Pharmacognosy -3
PHG 413

Prof. Dr. Amani S. Awaad
Professor of Pharmacognosy
Pharmacognosy Department,
College of Pharmacy Salman Bin Abdulaziz
University,
Al-Kharj. KSA.
Email: amaniawaad@hotmail.com
Welcome Back
Dears

Biologics
You should be able to know:

• **What is Antigens**
• **Diagnostic Antigens**
• **What are Toxins & Toxoids**
• **What are Biologics Related To Human Blood**
Antigens

Diagnostic Antigens

A number of antigen-containing preparations are employed as diagnostic aids to determine whether an individual has developed hypersensitivity to certain types of organisms. Small quantities of the diagnostic preparations are usually injected intradermally, and the developing reaction is usually read at 48 hours, although observations at 24 hours and at 72 hours are often helpful.

The usual type of positive response is a localized, well-defined wheal accompanied by erythema.

Antigen-containing diagnostic preparations that are commonly available include the tuberculins, histoplasmin, diphtheria toxin, and mumps skin test antigen.
Antigens

1. Tuberculins

Tuberculins are preparations obtained in a number of ways from the human and bovine strains of the tubercle bacillus.

The active substance of the tuberculin, which is apparently an albuminous derivative insoluble in alcohol, is elaborated by the organisms during their multiplication.

In both human and veterinary practice, tuberculin may be applied as a diagnostic agent to determine whether the person or animal is or has been infected with Mycobacterium.

Use And Dose. Old tuberculin is a diagnostic immunologic aid in testing patients suspected of having tuberculosis.

The usual dose of old tuberculin is 5 tuberculin units, intradermally. A positive test consists of an area of inflammation and definitely palpable induration or edema at least 5 mm in diameter.

It appears in 6 to 8 hours, reaches its maximum in 24 to 48 hours, and usually disappears in 6 to 10 days.

PRESCRIPTION PRODUCTS. Tuberculin, Old, Mono-Vacc Test®; Tuberculin, Old, Tine Test®
Antigens

Diagnostic Antigens

2. Histoplasmin

Histoplasmin is a sterile, standardized liquid concentrate of the soluble growth products developed by the fungus *Histoplasma capsulatum*. It is employed in skin tests to determine the presence of histoplasmosis, a disease that affects the reticuloendothelial system and usually results in enlargement of the liver, spleen, and lymph nodes.

Use And Dose. Histoplasmin is a diagnostic aid (dermal). The usual dose is 0.1 ml of a standardized sterile culture filtrate injected intradermally into the flexor surface of the forearm.

PRESCRIPTION PRODUCTS. Histoplasmin, Diluted®; Histolyn-CYL®
**3. Diphtheria Toxin**

*Diphtheria toxin or diphtheria toxin for the Schick test is a sterile solution of the diluted, standardized toxic products of growth of the diphtheria bacillus, *Corynebacterium diphtheriae*.  
*The test method involves the intradermal injection of 0.1 ml of the control solution into the flexor surface of the left forearm and an injection of 0.1 ml of the toxin into the right forearm.

*A positive reaction results in a circumscribed area of redness measuring 1 cm or more in diameter appearing in 24 to 36 hours on the right arm and reaching its greatest intensity on the 4th or 5th day. No reaction occurs on the control arm.*
Antigens

Diagnostic Antigens

4. Mumps Skin Test Antigen

Mumps skin test antigen is a sterile suspension of formaldehyde-inactivated mumps virus prepared from the extra-embryonic fluids of the mumps virus-infected chicken embryo. The mumps intradermal skin test is utilized to define an individual's previous experience with mumps virus.

Use And Dose. Mumps skin test antigen is a diagnostic aid, and the usual dose, intradermally, is 0.1 ml.
2-Acquired immunity

B. Active immunity

II-toxoid
Toxins & Toxoids

- Toxins are bacterial waste products that are considered poisonous to the animal body. Notwithstanding, they act as antigens because of their power to stimulate certain cells of the body to produce antibodies called antitoxins.

- In practice, toxins are modified to inactivate the toxicophore group of the molecule (The chemical group of a toxin that produces the poisonous effect), leaving the antigenic group unchanged.

- When toxins are excreted from the bacterial cells producing them and are dissolved in the surrounding culture medium, they are referred to as exotoxins. In other cases, when they are retained within the bacterial body, they are called endotoxins.

- The source of "the most poisonous poison" is Clostridium botulinum, a microorganism generally unable to grow in the body of a warm-blooded animal but capable of causing death if its exotoxins are ingested.

