Subject /Course	Pharmaceutical Biotechnology
Subject/Course ID	BP605T
Module Title	Types of immunity, Structure of Immunoglobulin's, Hypersensitivity reactions ,vaccines, Blood products
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Learning Outcome of module-3

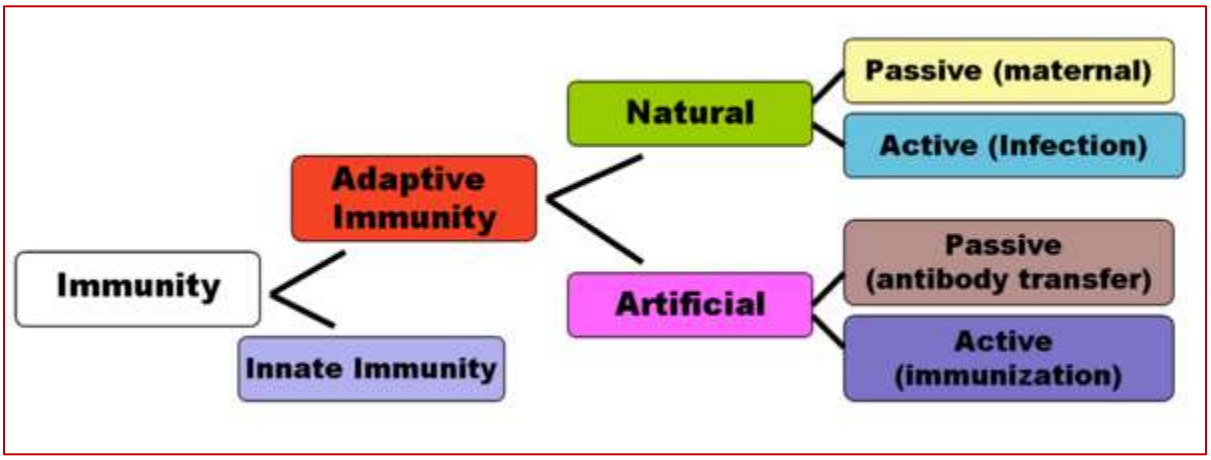
LO	Learning Outcome (LO)	Course Outcome Code
LO1	Upon completion of topic, students will be able to understand the concept of immunity and its type	BP605.3
LO2	They will be familiar with Immunoglobulin's concept and its functions	BP605.3
LO3	They will have knowledge about hypersensitivity reactions	BP605.3
LO4	They shall be able to understand the concept of vaccines and its preparation along with its storage	BP605.3

MODULE CONTENT TABLE

Topic
• Types of immunity- humoral immunity, cellular immunity. • Structure of Immunoglobulins. • Structure and Function of MHC • Hypersensitivity reactions, Immune stimulation and Immune suppressions. • General method of the preparation of bacterial vaccines, toxoids, viral vaccine, antitoxins, serum-immune blood derivatives and other products relative to immunity. • Storage conditions and stability of official vaccines. • Hybridoma technology- Production, Purification and Applications. • Blood products and Plasma Substitutes.

IMMUNITY

Immunity is your body's ability to recognize germs to prevent them from causing illness. The immune system's job is to help identify and eliminate dangerous germs that enter the body before they can cause disease or damage.



Innate Immunity

Innate immunity is the immune system that is present when you are born. It is your body's first line of defense against germs. It includes physical barriers, such as skin and mucous membranes, and special cells and proteins that can recognize and kill germs. The problem with these special cells and proteins is that they can kill a germ, but once the germ is dead, the innate immune system forgets it. It does not communicate any information about the germ to the rest of the body. Without this information, the body cannot prepare itself to fight this germ if it should reinfect the body.

Adaptive Immunity

Adaptive immunity is protection that your body builds when it meets and remembers antigens, which is another name for germs and other foreign substances in the body. When your body recognizes antigens, it produces antibodies to fight the antigens. It takes about 14 days for your body to make antibodies. More importantly, the body memorizes this fight so that if its meets the same antigen again, it can recognize and attack more quickly. Antibody production is one of the most important ways that immunity is developed.

There are two types of adaptive immunity: Active and Passive.

Active Immunity - antibodies that develop in a person's own immune system after the body is exposed to an antigen through a disease or when you get an immunization (i.e. a flu shot). This type of immunity lasts for a long time.

Passive Immunity - antibodies given to a person to prevent disease or to treat disease after the body is exposed to an antigen. Passive immunity is given from mother to child through the placenta before birth, and through breast milk after birth. It can also be given medically through blood products that contain antibodies, such as immune globulin. This type of immunity is fast acting but lasts only a few weeks or months.

There are two main mechanisms of immunity within the adaptive immune system – Humoral and Cellular.

