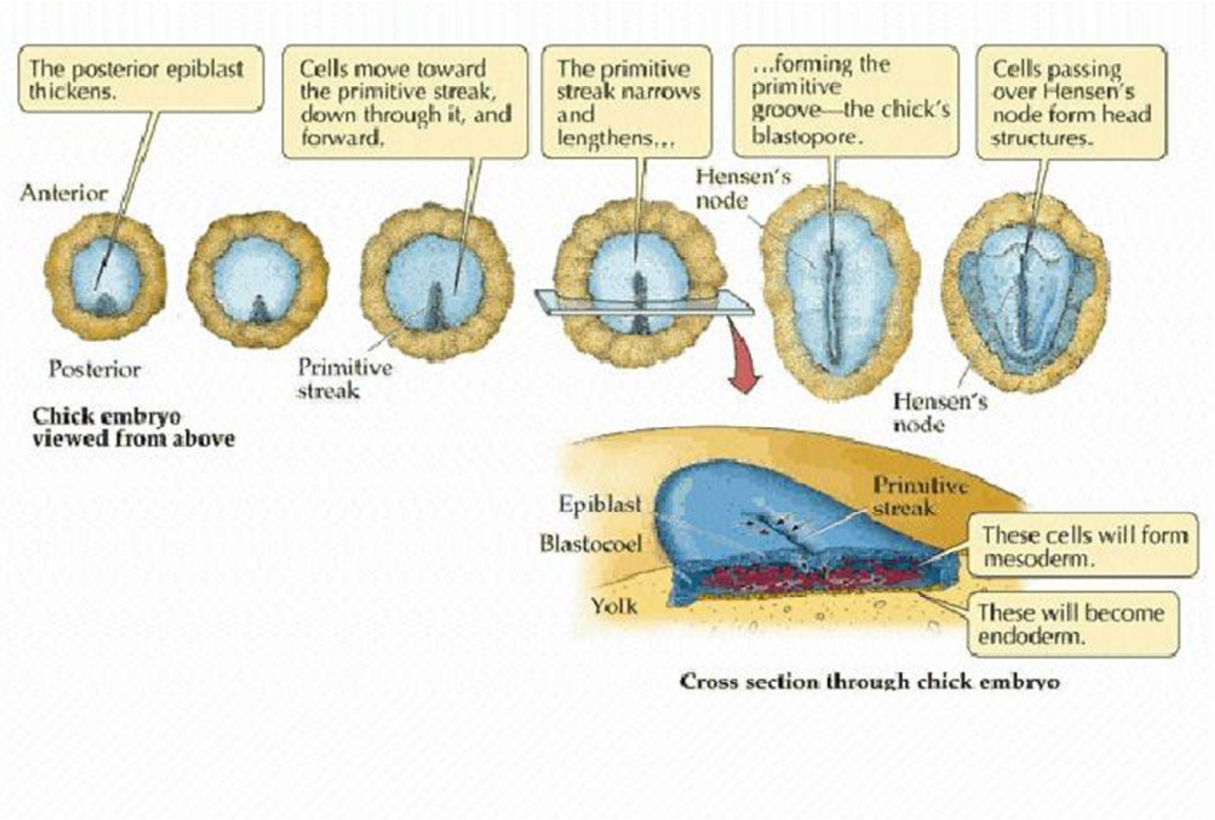


Fig. *Different steps of gastrulation in chick embryo*

During gastrulation in birds, epiblast cells converge at the midline and ingress at the primitive streak. Ingression of these cells results in formation of the mesoderm and replacement of some of the hypoblast cells to produce the definitive endoderm.

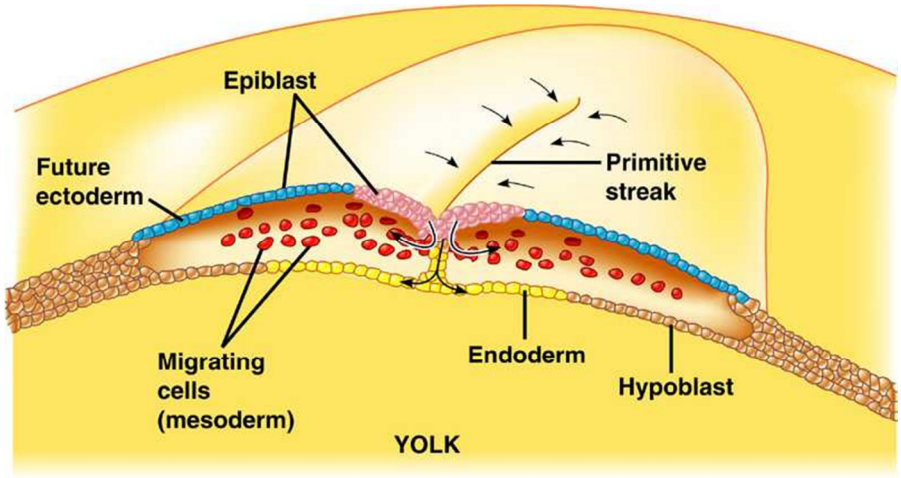


Fig. *Process of formation of germ layers in avian gastrula*

Gastrulation is an early stage in embryo development in which the blastula reorganizes into the three germ layers: the ectoderm, the mesoderm, and the endoderm. Gastrulation occurs after cleavage but before neurulation and organogenesis. Chicken embryo is a major model system in embryology. There were two suggested explanations of chick gastrulation. The first suggested that the mesoderm formed from the epiblast, the early stage totipotent layer of cells, and the mesoderm then differentiated into the endoderm. The other suggestion was that the epiblast and endoderm developed together first, followed by the mesoderm.

