TYPES OF ANTIGENS

TYPES ACCORDING TO ANTIGENIC SPECIFICITY

Species-specific antigen

- An antigen is specific in relation to a specific species of host only.

Organ specific antigen

- The antigen is specific in relation to a particular organ in a single species. For example, kidney protein is different from lung protein.

Heterophile antigens

- They are antigens of identical nature present in the cells of some bacterial species and also in the tissues of different animals. Antibody formed against one antigen cross-react with other antigens. There is a phenomenon of antigenic sharing.
- *Examples:*
    - Frossman antigens are a group of related heterophile antigens. They are present in the cell wall of many bacterial species (glycoprotein with carbohydrate side chain) belong to the genera streptococcus, shigella, salmonella and clostridium and also on the surface of red blood cells (glycoprotein) of horses, sheep, cats and mice. The animals having Frossman antigens in their tissues do not develop antibodies because the antigens are considered as 'self'
    - A heterophile antigen is found in some proteus strains (OX-19, OX -2, OX-K) and also certain Rickettsial organisms (e.g. *Rickettsia rickettsii*). This forms the basis of *Weil-Felix reaction*. An agglutination test is used to detect antibody in human beings against Rickettisal organisms using Proteus antigen.

Alloantigens (isoantigens)

- These are antigens present in one individual and are antigenic to some individuals of the same species. The corresponding antibodies are called alloantibodies. Example: Blood group antigen, Transplantation antigen etc.

Syngenic antigen

- The antigens present in the individuals of the same genetic make up. Example- antigens present in monozygotic twins.

Autoantigen

- In certain circumstances, own body tissues develop antigenic properties and antibody formed against the antigen. The auto antigens are sequestrated without contact with the lympho-reticular system but by any mishap when antigens are released, they provide an opportunity to produce autoantibody. Example: sperm, lens protein etc.

Super antigen

- A group of molecules that do not have to be processed by antigen presenting cells in order to activate T cells. Examples – Bacterial antigens (Streptococcal A antigen).

ANTIGENIC TYPES BASED ON T CELL RESPONSE

T dependent antigen

- Complex antigens such as RBC, serum proteins etc. They are rapidly metabolized, require T cell help and produce memory and class switching.

T independent antigen

- LPS of *E coli*, pneumococcal *polysaccharide, flagellin , Lectin, Con A PHA, Pokeweed mitogen etc.,* composed of repeating units. They are slowly metabolized, no memory or class switching.
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MICROBIAL AND NON-MICROBIAL ANTIGENS

Microbial antigens

- It includes bacterial antigens, viral antigens and other microbial antigens.

Non-microbial antigens

- They are certain dust particles, pollen grain, snake venom, etc.

BACTERIAL ANTIGENS

- There are two main groups
  - Soluble antigens: Some soluble substances produced by the bacteria, which are excreted into the environment. For example, toxins, enzymes etc.
  - Cellular antigens: They are the structural units of bacterial cell. Common bacterial antigens are:
    - *Somatic (O) antigen:* In gram negative bacteria (Salmonella, *E. coli*, Brucella etc.), somatic antigens are composed of lipopolysaccharide (LPS)–protein complex, which are good antigen and produce good immune response. But O antigens are highly variable (LPS consists of highly variable Oligosaccharides) and thus immunity against one 'O" antigen will not confer immunity against bacteria bearing other 'O" antigens. But a common core antigen (under laying core polysaccharide) has a potential use as vaccine.
    - *Capsular (K) antigen:* A variety of bacterial species have capsule (e.g. *Bacillus anthracis*, *E. coli*, Salmonella spp. etc) which is antigenic. Capsule commonly consists of polysaccharides (e.g. K antigen of *E.coli*) but some are composed of polypeptides (e.g. Poly-D-glutamic acid in case of *B.anthracis*).
    - *Flagellar (H) antigen:* Motile bacteria have flagella (e.g. *Salmonella* spp., *E.coli*, *Proteus* spp.). These Flagella is composed of protein (flagellin), which is antigenic.
    - *Fimbrial (F) antigen:* Fimbrial or Pili antigen are present on the surface of bacteria .
    - *Spore antigen:* Bacterial spores (e.g. *Bacillus* spp., *Clostridium* spp. etc.,) especially the exosporidium is antigenic.
    - Other significant bacterial antigens include the porins, heat shock proteins, the exotoxins etc.