Humoral immunity is also called antibody-mediated immunity. With assistance from helper T cells, B cells will differentiate into plasma B cells that can produce antibodies against a specific antigen. The humoral immune system deals with antigens from pathogens that are freely circulating, or outside the infected cells. Antibodies produced by the B cells will bind to antigens, neutralizing them, or causing lysis (dissolution or destruction of cells by a lysin) or phagocytosis.

Cellular immunity occurs inside infected cells and is mediated by T lymphocytes. The pathogen's antigens are expressed on the cell surface or on an antigen-presenting cell. Helper T cells release cytokines that help activated T cells bind to the infected cells' MHC-antigen complex and differentiate the T cell into a cytotoxic T cell. The infected cell then undergoes lysis.

IMMUNOGLOBULINS

Immunoglobulins, also known as antibodies, are glycoprotein molecules produced by plasma cells (white blood cells). They act as a critical part of the immune response by specifically recognizing and binding to particular antigens, such as bacteria or viruses, and aiding in their destruction. The antibody immune response is highly complex and exceedingly specific. The various immunoglobulin classes and subclasses (isotypes) differ in their biological features, structure, target specificity and distribution. Hence, the assessment of the immunoglobulin isotype can provide useful insight into complex humoral immune response. Assessment and knowledge of immunoglobulin structure and classes is also important for selection and preparation of antibodies as tools for immunoassays and other detection applications.

Immunoglobulin classes (isotypes)

The various antibodies produced by plasma cells are classified by isotype, each of which differs in function and antigen responses primarily due to structure variability. Five major antibody classes have been identified in placental mammals: IgA, IgD, IgE, IgG and IgM. This classification is based on differences in amino acid sequence in the constant region (Fc) of the antibody heavy chains. IgG and IgA are further grouped into subclasses (e.g., in human IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) based on additional small differences in the amino acid heavy chain sequences.

Based on differences in the amino acid sequence in the constant region of the light chain, immunoglobulins can be further sub-classified by determination of the type of light chain (kappa light chain or lambda light chain). A light chain has two successive domains: one constant domain and one variable domain. The ratio of these two light chains differs greatly among species, but the light chains are always either both kappa or both lambda, never one of each. Determination of individual subclasses is relevant in assessing primary immunodeficiencies or immune responses, especially if the total IgG or IgA concentration is not altered or elevated.

IgA: IgA antibodies are found in areas of the body such the nose, breathing passages, digestive tract, ears, eyes, and vagina. IgA antibodies protect body surfaces that are exposed to outside foreign substances. This type of antibody is also found in saliva, tears, and blood. About 10% to 15% of the antibodies present in the body are IgA antibodies. A small number of people do not make IgA antibodies.

IgG: IgG antibodies are found in all body fluids. They are the smallest but most common antibody (75% to 80%) of all the antibodies in the body. IgG antibodies are very important in fighting bacterial and viral infections. IgG antibodies are the only type of antibody that can cross the placenta in a pregnant woman to help protect her baby (fetus).

IgM: IgM antibodies are the largest antibody. They are found in blood and lymph fluid and are the first type of antibody made in response to an infection. They also cause other immune system cells to destroy foreign substances. IgM antibodies are about 5% to 10% of all the antibodies in the body.

IgE: IgE antibodies are found in the lungs, skin, and mucous membranes. They cause the body to react against foreign substances such as pollen, fungus spores, and animal dander. They are involved in

allergic reactions to milk, some medicines, and some poisons. IgE antibody levels are often high in people with allergies.

IgD: IgD antibodies are found in small amounts in the tissues that line the belly or chest. How they work is not clear.

IVIG is used to treat various autoimmune, infectious, and idiopathic diseases. IVIG is an approved treatment for multifocal motor neuropathy, chronic lymphocytic lymphoma, chronic inflammatory demyelinating polyneuropathy, Kawasaki disease and ITP.

MHC (Major histocompatibility complex)

The major histocompatibility complex (MHC) is a large locus on vertebrate DNA containing a set of closely linked polymorphic genes that code for cell surface proteins essential for the adaptive immune system. These cell surface proteins are called MHC molecules.

Classes of MHC

MHC Class I

MHC class I molecules are expressed in all nucleated cells and also in platelets—in essence all cells but red blood cells. It presents epitopes to killer T cells, also called cytotoxic T lymphocytes (CTLs). A CTL expresses CD8 receptors, in addition to T-cell receptors (TCR)s. When a CTL's CD8 receptor docks to a MHC class I molecule, if the CTL's TCR fits the epitope within the MHC class I molecule, the CTL triggers the cell to undergo programmed cell death by apoptosis. Thus, MHC class I helps mediate cellular immunity, a primary means to address intracellular pathogens, such as viruses and some bacteria, including bacterial L forms, bacterial genus Mycoplasma, and bacterial genus Rickettsia. In humans, MHC class I comprises HLA-A, HLA-B, and HLA-C molecules.