In chick embryos, the ectoderm, mesoderm, and endoderm cells ultimately give rise to different tissues and organs. Ectoderm cells generate the skin and neural tissue. Endoderm cells become the lining of the gastrointestinal and the respiratory tracts. Mesoderm cells differentiate into the circulatory system, kidneys, and skeletal compartments among many other features. Those tissues and organs are created during organogenesis. Gastrulation involves cells from the epiblast moving underneath through a line at the midline of the disk called the primitive streak. Some of these involuting cells form endoderm and some form mesoderm. The primitive streak marks the future anterior-posterior axis of the embryo. The primitive streak in the chick is equivalent to the blastopore in the frog (site through which the cells involute).

Answer No. 4.

Hox genes

Hox genes (also known as homeotic genes) are a group of related genes that control the body plan of an embryo along the anterior-posterior (head-tail) axis. After the embryonic segments have formed, the Hox proteins determine the type of segment structures (e.g. legs, antennae, and wings in fruit flies or the different types of vertebrae in humans) that will form on a given

segment. Hox proteins thus confer segmental identity, but do not form the actual segments themselves.

Hox genes are defined as having the following properties:

- Their protein product is a transcription factor
- They contain a DNA sequence known as the homeobox
- In many animals, the organization of the Hox genes on the chromosome is the same as the order of their expression along the anterior-posterior axis of the developing animal, and are thus said to display colinearity.

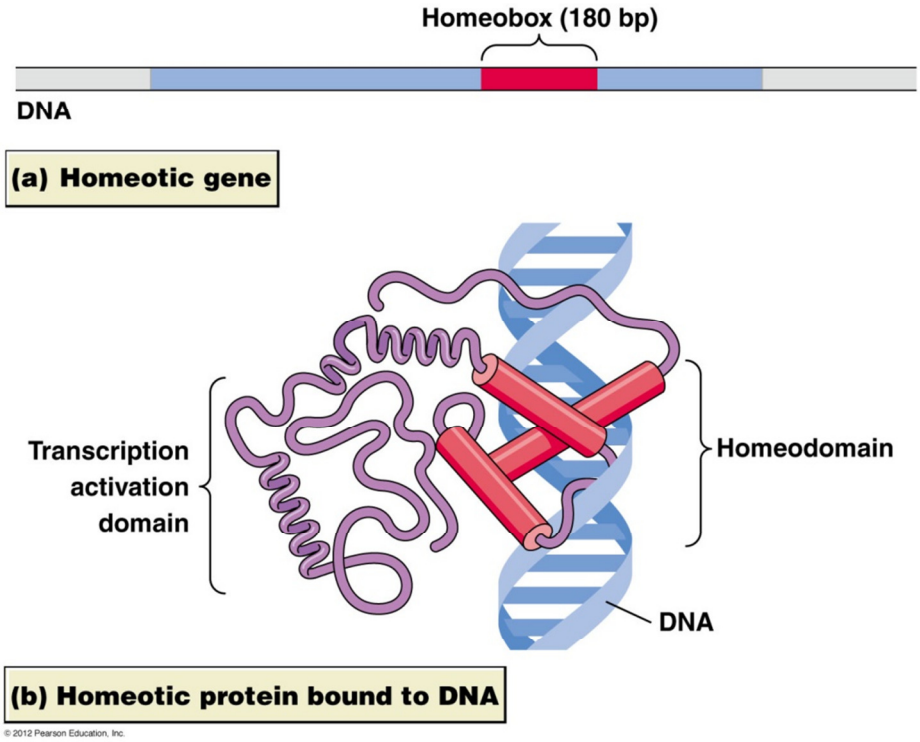


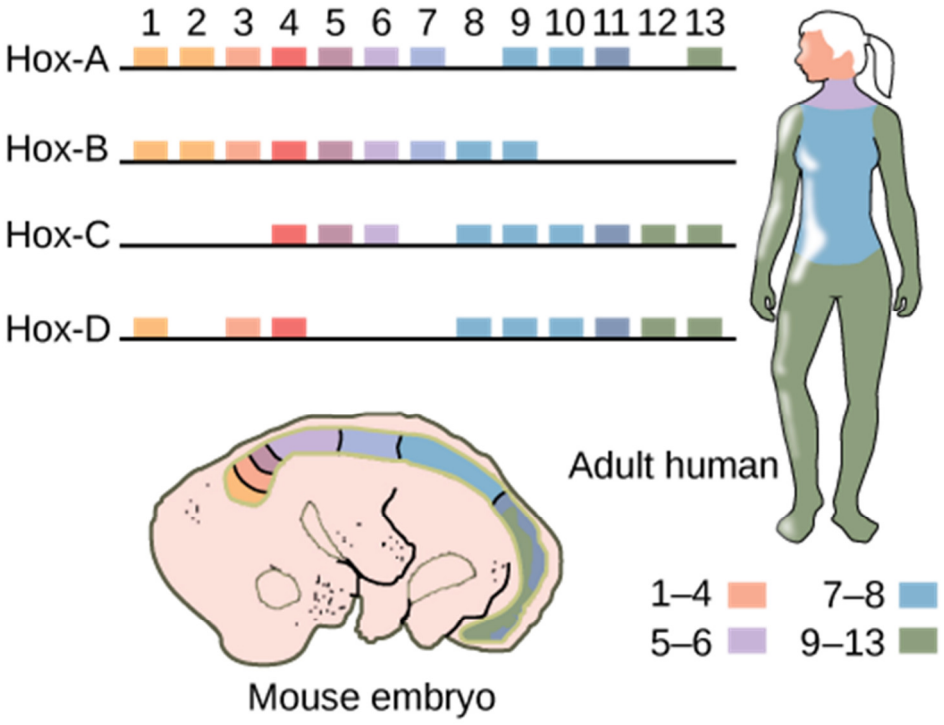
Fig. *Homeotic gene and homeotic protein*