VIRAL ANTIGENS

- Structural components (VP-Viral Protein) of the virus vary in their size and complexity.
- Capsid protein and envelope (consists of lipoprotein and glycoprotein) are antigenic.
- Examples, HN protein (glycoprotein) of Newcastle disease virus.

NON-MICROBIAL ANTIGEN

- Some food may contain substances that evoke immune response and cause allergic reaction.
- Pollen grains, fungal spores or some dust particles when inhaled, cause allergic reaction.

CELL SURFACE ANTIGEN

- Mammalian cell surface contain protein molecules within lipid bilayer.
- These proteins may act as antigen when injected into another animal of same species or different species.
- Important cell surface antigens are
  - Blood group antigen
  - Major histocompatibility complex (MHC) molecules
  - Cluster of differentiation (CD).

BLOOD GROUP ANTIGEN

- The antigens found on the surface of red blood cells are called blood group antigens or erythrocytes antigens.
- Earlier attempt of blood transfusion often resulted in disastrous consequences.
- Blood transfusion became scientifically feasible after the discovery of blood groups by Landsteiner (1900).
- Most of the blood group antigens are either glycoprotein or glycolipids and they are the integral components of cell membrane.
- They are not involved in antigen processing but they influence graft rejection.
- There are several human blood group system e.g., ABO, MN, Rh, Lewis, Kell, Duffy, Kidd, Colton etc.,
- Function:

- The ABO antigens in human are anion and glucose transporter proteins.
- The M and C antigen of sheep RBC are associated with membrane potassium pump and amino acid transport.

MAJOR HISTOCOMPATIBILITY COMPLEX MOLECULES

- MHC molecules are present on the surface of nucleated cells and also on red blood cells in some species (class I MHC).
- Some MHC antigens are present on the surface of macrophages, dendritic cells and B cells (MHC- class II molecules).
- Some MHC are not bound to cell surface but present in the secretion (MHC- class III molecules)
- They are protein or glycoprotein substances and provoke immune response.

CLUSTER DIFFERENTIATION

- It refers to different molecules present on the surface of lymphocytes, which perform specific function, and the receptors can be identified by monoclonal antibodies.
- Example CD_{8+} refers to T Cytotoxic cells.

ABO BLOOD GROUP SYSTEM

- The antigen found on the surface red blood cells (RBC) are called blood group antigen.
- The ABO system contains four blood groups and it is determined based on the presence or absence of two distinct antigens.
- RBC of group A carry antigen A, group B carry antigen B, O group have neither A nor B antigen and group AB carry both A and B antigen.
- Group A is subdivided into A1 (about 80%) and A2 (about 20%). The four antigens can be distinguished by two distinct *isoantibodies* present in the serum.
- 'A' groups people have anti B antibody, B groups have anti A antibody, O groups both anti A and anti B antibody, whereas AB groups will neither have anti A nor anti B antibodies. When erythrocytes are mixed with serum containing corresponding antibodies, agglutination occurs (table).
- Isoantibodies appear in the serum by about six months of age and persist thereafter.
- Since O groups do not have either A or B antigen, RBC from this group of people are not agglutinated by serum of any other blood groups, thus O groups are used as universal blood donor. But serum from O group contain both anti A and B antibodies and agglutinate erythrocyte of all other blood groups that means they can receive blood from group O only.
- AB groups do not have anti A or anti B antibodies and used as universal acceptor.

AGGLUTINATION REACTION WITH RBC AND CORRESPONDING ANTISERUM

Erythrocytes	Antiserum against			
	A	B	AB	O
A	-	+	-	+
B	+	-	-	+
AB	+	+	-	+
O	-	-	-	-

Rh SYSTEM AND ERYTHROBLASTOSIS FETALIS

Rh system

- Levine and Stetson (1939) demonstrated a new antibody in the serum of women who developed reaction following blood transfusion and she recently delivered stillborn baby with hemolytic disease.
- Landsteiner and Wiener (1940) found that rabbit antiserum to rhesus monkey RBC agglutinated RBC of 80% normal people. This antigen or RBC is called *Rhesus or Rh factor*.
- Very large number of antigens are detected in Rh system, they cross react and weakly immunogenic except 'D' or Rho antigen which is most powerful antigen and responsible for majority of Rh incompatibility reaction. Thus people are divided into Rh positive and Rh-negative groups.
- Rh antigens are determined by three pair of closely linked allelomorphic genes (Cc, Dd, and Ee).