MHC class II

This class can be conditionally expressed by all cell types, but normally occurs only on "professional" antigen-presenting cells (APCs): macrophages, B cells, and especially dendritic cells (DCs). An APC takes up an antigenic protein, performs antigen processing, and returns a molecular fraction of it—a fraction termed the epitope—and displays it on the APC's surface coupled within an MHC class II molecule (antigen presentation). On the cell's surface, the epitope can be recognized by immunologic

structures like T-cell receptors (TCRs). The molecular region which binds to the epitope is the paratope.

On surfaces of helper T cells are CD4 receptors, as well as TCRs. When a naive helper T cell's CD4 molecule docks to an APC's MHC class II molecule, its TCR can meet and bind the epitope coupled within the MHC class II. This event primes the naive T cell. According to the local milieu, that is, the balance of cytokines secreted by APCs in the microenvironment, the naive helper T cell (Th0) polarizes into either a memory Th cell or an effector Th cell of phenotype either type 1 (Th1), type 2 (Th2), type 17 (Th17), or regulatory/suppressor (Treg), as so far identified, the Th cell's terminal differentiation.

Class III

These molecules have physiologic roles unlike classes I and II, but are encoded between them in the short arm of human chromosome 6. Class III molecules include several secreted proteins with immune functions: components of the complement system (such as C2, C4, and B factor), cytokines (such as TNF-α, LTA, and LTB), and heat shock proteins.

Functions

The function of MHC molecules is to bind peptide fragments derived from pathogens and display them on the cell surface for recognition by the appropriate T cells. The consequences are almost always deleterious to the pathogen—virus-infected cells are killed, macrophages are activated to kill bacteria living in their intracellular vesicles, and B cells are activated to produce antibodies that eliminate or neutralize extracellular pathogens. Thus, there is strong selective pressure in favor of any pathogen that has mutated in such a way that it escapes presentation by an MHC molecule.

Two separate properties of the MHC make it difficult for pathogens to evade immune responses in this way. First, the MHC is polygenic: it contains several different MHC class I and MHC class II genes, so that every individual possesses a set of MHC molecules with different ranges of peptide-binding specificities. Second, the MHC is highly polymorphic; that is, there are multiple variants of each gene within the population as a whole. The MHC genes are, in fact, the most polymorphic genes known. In this section, we will describe the organization of the genes in the MHC and discuss how the variation in MHC molecules arises. We will also see how the effect of polygeny and polymorphism on the range of peptides that can be bound contributes to the ability of the immune system to respond to the multitude of different and rapidly evolving pathogens.

HYPERSENSITIVITY REACTIONS

Hypersensitivity (also called hypersensitivity reaction or intolerance) refers to undesirable reactions produced by the normal immune system, including allergies and autoimmunity. They are usually referred to as an over-reaction of the immune system and these reactions may be damaging and uncomfortable. This is an immunologic term and is not to be confused with the psychiatric term of being hypersensitive which implies to an individual who may be overly sensitive to physical (ie sound, touch, light, etc.) and/or emotional stimuli. Although there is a relation between the two - studies have shown that those individuals that have ADHD (a psychiatric disorder) are more likely to have hypersensitivity reactions such as allergies, asthma, eczema than those who do not have ADHD.

Types of hypersensitivity reactions

Hypersensitivity reactions can be classified into four types.

Type I: IgE mediated immediate reaction

Type II: Antibody-mediated cytotoxic reaction (IgG or IgM antibodies)

Type III: Immune complex-mediated reaction

Type IV: Cell-mediated, delayed hypersensitivity reaction

The first three types are considered immediate hypersensitivity reactions because they occur within 24 hours. The fourth type is considered a delayed hypersensitivity reaction because it usually occurs more than 12 hours after exposure to the allergen, with a maximal reaction time between 48 and 72 hours.

Type I hypersensitivity occurs as a result of exposure to an antigen. The response to the antigen occurs in two stages: the sensitization and the effect stage. In the "sensitization" stage, the host experiences an asymptomatic contact with the antigen. Subsequently, in the "effect" period, the pre-sensitized host is re-introduced to the antigen, which then leads to a type I anaphylactic or atopic immune response.

Type II hypersensitivity reaction refers to an antibody-mediated immune reaction in which antibodies (IgG or IgM) are directed against cellular or extracellular matrix antigens with the resultant cellular destruction, functional loss, or damage to tissues.