They all cluster together on the genome and play a major role in the development of animal segments with different *Hox* genes being expressed in different segments. *Hox* gene evolution played a big role in the diversification of these segments.

In vertebrates (animals that have backbones), the entire Hox cluster has been duplicated multiple times. Mice and other mammals have four Hox clusters. All four are similar, but each is different.

Mammalian Hox genes

Hox genes are evolutionarily conserved transcription factors that play important roles in establishing the basic body plan of animals. Mammals have about 39 *Hox* genes clustered into four chromosomal complexes. This gene family regulates the regional character and patterning of diverse structures along the anterior–posterior (A/P) axis of the embryo. Nested patterns of *Hox* gene expression generate a Hox combinatorial protein code that orchestrates the morphogenesis of structures in the nervous system, axial skeleton, limbs, intestine and many other tissues. In light of their key role in regulating morphogenesis across animal species, modulation of *Hox* expression or function over the course of evolution is believed to have been important in generating diversity.



Hox genes

Hox genes are highly-conserved genes encoding transcription factors that determine the course of embryonic development in animals. In vertebrates, the genes have been duplicated into four clusters: Hox-A, Hox-B, Hox-C, and Hox-D. Genes within these clusters are expressed in certain body segments at certain stages of development. Shown here is the homology between Hox genes in mice and humans.

Mammalian Hox genes expressed along dorsal axis in neural tube, neural crest, paraxial mesoderm and surface ectoderm and in derivatives of these tissues.

Homeobox (HOX) genes encode a group of homeodomain-containing transcription factors. This gene family was initially described in Drosophila melanogaster, where it was shown to control segmental patterning during development. Homeodomains are also found in genes other than the HOX family, including transcription factors involved in developmental processes such as pluripotency and differentiation. In mammalian genomes, HOX genes are encoded from 4 clusters and are expressed in a temporal manner during development. In addition, the spatial developmental control of a particular HOX gene depends on its location within its cluster. Recently, their importance has been reemphasized by stem cell and cancer researchers. HOX genes have been identified as oncogenes as well as tumor suppressor genes, depending on the specific cancer under study. HOX gene dysregulation can also affect biological processes such as apoptosis, proliferation, and signal transduction during oncogenesis.

Answer No. 5.

Dictyostelium is a soil-living amoeba belonging to the slime mold (Mycetozoa). It is a eukaryote that transitions from a collection of unicellular amoebae into a multicellular slug and then into a fruiting body within its lifetime. It has a unique asexual lifecycle that consists of four stages: vegetative, aggregation, migration, and culmination. The life cycle of *Dictyostelium* is relatively short, that undergoes movement, chemical signaling, and development. The simplicity of its life cycle makes *Dictyostelium* a valuable model organism to study genetic, cellular, and biochemical processes in other organisms.

Life Cycle

The life cycle of *Dictyostelium* begins as spores are released from a mature sorocarp (fruiting body). Myxamoebae hatch from the spores under warm and moist conditions. During their vegetative stage, the myxamoebae divide by mitosis as they feed on bacteria. The bacteria secrete folic acid, attracting the myxamoebae. When the supply of bacteria is depleted, the myxamoebae enter the aggregation stage.

During aggregation, starvation initiates the creation of a biochemical machinery that includes glycoproteins and adenylyl cyclase. The glycoproteins allow for cell-cell adhesion, and adenylyl cyclase creates cyclic AMP. Cyclic AMP is secreted by the amoebas to attract neighboring cells to a central location. As they move toward the signal, they bump into each other and stick together by the use of glycoprotein adhesion molecules.