Modification of Toxin to Toxoid

- Toxin
- chemical modification
- Toxoid

Tetanus bacteria emitting toxin
Tetanus toxin
Tetanus toxoid
Antitoxins

Antitoxins are prepared from the blood of animals, usually horses, that have been immunized by repeated injections of specific bacterial exotoxins. The toxin, in constantly increasing doses, induces the formation of antitoxin in the blood of the injected animal. After tests have been conducted to determine the antitoxin titer of the serum, the animal is bled, the clot is permitted to form, and the clear supernatant serum is separated for processing.

1. Diphtheria Antitoxin

Diphtheria antitoxin is a sterile, nonpyrogenic solution of the refined and concentrated proteins, chiefly globulins, containing antitoxic antibodies obtained from the blood serum or plasma of healthy horses that have been immunized against diphtheria toxin or toxoid.

Uses And Dose
The usual prophylactic dose, intramuscularly or intravenously, is 1000 to 10,000 units; the therapeutic dose is 20,000 to 120,000 units.
**Antitoxins**

**2. Tetanus Antitoxin**

Tetanus antitoxin is a sterile, nonpyrogenic solution of the refined and concentrated proteins, containing antitoxic antibodies obtained from the blood serum or plasma of healthy horses that have been immunized against tetanus toxin or toxoid.

**Uses And Dose.** Tetanus antitoxin is employed in the treatment and prophylaxis of tetanus. It creates passive immunity to tetanus. Like diphtheria antitoxin, it is a valuable therapeutic agent when used early in the disease. The usual prophylactic dose, intramuscularly or subcutaneously, is 1500 to 5000 units; the therapeutic dose is 50,000 to 100,000 units or more with at least part of the dose given intravenously.

**3. Botulism Antitoxin**

Botulism antitoxin is a sterile, nonpyrogenic solution of the refined and concentrated antitoxic antibodies, chiefly globulins, obtained from the blood serum or plasma of healthy horses that have been immunized against the toxins produced by both the type A and type B and/or type E strains of Clostridium botulinum. A multivalent antitoxin is advantageous because the prescribing physician is not required to wait for a determination of the type of the causative organism.

**Use And Dose.** Botulism antitoxin is classed as a passive immunizing agent to be used in the treatment of botulism. The usual dose is, intravenously, 20,000 units, repeated at 2- to 4-hour intervals, as necessary.
Venoms and Antivenins

Venoms are poisonous excretions produced by animals; they can be compared with the toxic waste products (exotoxins) of bacteria. Poisonous snakebites often cause severe pain and can lead to tissue necrosis, amputation, and death. The venom of the rattlesnake is a complex mixture, chiefly of proteins, many of which have enzymatic activity and a nonenzymatic neurotoxic fraction.

Similarly, the venoms of the tarantula, scorpion, black widow spider, honeybee, wasp, and other arthropods produce various deleterious effects, depending on the amount, time of year, and other conditions. Chemical examinations of the poisons of toads have revealed that both skin and glandular secretions possess toxic substances called bufotoxins.
Antiserums

Antiserums are biologics prepared in a manner similar to that for antitoxins and antivenins except that bacteria or viruses are used to stimulate the production of specific antibodies in a healthy animal such as the horse. Viral or bacterial cells, as found in vaccines, serve as the antigenic substances; these are introduced into the animal body in gradually increasing doses and are continued until the proper antibody titer of the blood serum is achieved.

The destruction of the injected cells by phagocytes liberates antigenic materials with the subsequent development of corresponding antibodies. Antiserum against rabies is an example of this type of immunizing agent. The therapeutic effectiveness of anti-serums is based on their production of artificial passive immunity. Thus, each anti-serum is a specific biologic employed to provide a supply of ready-made antibodies to combat the disease.

Antiserum against rabies is useful in modern therapy, but many antiserums against bacteria that were formerly employed in therapy have been replaced by antibiotics.
**Immune Globulins**

**Immune globulins** are immunizing biologics that contain specific antibodies derived from the blood of humans who have survived an attack of a specific disease or who have been immunized in some other manner. Chances of sensitization are less with human serum derivatives than with immune sera from animal sources.

1. **Immune Globulin**

*Immune globulin, immune serum globulin (human), immune globulin intramuscular, or gamma globulin* is a sterile, nonpyrogenic solution of globulins and contains many antibodies normally present in adult human blood. Each lot of immune globulin is prepared by pooling approximately equal amounts of material (source blood, plasma, serum, or placentas) from at least 1000 individuals. Immune globulin has some prophylactic value in chicken pox, hepatitis A, rubella, and other diseases.