In type III hypersensitivity reaction, an abnormal immune response is mediated by the formation of antigen-antibody aggregates called "immune complexes". They can precipitate in various tissues such as skin, joints, vessels, or glomeruli, and trigger the classical complement pathway. Complement

activation leads to the recruitment of inflammatory cells (monocytes and neutrophils) that release lysosomal enzymes and free radicals at the site of immune complexes, causing tissue damage. The most common diseases involving a type III hypersensitivity reaction are serum sickness, post-streptococcal glomerulonephritis, systemic lupus erythematosus, farmers' lung (hypersensitivity pneumonitis), and rheumatoid arthritis.

Type IV hypersensitivity reactions are, to some extent, normal physiological events that help fight infections, and dysfunction in this system can predispose to multiple opportunistic infections. Adverse events can also occur due to these reactions when an undesirable interaction between the immune system and an allergen happens.

IMMUNE STIMULATION AND IMMUNOSUPRESSION

Immune stimulation refers to the stimulation of the immune system by an external source. The stimulation can confer a protective effect against microorganisms . As well, immune stimulation shows promise as a means of obtaining an immune response to conditions such as cancer. Immunostimulants, also known as immunostimulators, are substances (drugs and nutrients) that stimulate the immune system by inducing activation or increasing activity of any of its components. One notable example is the granulocyte macrophage colony-stimulating factor.

There are two main categories of immunostimulants.

Specific immunostimulants provide antigenic specificity in immune response, such as vaccines or any antigen.

Non-specific immunostimulants act irrespective of antigenic specificity to augment immune response of other antigen or stimulate components of the immune system without antigenic specificity, such as adjuvants and non-specific immunostimulators.

Immunosuppressants are drugs or medicines that lower the body's ability to reject a transplanted organ. Another term for these drugs is anti-rejection drugs.Immunosuppressants stop your immune system from damaging healthy cells and tissues. People with organ transplants and stem cell transplants take these medicines to prevent transplant rejections. The drugs also treat autoimmune disease symptoms. Immunosuppressants are powerful drugs that require careful monitoring to avoid problems.

VACCINES

Vaccines are substances administered to generate a protective immune response. They can be live attenuated or killed. Toxoids are inactivated bacterial toxins. They retain the ability to stimulate the formation of antitoxins, which are antibodies directed against the bacterial toxin.Vaccines can be divided into a number of different types, but ultimately work on the same principle. This is to stimulate the immune response to recognise a pathogen (a disease-causing organism) or part of a pathogen. Once the immune system has been trained to recognise this, if the body is later exposed to the pathogen, it will be removed from the body. Specifically, the immune system recognises foreign 'antigens', parts of the pathogen on the surface or inside the pathogen that are not normally found in the body.

Whole Pathogen Vaccines

The oldest and most well-known method of vaccination is to use the whole disease-causing pathogen in a vaccine to produce an immune response similar to that seen during natural infection. Using the pathogen in its natural state would cause active disease and could potentially be dangerous to the individual receiving it and risk the disease spreading to others. To avoid this, modern vaccines use pathogens that have been altered.

Live attenuated Vaccines

Live attenuated vaccines contain whole bacteria or viruses which have been "weakened"(attenuated) so that they create a protective immune response but do not cause disease in healthy people. For most modern vaccines this "weakening" is achieved through genetic modification of the pathogen either as a naturally occurring phenomenon or as a modification specifically introduced by scientists. Live vaccines tend to create a strong and lasting immune response and include some of our best vaccines. However, live vaccines may not suitable for people whose immune system doesn't work, either due to drug treatment or underlying illness. This is because the weakened viruses or bacteria could in some cases multiply too much and might cause disease in these people.

Inactivated Vaccines

Inactivated vaccines contain whole bacteria or viruses which have been killed or have been altered, so that they cannot replicate. Because inactivated vaccines do not contain any live bacteria or viruses, they cannot cause the diseases against which they protect, even in people with severely weakened immune systems. However, inactivated vaccines do not always create such a strong or long-lasting immune response as live attenuated vaccines.

Subunit Vaccines

Most of the vaccines in the UK schedule are subunit vaccines which do not contain any whole bacteria or viruses at all. Instead, these vaccines typically contain one or more specific antigens (or "flags") from the surface of the pathogen. The advantage of subunit vaccines over whole pathogen vaccines is that the immune response can focus on recognising a small number of antigen targets ("flags"). Subunit vaccines do not always create such a strong or long-lasting immune response as live attenuated vaccines. They usually require repeated doses initially and subsequent booster doses in subsequent years. Adjuvants are often added to subunit vaccines. These are substances which help to strengthen and lengthen the immune response to the vaccine. As a result, common local reactions (such as a sore arm) may be more noticeable and frequent with these types of vaccines.