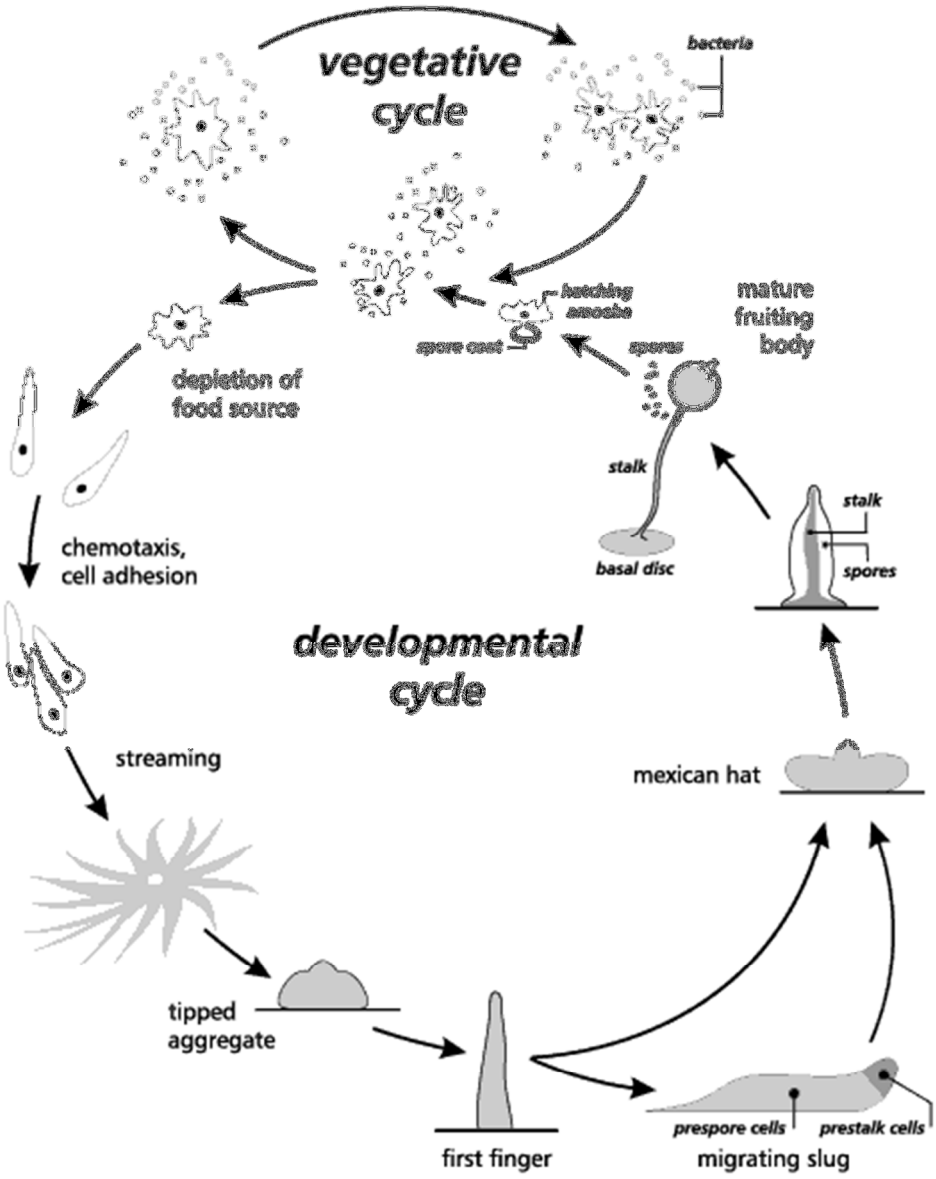


Fig. Life cycle of Dictyostelium

The migration stage begins once the amoebas have formed a tight aggregate and the elongated mound of cells tip over to lie flat on the ground. The amoebas work together as a motile pseudoplasmodium, also known as a slug. The slug is approximately 2–4 mm long, composed of up to 100,000 cells, and is capable of movement by producing a cellulose sheath in its anterior cells through which the slug moves. Part of this sheath is left behind as a slimy trail as it moves toward attractants such as light, heat, and humidity in a forward-only direction. cAMP and a substance called differentiation-inducing factor (DIF), help to form different cell types. The slug becomes differentiated into prestalk and prespore cells that move to the anterior and posterior ends, respectively. Once the slug has found a suitable environment, the anterior end of the slug will form the stalk of the fruiting body and the posterior end will form

the spores of the fruiting body. After the slug settles into one spot, the posterior end spreads out with the anterior end raised in the air, forming what is called the "Mexican hat," and the culmination stage begins.

The prestalk cells and prespore cells switch positions in the culmination stage in order to form the mature fruiting body. The anterior end of the Mexican hat forms a cellulose tube, which allows the more posterior cells to move up the outside of the tube to the top, and the prestalk cells move down. This rearrangement forms the stalk of the fruiting body made up of the cells from the anterior end of the slug, and the cells from the posterior end of the slug are on the top and now form the spores of the fruiting body. At the end of this 8– to 10-hour process, the mature fruiting body is fully formed. This fruiting body is 1–2 mm tall and is now able to start the entire cycle over again by releasing the mature spores that become myxamoebae.

Answer No. 6.

The complement system is a complex system of proteins that acts as a cascade. Each protein within the system is assigned a number and they react in sequence once the system has been activated. Many of the proteins are pro-enzymes that require proteolytic cleavage in order to become active. The complement cascade forms part of the body's innate immune system and is involved in host defense against infection, the initiation of an inflammatory response and the destruction of certain bacteria and viruses.