Erythroblastosis fetalis

- When Rh-negative women carries Rh-positive fetus (when husband is Rh positive), she develops antibodies to Rh antigen as fetal blood enter to maternal circulation (minor transplacental leakage occur during pregnancy but during delivery large amount of fetal blood enter into maternal circulation).
- Mother develops immunity during first pregnancy.
- During subsequent pregnancy, Rh antibodies (IgG class) pass from mother to fetus and cause haemolysis or jaundice.

HISTOCOMPATIBILITY ANTIGEN

- When an organ is grafted, normally the graft is rejected because of immune response.
- The antigen present on the cells of the graft tissues trigger the immune response and these antigens are called *histocompatibility antigen* .
- Every animal has its own histocompatibility antigen, which is inherited from its parents.
- The histocompatibility antigens vary in their ability to provoke immune response, some are not significant while others are potent to evoke immune response or rejection of graft.
- These potent antigens are inherited from parent through a set of genes known as *major histocompatibility complex(MHC).*
- MHC is an organized cluster of genes that control antigen processing and presentation. They are found in multiple systems.
- Immunological response to antigens are controlled by specific genes called immune response (Ir) genes, which are believed to be located in the HLA class-II region, probably in the DR Locus.
- All vertebrate animals have MHC genes that are maintained as linked genes. But the arrangements of genes differ with species.
- The genes are labeled A, B, C and D and they are co-dominant.
- Only one gene of each pair can code for antigen in a given individual and these antigens are different form one individual to others. Collectively the genes of
    - Human MHC are called HLA (Human leukocyte antigen)
    - Cattle - BOLA (Bovine leukocyte antigen)
    - Sheep – OLA (Ovine leukocyte antigen)
    - Horse – ELA (Equine leukocyte antigen)
    - Swine –SLA (Swine leukocyte antigen)
    - Dog- DLA (dog leukocyte antigen),
    - Mouse – H_2 (Histocompability),
    - Chicken – B
- MHC plays an important role in recognition of protein antigens by T cells. T cells do not recognize free soluble antigens but recognize peptide antigens that are non-covalently bound to MHC molecules, i.e. either Class I or Class II molecules.

MHC DISTRIBUTIONS

Class- I

- Expressed on the cell surface of nucleated cells (including B cells, T cells, macrophages) except Erythrocytes.

Class-II

- Expressed on the cell surface of antigen presentating cells mainly B-lymphocytes, macrophages, and dedritic cells.

Class-III

- Serum proteins and component of complement system.

MHC RESTRICTIONS

- The importance of MHC antigens is to present antigen by macrophages or other cells to T lymphocyte for immune response.

- *MHC restriction* means the antigen (foreign) will be recognized by T lymphocytes only if it is presented in association with self MHC antigen (class I or class II). For example, in case of virus-infected cells, T cytotoxic cell destroy the virus-infected cells (target cells) after recognition of antigen along with MHC -class I.
- Helper T (CD_4^+) lymphocytes can recognize antigen presented by antigen presentating cells on their surface along withMHC class II.

ANTIGEN PROCESSING AND PRESENTATION

Processing of Exogenous antigen

- The processing and presentation of exogenous protein antigen is mainly done by the antigen presentating cells viz. macrophages, dendritic cells and B-cells, controlled by MHC-Class II molecule. These cells can phagocytose exogenous antigen and process this antigen in the phagosome and finally phagosome containing processed peptides fused with the endosome containing MHC-Class -II molecules.
- In the phago-endosome the processed peptides are loaded on to the MHC-class II molecules and then presented on to their surface. $CD4^+$T helper cells recognize these peptides along with MHC- Class II on the surface of antigen presentating cells for the initiation of immune response.

Processing of Endogenous antigen

- Cytotoxic T cells recognize antigen in the context of MHC class I antigen on the surface of viral infected cells or transformed cells in the body. The endogenous antigens (viral antigens or transformed proptein molecules) are processed by the immunoproteosomes in the cytosol of a cell and appropriate peptide is selected by the two transporter proteins - TAP1 & TAP2 and transported to the endoplasmic reticulum for loading to the MHC class I molecule. Then the peptide along with MHC class I molecules is transported to the srface of cell which is now recognozed by the cytotoxic T cells for its lysis.

Presentation of Non peptide antigen

- It is well known that non proten antigen like glyolipids and lipids are recognized by T cells. These non-protein antigens arepresented by the members of CD1 family of non-classical class I molecules.