Recombinant Protein Vaccines

Recombinant vaccines are made using bacterial or yeast cells to manufacture the vaccine. A small piece of DNA is taken from the virus or bacterium against which we want to protect and inserted into the manufacturing cells. For example, to make the hepatitis B vaccine, part of the DNA from the hepatitis B virus is inserted into the DNA of yeast cells. These yeast cells are then able to produce one of the surface proteins from the hepatitis B virus, and this is purified and used as the active ingredient in the vaccine. Most of the vaccines in the UK schedule are subunit vaccines which do not contain any whole bacteria or viruses at all. ('Acellular' means 'not containing any whole cells'.) Instead these kind of vaccines contain polysaccharides (sugars) or proteins from the surface of bacteria or viruses. These polysaccharides or proteins are the parts that our immune system recognises as 'foreign', and they are referred to as antigens. Even though the vaccine might only contain a few out of the thousands of proteins in a bacterium, they are enough in themselves to trigger an immune response which can protect against the disease.

Toxoid Vaccines

Some bacteria release toxins (poisonous proteins) when they attack the body, and it is the toxins rather than the bacteria itself that we want to be protected against. The immune system recognises these toxins in the same way that it recognises other antigens on the surface of the bacteria, and is able to mount an immune response to them. Some vaccines are made with inactivated versions of these toxins. They are called 'toxoids' because they look like toxins but are not poisonous. They trigger a strong immune response.

Conjugate Vaccines

'Conjugate' means 'connected' or 'joined'. With some bacteria, to get protection from a vaccine you need to train the immune system to respond to polysaccharides (complex sugars on the surface of bacteria) rather than proteins. But in the early days of polysaccharide vaccines it was found that they did not work well in babies and young children. Researchers discovered that they worked much better if the polysaccharide was attached (conjugated) to something else that creates a strong immune response. In most conjugate vaccines, the polysaccharide is attached to diphtheria or tetanus toxoid protein (see 'Toxoid vaccines' above). The immune system recognises these proteins very easily and this helps to generate a stronger immune response to the polysaccharide.

RNA vaccines

RNA vaccines use mRNA (messenger RNA) inside a lipid (fat) membrane. This fatty cover both protects the mRNA when it first enters the body, and also helps it to get inside cells by fusing with the cell membrane. Once the mRNA is inside the cell, machinery inside the cell translates it into the antigen protein. This mRNA typically lasts a few days, but in that time sufficient antigen is made to stimulate an immune response. It is then naturally broken down and removed by the body. RNA vaccines are not capable of combining with the human genetic code (DNA).

There are two RNA vaccines authorised for emergency use in the UK at present. The Pfizer BioNTech and the Moderna COVID-19 vaccines are both RNA vaccines.

DNA vaccines

DNA is more stable than mRNA so doesn't require the same initial protection. DNA vaccines are typically administered along with a technique called electroporation. This uses low level electronic waves to allow the bodies' cells to take up the DNA vaccine. DNA must be translated to mRNA within the cell nucleus before it can subsequently be translated to protein antigens which stimulate an immune response. There are currently no licenced DNA vaccines, but there are many in development.