The following are the basic functions of complement:

1. **Opsonization** - enhancing phagocytosis of antigens
2. **Chemotaxis** - attracting macrophages and neutrophils
3. **Cell Lysis** - rupturing membranes of foreign cells
4. **Agglutination**- clustering and binding of pathogens together (sticking)

There are three distinct pathways through which complement can be activated on pathogen surfaces. These pathways depend on different molecules for their initiation, but they converge to generate the same set of effector molecules.

The pathways are as follows-

1. Classical Pathway
2. Alternative Pathway
3. Lectin Pathway

1. **Classical Pathway**

This pathway involves complement components **C1**, **C2** and **C4**. The pathway is triggered by **antibody-antigen complexes** binding to **C1**, which itself has three subcomponents **C1q**, **C1r** and **C1s**. The pathway forms a C3 convertase, **C4b2a**, which splits C3 into two fragments; the large fragment, **C3b**, can covalently attach to the surface of microbial pathogens and **opsonise** them; the small fragment, **C3a**, activates **mast cells**, causing the release of vasoactive mediators such as histamine.

2. **Alternative Pathway**

This pathway involves various factors, **B, D, H** & **I**, which interact with each other, and with C3b, to form a C3 convertase, **C3bBb**, that can activate more C3, hence the pathway is sometimes called 'the amplification loop'. Activation of the loop is promoted in the presence of bacterial and fungal cell walls, but is inhibited by molecules on the surface of normal mammalian cells.

3. **Mannose-binding Lectin Pathway**

This pathway is activated by the binding of **mannose-binding lectin** (**MBL**) to mannose residues on the pathogen surface. This in turn activates the MBL-associated serine proteases, **MASP-1** and **MASP-2**, which activate **C4** and **C2**, to form the C3 convertase, **C4b2a**.

Classical Pathway:

It is triggered by antigen-bound antibody molecules. C1 is a macromolecular complex made up of subunits C1q, C1r, and C1s. When the intact macromolecular C1 binds to the exposed regions of at least two antigen-bound antibodies, the C1r and C1s subunits are activated and are responsible for the cleavage of the next two involved complement components, C4 and C2. C4 is cleaved into two fragments. The larger C4b molecule attaches to the target membrane nearby while the small C4a molecule floats away. An exposed site on deposited C4b is available to interact with the next complement component, C2. Again, activated C1s cleaves the C2 molecule into two pieces. In this case, the fragment that remains is C2b. The smaller C2a fragment floats away. What remains bound to the membrane is C4b2b, also known as the C3 convertase because its role is to convert the next complement component, C3, into its active form.The C3 convertase of the classical pathway splits C3 into two fragments, C3a and C3b. The convertase has the ability to cleave multiple C3 molecules, forming hundreds of C3a and C3b fragments. The C3a fragments float away and have a role in inducing an inflammatory response.

The C5 convertase, much like the C3 convertase before it, catalyzes the cleavage of hundreds to thousands of C5 complement components into C5a and C5b, before it reverts to inactivity. C5a floats away and contributes to inflammation while the C5b fragment binds to the antigen surface. This binding of C5b is the initial step in the formation of the membrane attack complex (MAC). The membrane-bound complement component C5b is bound by the next complement molecule, C6.

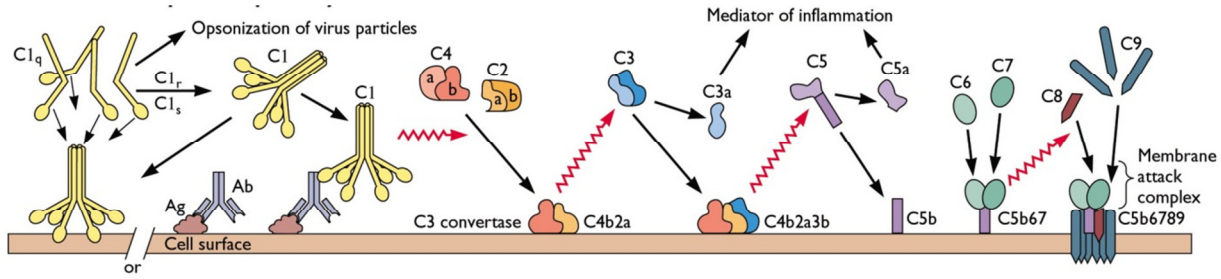


Fig. Consecutive steps of classical complement pathway

The resulting bimolecular complex then binds C7 and then C8. The C5b-8 complex acts as a receptor for a variable number of membrane-disrupting C9 molecules. The resultant C5b-8 complex and poly-C9 is given the name "membrane attack complex." The MAC creates a transmembrane pore leading to the lysis of the target cell.

Alternative Pathway

This pathway is triggered when the C3b protein directly binds the microbe. It is initiated by the spontaneous hydrolysis of C3, which is abundant in the blood plasma. The spontaneous cleavage of the thioester bond in C3 forms C3 (H_2O). This change in shape allows the binding of plasma protein Factor B, which allows Factor D to cleave Factor B into Ba and Bb. Bb remains part of the C3(H_2O) to form C3(H_2O)Bb. This complex is also known as a fluid-phase C3-convertase. This convertase, although only produced in small amounts, can cleave multiple C3 proteins into C3a and C3b.

The alternative pathway C3-convertase consists of the activated B and C3b factors, forming an unstable compound that can become stable after binding properdin, a serum protein.