**Use And Dose.** Immune globulin is a passive immunizing agent. The dosage is based on body weight and varies with the intended use. The usual intramuscular dose is 0.2 ml per kg for measles prophylaxis and 0.02 ml per kg for prophylaxis against hepatitis A. It is also given to treat gamma globulin deficiency for the prevention of recurrent infections. **Prescription Products.** Gamastan®, Immuglobin®, Gammar®

*Immune globulin intravenous (IGIV) provides immediate antibody levels, whereas intramuscular administration involves a 2- to 5-day delay before adequate serum levels are attained. It is used in the treatment of immunodeficiency syndrome, especially in patients who require an immediate increase in immunoglobulin blood levels. The usual dose is 100 to 200 mg per kg, administered once a month by intravenous infusion.**PRESCRIPTION PRODUCTS. Gamimune®, Sandoglobulin®
Immune Globulins

2. Pertussis Immune Globulin

*Pertussis immune globulin or pertussis immune globulin (human) is a sterile, nonpyrogenic solution of globulins derived from the blood plasma of adult human donors who have previously been immunized with pertussis vaccine.

Use And Dose. Pertussis immune globulin is used in the prophylaxis and treatment of pertussis. The usual intramuscular prophylactic dose is 1.25 to 2.5 ml, repeated in 1 or 2 weeks as necessary. The therapeutic dose range is the same, but administration is repeated in 1 or 2 days, depending on the clinical response. Prescription Product. Hypertussis®

3. Tetanus Immune Globulin

Tetanus immune globulin or tetanus immune globulin (human) is a sterile, nonpyrogenic solution of globulins derived from the blood plasma of adult human donors who have been immunized with tetanus toxoid. This immune globulin is especially useful for passive immunization against tetanus in individuals with wounds that may have been contaminated with tetanus microorganisms.

Use And Dose. Tetanus immune globulin is employed in the prophylaxis and treatment of tetanus. The usual intramuscular prophylactic dose is 250 units as a single injection. The therapeutic dose range is 3000 to 6000 units. Prescription Products. Homo-Tet®, Hu-Tet®, Hyper-Tet®
Biologics Related To Human Blood

*A number of human blood products that have no immunizing property or function are considered biologics.*

*These products include whole blood, red blood cells, and various blood fractions.*

Such blood derivatives have specialized application.

*Recent years have been characterized by an increasing sophistication in the availability and use of blood products.*

1. Whole Blood

*Whole blood or whole blood (human) is blood that has been drawn from a selected donor under rigid aseptic conditions.*

*It contains citrate ion or heparin as an anticoagulant. It should be stored at a constant temperature of between 1 and 6°C.*

*It is used as a blood replenisher. It is administered intravenously, usually in a volume of 1 unit or 500 ml, as necessary.*

The expiration date is 21 days after the date of bleeding if the anticoagulant is citrate dextrose solution or citrate phosphate dextrose solution, 35 days if the anticoagulant is citrate phosphate dextrose adenine solution, and 48 hours if the anticoagulant is heparin.
Biologics Related To Human Blood

2. Red Blood Cells

Red blood cells is whole blood from which plasma has been removed. Red blood cells may be prepared at any time during the dating period of the whole blood from which it is derived by centrifugation or undisturbed sedimentation. It contains a portion of the plasma sufficient to ensure optimal cell preservation or contains a cryomphylactic substance if it is used for extended manufacturers' storage at -65° C or colder.

The expiration date for frozen red blood cells is not later than that of the whole human blood from which it was derived. The expiration date for frozen red blood cells, stored at -65° C or colder, is not later than 3 years after the date of collection of the source blood. It is useful in cases of anemia, when the additional volume of plasma is undesirable.
3. Albumin Human

*Human serum albumin is the most abundant protein in human blood plasma.
*It is a sterile, nonpyrogenic preparation of serum albumin obtained by fractionating material (source blood, plasma, serum, or placentas) from healthy, human donors.
*This material is then tested for the absence of hepatitis B surface antigen.

Albumin is essential for maintaining the osmotic pressure needed for proper distribution of body fluids between intravascular compartments and body tissues.
Albumin human is a blood-volume supporter. The usual dose, intravenously, is a volume equivalent to 25 g of albumin.

Prescription Products. Albutein®, Buminate®, Albuminar®, Plasbumin
Biologics Related To Human Blood

4. Plasma Protein Fraction

Plasma protein fraction or plasma protein fraction (human) is a sterile solution of selected proteins derived by fractionating material (source blood, plasma, or serum) from healthy human donors and testing for the absence of hepatitis B surface antigen. It contains not less than 4.5 g and not more than 5.5 g of protein per 100 ml, of which not less than 83% is albumin, and not more than 17% is alpha and beta globulins.

This substance is a human blood fraction that is indicated for restoration of blood volume when the patient is in a state of shock caused by burns, crushing injuries, and any other causes, in which loss of plasma fluids, not loss of red blood cells, is predominant.

USE AND DOSE. Plasma protein fraction is a blood-volume supporter. The usual dose is 250 to 500 ml by intravenous infusion at a rate not exceeding 10 ml per minute.

Prescription Products. Plasmanate®, Protenate®, Plasma-Plex®, Plasmatein®
thanks