HYBRIDOMA TECHNOLOGY

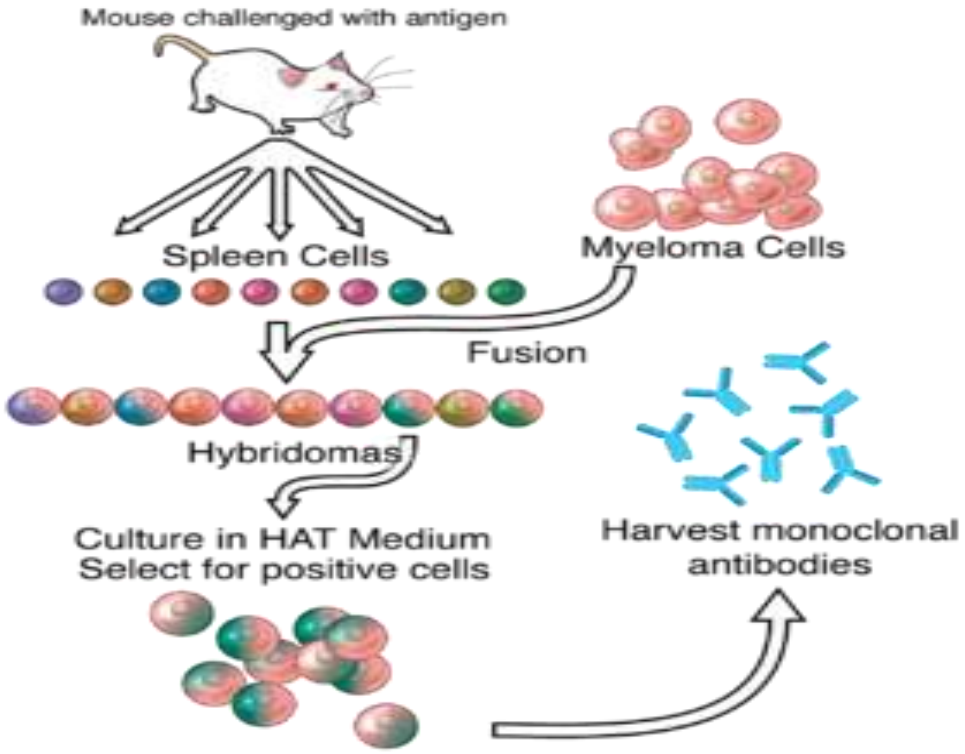
Hybridoma technology is a method for producing large numbers of identical antibodies (also called monoclonal antibodies). This process starts by injecting a mouse (or other mammal) with an antigen that provokes an immune response. A type of white blood cell, the B cell, produces antibodies that bind to the injected antigen. These antibody producing B-cells are then harvested from the mouse and, in turn, fused with immortal B cell cancer cells, a myeloma,[clarification needed] to produce a hybrid cell line called a hybridoma, which has both the antibody-producing ability of the B-cell and the longevity and reproductivity of the myeloma. The hybridomas can be grown in culture, each culture starting with one viable hybridoma cell, producing cultures each of which consists of genetically identical hybridomas which produce one antibody per culture (monoclonal) rather than mixtures of different antibodies (polyclonal). The myeloma cell line that is used in this process is selected for its ability to grow in tissue culture and for an absence of antibody synthesis. In contrast to polyclonal antibodies, which are mixtures of many different antibody molecules, the monoclonal antibodies produced by each hybridoma line are all chemically identical.

The production of monoclonal antibodies was invented by César Milstein and Georges J. F. Köhler in 1975. They shared the Nobel Prize of 1984 for Medicine and Physiology with NielsKaj Jerne, who made other contributions to immunology. The term hybridoma was coined by Leonard Herzenberg during his sabbatical in César Milstein's laboratory in 1976–1977.

Applications of Hybridoma Technology

The use of monoclonal antibodies is numerous and includes the prevention, diagnosis, and treatment of disease. For example, monoclonal antibodies can distinguish subsets of B cells and T cells, which is helpful in identifying different types of leukaemias. In addition, specific monoclonal antibodies have been used to define cell surface markers on white blood cells and other cell types. This led to the cluster of differentiation series of markers. These are often referred to as CD markers and define several hundred different cell surface components of cells, each specified by binding of a particular monoclonal antibody. Such antibodies are extremely useful for fluorescence-activated cell sorting, the specific isolation of particular types of cells. In diagnostic histopathology with the help of monoclonal antibodies, tissues and organs can be classified based on their expression of certain defined markers, which reflect tissue or cellular genesis. Prostate specific antigen, placental alkaline phosphatase, human

chorionic gonadotrophin, α-fetoprotein and others are organ-associated antigens and the production of monoclonal antibodies against these antigens helps in determining the nature of a primary tumor.



Monoclonal antibodies are especially useful in distinguishing morphologically similar lesions, like pleural and peritoneal mesothelioma, adenocarcinoma, and in the determination of the organ or tissue origin of undifferentiated metastases. Selected monoclonal antibodies help in the detection of occult metastases (cancer of unknown primary origin) by immuno-cytological analysis of bone marrow, other tissue aspirates, as well as lymph nodes and other tissues and can have increased sensitivity over normal histopathological staining.

Immuno-cytochemistry using tumor-associated monoclonal antibodies has led to an improved ability to detect occult breast cancer cells in bone marrow aspirates and peripheral blood, further development of this method is necessary before it can be used routinely.

Another application of immuno-cytochemical staining is for the detection of two antigens in the same smear. Double staining with light chain antibodies and with T and B cell markers can indicate the neoplastic origin of a lymphoma.

BLOOD PRODUCT AND PLASMA SUBSITUTES

Whole Human Blood

Blood should be collected only by a licensed blood bank. Blood should be drawn from the donor by a qualified physician or under his/her supervision by assistants trained in the procedure. A physician should be present on the premises when the blood is being collected. Blood should be collected by single venepuncture and flow of blood should be continuous. The blood donor area should be clean, congenial, comfortable and conveniently approachable. As the temperatures vary widely in different seasons, it is mandatory to have air-conditioned rooms to make the donor comfortable and to minimise chances of contamination.

Method

A strict standardised procedure should be in use to achieve surgical cleanliness for preparing venepuncture site to provide maximum possible assurance of sterile product.