After the creation of C3 convertase, the complement system follows the same path regardless of the means of activation (alternative, classical, or lectin). Binding of another C3b-fragment to the C3-convertase of the alternative pathway creates a C5-convertase analoguous to the lectin or classical pathway.

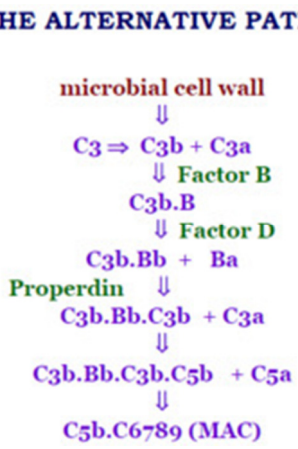


Fig. Consecutive steps of alternative complement pathway

The C5-convertase of the alternative pathway consists of C3bBbC3b also referred to as $C3b_2Bb$ (instead of C4b2a3b in the other pathways).

Difference between Classical ad Alternative Pathways:

Feature	Classical Pathway	Alternative Pathway
Initiated by	Ag-Ab complex (*immune complex*)	Cell surface constituents foreign to host, *e.g.*, bacteria
Initiation reaction	C1 binds Fc region of Ab in Ag-Ab complex	C3b* binds foreign cell surface
Cleavage of C3	By C3 convertase ($\overline{C4b2a}$)	Initially, spontaneous; later by $\overline{C3bBb}$ that has C3 convertase activity
Progresses through	C1 → C4 → C2 → C3 → C5	C3 → Factor B → (FactorD)[1] → (Properdin)[2] → C5
Products	Anaphylatoxin (C4a, C3a) Opsonin (C3b, major major opsonin) Membrane-attack complex (C5b6789) causing cell lysis	Anaphylatoxin (C3a) Opsonin (C3b major opsonin) Membrane-attack complex (C5b6789); cell lysis

Answer No. 7.

Antigens are considered as the macromolecules that elicit an immune response in the body. Antigens can be proteins, polysaccharides or conjugates of lipids with proteins (lipoproteins) and polysaccharides (glycolipids).

There are generally two categories of antigens

1. **Exogenous antigens**

Exogenous antigens (inhaled, ingested, or injected) are taken up by **antigen-presenting cells** (**APCs**). These include:

- **phagocytic cells** like **dendritic cells** and **macrophages**;
- **B lymphocytes** ("**B cells**"); which are responsible for producing **antibodies** against the antigen.

2. **Endogenous antigens**

Antigens that are generated within a cell (e.g., viral proteins in **any** infected cell).

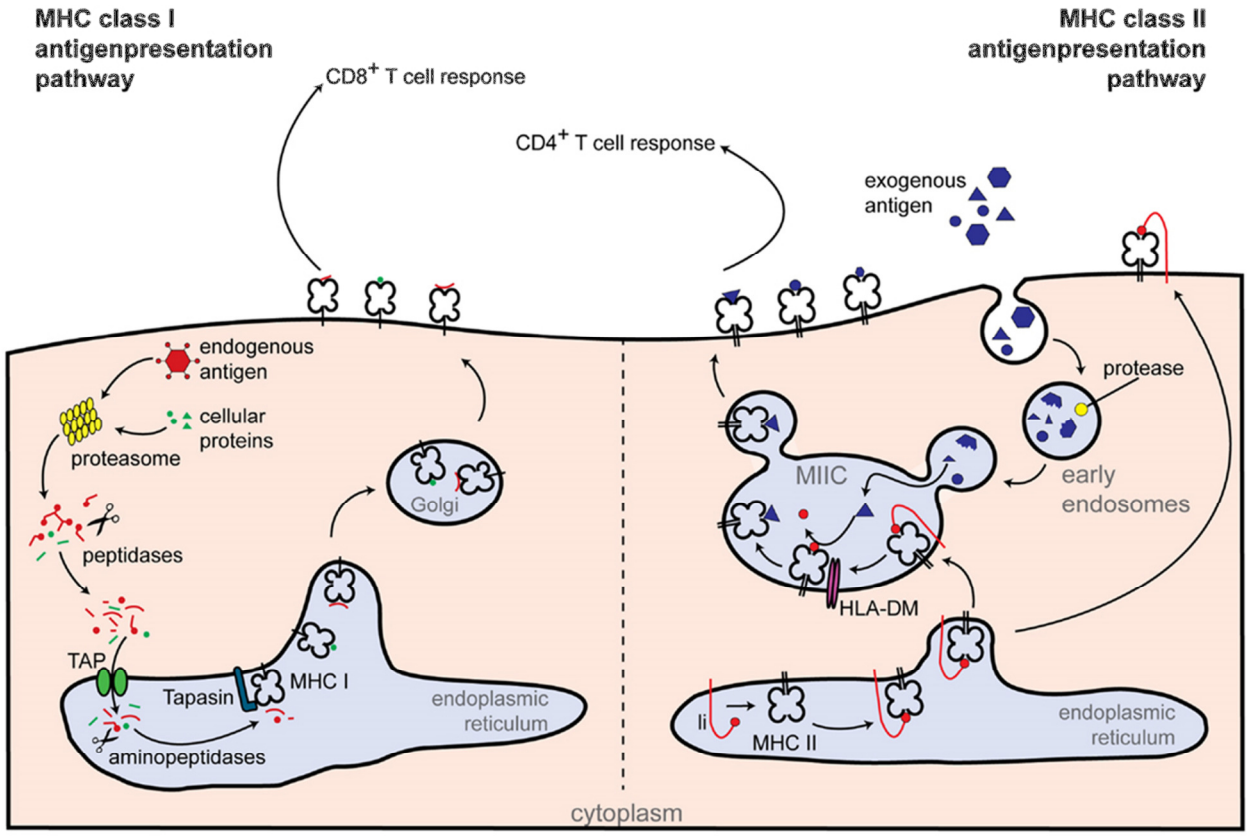
MHC (Major histocompatibility complex)

The **major histocompatibility complex** (**MHC**) is a set of cell surface molecules encoded by a large gene family which controls a major part of the immune system in all vertebrates. The major function of MHCs are to bind to peptide fragments derived from pathogens and display them on the cell surface for recognition by the appropriate T-cells.

MHC class I presentation (for endogenous antigens)

Endogenous antigens are produced mainly by viruses replicating within a host cell, though antigens here can also derive from cytoplasmic bacteria or the host cell's own proteins. The host cell digests cytoplasmic proteins by the proteasome into small peptides. A specialized carrier, the Transporter associated with Antigen Processing (TAP) complex moves the peptide into the endoplasmic reticulum, allowing the antigenic peptide to be coupled to an MHC Class I molecule and transported to the cell surface.

MHC Class I molecules present antigen to CD8+ cytotoxic T cells and are expressed on all nucleated cells. Cytotoxic T cells (also known as TC, killer T cell, or cytotoxic T-lymphocyte (CTL)) are a population of T cells that are specialized for inducing the death of other cells. Recognition of antigenic peptides through Class I by CTLs leads to the killing of the target cells, which is infected by virus, intra cytoplasmic bacterium, or are in damaged condition.



MHC class II presentation (for exogenous antigens)

This type of MHC is generally shown by APC (Antigen presenting cells). Expression of Class II is more restricted than Class I. High levels of Class II are found on dendritic cells, but can also be observed on activated macrophages, B cells, and several other host cell types in inflammatory conditions. Dendritic cells (DCs) phagocytose exogenous pathogens such as bacteria, parasites, and toxins in the tissues and then migrate, via chemotactic signals, to T cell-enriched lymph nodes. During migration, DCs undergo a process of maturation in which they lose phagocytic capacity and develop an increased ability to communicate with T-cells in the lymph nodes. This maturation process is dependent on signaling from other pathogen-associated molecular pattern (PAMP) molecules through pattern recognition receptors, such as the members of the Toll-like receptor family.

The DC uses lysosome-associated enzymes to digest pathogen-associated proteins into smaller peptides. In the lymph node, the DC will display these antigenic peptides on its surface by coupling them to MHC Class II molecules. This MHC:antigen complex is then recognized by T cells passing through the lymph node. Exogenous antigens are usually displayed on MHC Class II molecules, which interact with $CD4^+$ helper T cells. $CD4^+$ lymphocytes, or TH, are immune

response mediators, and play an important role in establishing and maximizing the capabilities of the adaptive immune response.

Answer No. 8.

This condition is called as **Autoimmunity** or **Auto immune disease**.

Autoimmunity

Autoimmunity is the system of immune responses of an organism against its own cells and tissues. Any disease that results from such an aberrant immune response is termed an autoimmune disease. Autoimmunity can be defined as breakdown of mechanisms responsible for self-tolerance and induction of an immune response against components of the self.

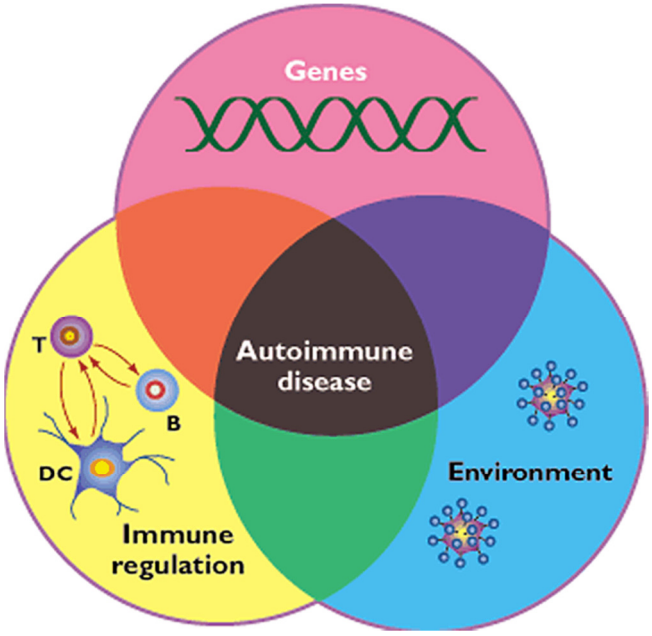
Examples includes Celiac disease, diabetes mellitus type 1, Sarcoidosis, systemic lupus erythematosus (SLE), Sjögren's syndrome, Churg-Strauss Syndrome, Hashimoto's thyroiditis, Graves' disease, idiopathic thrombocytopenic purpura, Addison's Disease, rheumatoid arthritis (RA), Polymyositis (PM), and Dermatomyositis (DM). Autoimmune diseases are very often treated with steroids.