Equipment

The blood bags for collection of blood should be sterile, pyrogen free and disposable, with a closed system of collection as per standards provided by ISO / ISI. Multiple interconnected plastic bags should be used for blood component preparation (closed system). Venting of any container should be done under laminar airflow bench and such container should be used within 24 hours. To avoid venting in case of paediatric use, multiple inter-connected closed containers should be used.

Anticoagulant solutions

The anticoagulant solution should be sterile and pyrogen free. One of the following solutions should be used in the indicated volumes.

1) Citrate-Phosphate-Dextrose (CPD) Solution. 14 ml solution is required for 100 ml of blood.

2) Citrate-Phosphate-Dextrose-Adenine (CPD1) solution. 14 ml solution is required for 100 ml of blood. 3 100 ml SAM/ADSOL or any approved additive solution containing saline adenine and glucose (or with mannitol) is added to packed cells after separation of plasma for storage.

Volume of blood

Volume of blood collected should be proportionate to the volume of anti-coagulant, with ±10% variation and should not exceed 10 ml/kg body weight limited to a volume of 500 ml. Units of blood where volume collected is out of the permitted limits should not be used for transfusion. No attempt should be made to collect blood from such donor during the same session.

Samples for laboratory tests

The blood samples in the pilot tubes (clotted and anticoagulated) should be collected at the time of collection of blood by the same person who collects blood. They should be marked before collection to be identified with the unit of blood. The integral donor tubing of plastic bag should be filled with anticoagulated blood and sealed in such a manner that it will be available with segment numbers for traceability for subsequent compatibility tests.

Identification

Each container of blood/blood components /pilot tubes should be identified by a numeric or alpha numeric at the time of collection of blood, so that it can be traced back to the donor and also to the recipient. The segment number printed on the integral donor tubing should be recorded.

Storage

Immediately after collection, the blood should be placed at 40C to 60C ± 2®C.

DRIED HUMAN PLASMA

Preparation

Plasma is a Yellow coloured fluid and consists of 55% blood. This is used for Plasma transfusion. The preparation of dried human plasma starts with centrifugation of 400ml Whole Human blood collected from an eligible donor and packed in sterile, Bacteria proof container, at 18 degree Celsius to separate the serum. This is followed by Primary drying in chamber where the horizontally placed bottles are dried at 50 degree Celsius. Primary drying takes about 2 weeks. This is followed by Secondary drying in a Vacuum or in a desiccators for one day. After completion of this drying the residual moisture should be 0.5%.

Storage

The dried human Plasma should be stored at 28 degree Celsius,protected from moisture and Sunlight, where it is stable for 5 years.

Plasma substitutes

Dextran 70 and polygeline are macromolecular substances which are metabolized slowly; they may be used to expand and maintain blood volume in shock arising from conditions such as burns or septicaemia. They are rarely needed when shock is due to sodium and water depletion as, in these circumstances, the shock responds to water and electrolyte repletion.

Plasma substitutes should not be used to maintain plasma volume in conditions such as burns or peritonitis where there is loss of plasma protein, water and electrolytes over periods of several days. In these situations, plasma or plasma protein fractions containing large amounts of albumin should be given.

Plasma substitutes may be used as an immediate short-term measure to treat massive haemorrhage until blood is available, but large volumes of some plasma substitutes can increase the risk of bleeding by depleting coagulation factors. Dextran may interfere with blood group cross-matching or biochemical measurements and these should be carried out before the infusion is started.

Dextran 70

Dextran is a representative plasma substitute. Various preparations can serve as alternatives

Infusion (Solution for infusion), dextran 70 6% in glucose intravenous infusion 5% or sodium chloride intravenous infusion 0.9%

Uses:

Short-term blood volume expansion

Contraindications:

Severe congestive heart failure, renal failure; bleeding disorders such as thrombocytopenia and hypofibrinogenaemia

Precautions:

cardiac disease or renal impairment; monitor urine output; avoid haematocrit falling below 25–30%; where possible, monitor central venous pressure; can interfere with blood group cross-matching and biochemical tests—take samples before start of infusion; monitor for hypersensitivity reactions; pregnancy

Dosage:

Short-term blood volume expansion, by rapid intravenous infusion , adult 500–1000 ml initially, followed by 500 ml if necessary; total dosage should not exceed 20 ml/kg during the initial 24 hours; if required 10 ml/kg daily may be given for a further 2 days (treatment should not continue for longer than 3 days); child total dosage should not exceed 20 ml/kg

Adverse effects:

Hypersensitivity reactions including fever, nasal congestion, joint pains, urticaria, hypotension, bronchospasm—rarely severe anaphylactoid reactions; transient increase in bleeding time

Polygeline

Polygeline is a representative partially degraded gelatin. Various preparations can serve as alternatives