An immune response to "self" antigens defines a state of autoimmunity.
Autoimmune responses may result from two general causes. In one case, antigens normally "hidden" from the immune system ("sequestered" antigens) may be released into the circulation and trigger a response by the immune system. In this case no state of peripheral tolerance need exist, and the immune system is capable of generating an effective response on exposure to the antigen. A different situation exists when the normally effective tolerant state of the immune system to "self" antigens is for some reason abrogated. The final result of such a breakdown of tolerance, however, is the same as in the case above: a damaging and potentially fatal autoimmune reaction.

Breaking of the normal tolerant state of an organism's immune system may result from a variety of influences:
i) Decrease in Treg activity.
ii) Increase in TH activity (e.g., with adjuvants).
iii) Immune response to foreign antigens which happen to cross-react with "self"

Three general factors are considered to be the cause of auto immune disease. They can affect the immune system either by combined way or singly. They are as follows:

a. Some **genes** may be responsible
b. Some fault/disturbance in **Immune regulation**
c. Some **environmental factors**



Effector mechanisms in autoimmune disease

a. Antibody mediated damage
b. Cell mediated damage

Antibody-mediated damage

Antibodies are a family of glycoproteins present in the serum and tissue fluids of all mammals. Antibodies can be carried on the surface of B cells, acting as receptors, or free in the blood or lymph. Specific binding of antigens (self or foreign) causes B cells to produce large amounts of antigen-specific antibody. These antibodies provide critical protection against infectious microorganisms immediately following infection and are the key protective immune response induced by vaccination. Similarly, self-reactive or autoantibodies are important in clearing cellular debris induced by inflammation or physical damage to the body. A common feature of all autoimmune diseases is the presence of autoantibodies, which are an important factor in the diagnosis or classification of the autoimmunedisease. Due to the chronic nature of most autoimmune diseases, autoantibodies appear long before clinical symptoms, providing a good predictive marker for the potential to develop disease. Autoantibodies can induce damage to the body by binding to self-tissues, activating the complement cascade and inducing lysis and/or removal of cells by phagocytic immune cells. This occurs in certain forms of haemolytic anaemia when autoantibodies bind to red blood cell surface antigens inducing lysis of red blood cells. Autoantibodies can also interact with cell-surface receptors, altering their function. Autoantibodies to the acetylcholine receptor block transmission at the neuromuscular junction resulting in myasthenia gravis, while autoantibodies to the thyrotropin receptor block thyroid cell stimulation resulting in Graves' disease. Self-antigen, autoantibodies and complement can

combine to form injurious immune complexes that deposit in vessels or joints as is observed in lupus, inflammatory heart disease and arthritis.

Cell-mediated damage

Damage induced by cells of the immune system play a major pathogenic role in many autoimmune diseases. The predominant infiltrating cells include phagocytic macrophages, neutrophils, self-reactive CD4+ T helper cells and self-reactive CD8+ cytolytic T cells, with smaller numbers of natural killer cells, mast cells and dendritic cells. Immune cells damage tissues directly by killing cells or indirectly by releasing cytotoxic cytokines, prostaglandins, reactive nitrogen or oxygen intermediates. Tissue macrophages and monocytes can act as antigen-presenting cells to initiate an autoimmune response, or as effector cells once an immune response has been initiated. Macrophages act as killer cells through antibody-dependent cell-mediated cytotoxicity and by secreting cytokines, such as tumour necrosis factor (TNF) or interleukin (IL)-1, which act as protein signals between cells. Macrophages and neutrophils damage tissues (and microorganisms) by releasing highly cytotoxic proteins like nitric oxide and hydrogen peroxide. Cytokines and other mediators released by macrophages recruit other inflammatory cells, like neutrophils and T cells, to the site of inflammation. CD4+ T cells have been classified as T helper 1 (TH1) or T helper 2 (TH2) cells depending on the release of the cytokines interferon-g (IFN-g) or IL-4, respectively. IFN-g is a proinflammatory cytokine associated with many organ-specific autoimmune diseases like type I diabetes and thyroiditis, while IL-4 activates B cells to produce antibodies and is associated with autoantibody/immune complex-mediated autoimmune diseases like lupus and arthritis. Suppressor or regulatory T-cell populations, including activated CD25+CD4+ regulatory T cells, exist in peripheral tissues and are important in controlling inflammation and autoimmune responses by killing autoreactive cells. These regulatory cells also secrete anti-inflammatory cytokines like IL-10 and transforming growth factor (TGF)-b that further inhibit TH1 immune responses, thereby reducing inflammation and autoimmune disease. If regulation of self-reactive T-cells and autoantibody production by regulatory T-cell populations is disrupted by environmental agents like infections o toxins, then chronic autoimmune disease may result.

Classification of Autoimmune Diseases

It can be considered as of two types

2. **Systemic-** Auto-immunity is directed against an antigen that is present at many different sites and can include involvement of several organs**.**
3. **Organ specific -** Organ specific means the auto-immunity is directed against a component of one particular type of organ.

:Resources: from Wikipedia and different other web sites