Infusion (Solution for infusion), polygeline 3.5% with electrolytes, 500-ml bottle

Uses: Correction of low blood volume

Contraindications: severe congestive heart failure; renal failure

Precautions: Blood samples for cross-matching should be taken before infusion; haemorrhagicdiasthesis; congestive heart failure, renal impairment, hypertension, oesophagealvarices; interactions:

Dosage: Correction of low blood volume, by intravenous infusion , initially 500–1000 ml of a 3.5% solution

Adverse effects: hypersensitivity reactions including urticaria—rarely severe anaphylactoid reactions; transient increase in bleeding time

Plasma fractions for specific use

Factor VIII is essential for blood clotting and the maintenance of effective haemostasis; von Willebrand factor is a mediator in platelet aggregation and also acts as a carrier for factor VIII. Blood coagulation factors VII, IX, and X are essential for the conversion of factor II (prothrombin) to thrombin. Deficiency in any of these factors results in haemophilia. Bleeding episodes in haemophilia require prompt treatment with replacement therapy. Factor VIII , used for the treatment of haemophilia A, is a sterile freeze-dried powder containing the blood coagulation factor VIII fraction prepared from pooled human venous plasma. Standard factor VIII preparations also contain von Willebrand factor and may be used to treat von Willebrand disease. Highly purified preparations, including recombinant factor VIII, are available; they are indicated for the treatment of haemophiliaA but do not contain sufficient von Willebrand factor for use in the management of von Willebrand disease.

Factor IX Complex is a sterile freeze-dried concentrate of blood coagulation factors II, VII, IX and X derived from fresh venous plasma. Factor IX complex which is used for the treatment of haemophilia B may also be used for the treatment of bleeding due to deficencies of factor II, VII, and X. High purity preparations of factor IX which do not contain clinically effective amounts of factor II, VII, and X are available. A recombinant factor IX preparation is also available.

Factor VIII concentrate

Plasma fractions should comply with the WHO Requirements for the Collection, Processing and Quality Control of Blood, Blood Components and Plasma Derivatives (Revised 1992). WHO Technical Report Series, No. 840, 1994, Annex 2

Factor VIII concentrate is a complementary preparation and a representative coagulation factor preparation. Various preparations can serve as alternatives

Infusion (Powder for solution for infusion), factor VIII 250–1500 units

Uses:

Control of haemorrhage in haemophilia A

Precautions:

intravascular haemolysis after large or frequently repeated doses in patients with blood groups A, B, or AB (less likely with high potency, highly purified concentrates) Dosage: Haemophilia A, by slow intravenous infusion , ADULT and CHILD according to patient's needs

Adverse effects: allergic reactions including chills, fever

Factor IX complex (coagulation factors II, VII, IX, X) concentrate

Plasma fractions should comply with the WHO Requirements for the Collection, Processing and Quality Control of Blood, Blood Components and Plasma Derivatives (Revised 1992). WHO Technical Report Series, No. 840, 1994, Annex 2

Factor IX complex concentrate is a complementary preparation and a representative coagulation factor preparation. Various preparations can serve as alternatives Infusion (Powder for solution for infusion), factor II, VII, IX, and X 500–1500 units

Uses: replacement therapy for factor IX deficiency in haemophilia; bleeding due to deficiencies of factors II, VII or X

Contraindications: disseminated intravascular coagulation

Precautions: risk of thrombosis (probably less risk with highly purified preparations)

Dosage: Haemophilia B, by slow intravenous infusion , ADULT and CHILD according to patient's needs and specific preparation used

Treatment of bleeding due to deficiencies in factor II, VII or X as well as IX, by slow intravenous infusion, ADULT and CHILD according to patient's needs

Adverse effects: allergic reactions including chills, fever.

IMPORTANT QUESTION

2 Marks Question

1. Define Immunity.
2. Diffrentiate between Humoral and Cellular immunity.
3. What are Hypersensitivity reactions?
4. Define Immuboglobulins.
5. Define Vacines, Toxoids, Antitoxins and Serum immune blood derivatives.
6. What are Plasma Subsitutes?
7. What is Hybridoma technology?
8. What are Immuno suppressions?
9. Define Immunostimulants.
10. Enlist blood components.
11. What are Anticoagulants?
12. Define Hartman Solution.
13. Classify Antigens.
14. Define Immunological Tolerance.

5 Marks Questions

1. Give method of preparation of bacterial vaccines, toxoids, viral vaccines and antitoxins.
2. Explain production, purification and applications of Hybridoma Technology.
3. Describe and explain different types of Immunity.

10 Marks Questions

1. Explain the structure of immunoglobulins with its applications.
2. Explain structure and functions of MHC.
3. Write a note on Immune Suppressions.
4. Explain Plasma Substitutes with examples