PACKAGING OF PARENTERAL PRODUCTS

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- Parenteral Preparations and other sterile products must be packaged in a way that :

  - Maintains product sterility until the time of use .

  - Prevents contamination of contents during opening .

A . Types of containers

1 . **Ampules** , the oldest type of Parenteral product containers, are made entirely of **glass** .

- lntended for **single use only**, amplues are opened by breaking the glass at a score line on the neck.

- **Disadvantage**s . Because glass particles may become dislodged during ampule opening, the product must be filtered before it administered.

A . Types of containers

- 2. **Vials** are glass or plastic containers closed with a rubber stopper and sealed with an aluminum crimp.
  - **a.** *Vials have several* ***advantages*** *over ampoules.*
    - Vials can be designed to **hold multiple doses** (if prepared with a bacteriostatic agent).
    - The drug product is **easier to remove from** vials than from ampules.
    - Vials **eliminate the risk of glass particle contamination** during opening.

A . Types of containers

- **b.** *However,Vials also have certain* ***disadvantages***

  - The rubber stopper can become **cored**, causing a small bit of rubber to enter the solution.

  - Multiple withdrawals (as with multiple-dose vials) can result in microbial contamination.

A . Types of containers

- **c.** *Some drugs that are unstable in solution are packaged in vials un-reconstituted and must be* ***reconstituted*** *with a diluents before use. Sterile water or sterile sodium chloride for injection are the most commonly used drug diluents.*

  - **(1)** To accelerate the dissolution rate and permit rapid reconstitution, many **powders are lyophilized** (freeze dried).

A . Types of containers

- **(2)** Some of these drugs come in vials that contain a **double chamber.**

  (a) The top chamber, containing sterile water for injection, is spread from the unreconstituted drug by a rubber closure.

  (b) To dislodge the inner closure and mix the contents of the compartments, External pressure is applied to the outer rubber closure. This system eliminates the need to enter the Vial twice, thereby reducing the risk of microbial contamination.

A . Types of containers

- **3.** Some drugs come in vials that may be attached to an diluents containing bag for reconstitution and administration (**ADD-Vantage** by abbott) .
- Premeasured drug and diluents may also be stored in separate compartments within a delivery system then combined at the point of use. (Duplex by B. braun).
  - **a.** The ADD-Vantage Vial is screwed into the top of an ADD-Vantage diluent bag, and the rubber diaphragm is dislodged from the vial, allowing the diluent solution to dissolve the drug.
  - **b.** The reconstituted ADD-Vantage vial and IV bag are ready for administration when hung.

A . Types of containers

- **c.** The Duplex system has two-compartments where a seal is broken and drug and diluents are mixed to form a solution. The reconstituted drug is ready for patient administration .

A . Types of containers

- **4. Prefilled syringes** and **cartridges** are designed for maximum convenience .

a. Prefilled syringes. Drugs administration in an **emergency** (e.g., atropine, epinephrine) are available for immediate injection when packaged in prefilled syringes.

A . Types of containers

- **b. Prefilled cartridges**
  - Are ready-to-use parenteral packages that offer improved sterility and accuracy.
  - They consist of a plastic cartridges holder and prefilled medication cartridge with a needle attached.
  - The medication is premixed and premeasured
  - E.g. Enoxaparin .

A . Types of containers

5. Infusion solutions.

- Are divided into two categories**:**
  - **Small-volume parenterals** (SVPs), Those having a volume less than 100 mL.
  - **large-volume parenterals** (LVPs), Those having a volume of 100 mL or greater. Infusion solution are used for the intermittent or continuous infusion of fluids or drugs .

B. Packing materials.

- Materials used to package parenteral products include **glass** and **plastic** polymers.

- **1. Glass**, The original Parenteral packaging material, has superior clarity, facilitating inspection for particulate matter. Compared to plastic, **glass less frequently interacts with the preparation it contains.**

B. Packing materials.

2. **Plastic polymers** used for parenteral packages include polyvinylchloride (PVC) and polyolefin.
   - **a. PVC** is flexible and nonrigid.
   - **b. Polyolefin** is semirigid; unlike PVC, it can be stored upright.
   - **c.** Both types of plastic offer several **advantages over glass, including** durability, easier storage and disposal, reduced weight, and improved safety.

PARENTERAL ADMINISTER ROUTES.

Parental preparations may be given by a variety of administration routes.

- **A . Subcutaneous (SC or SQ)**
  - Administration refers to injection into the Subcutaneous tissue beneath the skin layers, usually of the **abdomen, arm, or thigh**.
  - Insulin is an example of a Subcutaneously administered drug.

PARENTERAL ADMINISTER ROUTES.

- **B. Intramuscular (IM)** administration means injection into **a muscle mass**. The mid-deltoid area and gluteus medius are injection sites.

- **1.** No **more than 5 mL** of a solution should be injected by this route.

- **2.** Drugs intended for prolonged or delayed absorption such as medroxyprogesterone (**Depo**-provera) and methylprednisolone (**Depo**-Medrol) commonly are administrated intramuscularly.

PARENTERAL ADMINISTER ROUTES.

- **C. Intravenous (IV)**
  - Administration is **the most important** and the most common parenteral administration route.
  - It allows an immediate therapeutic effect by delivering the drug directly into the circulation.
  - However, this route precludes recall of an inadvertent drug overdose.
  - Antibiotics, cardiac medications, and many other drugs are given intravenously.

PARENTERAL ADMINISTER ROUTES.

- **D. Intradermal (ID)**
  - Administration involves injection into the most **superficial skin layers**.
  - Because the route can be deliver only a **limited drug volume**, its use generally is restricted to skin tests and certain vaccines.

PARENTERAL ADMINISTER ROUTES.

- **E. Intra-arterial (IA)**
  - Administration is injected directly into an **artery.**
  - It delivers a high drug concentration to the target site with a little dilution by the circulation.
  - Generally this route is used only for radiopaque materials, thrombolytic agents, and some antineoplastic agents.

- **F. Intracardiac** (IC) administration is injection of a drug directly into the **heart**.

PARENTERAL ADMINISTER ROUTES.

- **G. Hypodermoclysis**
  - Refers to injection of large volume of a solution into Subcutaneous tissue to provide a continuous, abundant drug supply.
  - This route occasionally is used for antibiotic administration in children.
- **H. Intraspinal**

➢ Administration refers to injection into the **spinal column**.

➢ Local anesthetics (e.g., methyl-lidocaine, bupivacaine) are frequently administered via this route during surgical procedures.

PARENTERAL ADMINISTER ROUTES.

- **I. Intra-articular**
  - Administration means injection into **a joint space**.
  - Corticosteroids (e.g., methyl-prednisolone, hydrocortisone) use this route for the treatment of arthritis.
- **J. Intrasynovial**
  - Administration refers to injection into the **joint fluid**.

K. Intrathecal (IT)

- Administration is injection into the spinal fluid; it sometimes is used for antibiotics and cancer chemotherapy

PARENTERAL ADMINISTER ROUTES.

- **L. Epidural (ED)**
  - Administration refers to the injection of medications, usually **local anesthetics and/or narcotics** near or outside the dura mater of the central nervous system.

  - This route is frequently used during childbirth.
  - E.g. fentnyl

PARENTERAL PREPARATIONS

- **A . IV admixture**
  - These preparation consist of **one or more** sterile drug products added to an IV fluid, generally dextrose or sodium chloride solution alone or in combination.
  - IV admixtures are used for drugs intended for **continuous infusion**.
  - Drugs that may cause irritation or toxicity when given as a **rapid** direct IV injection are also prepared as IV admixture.

B. IV fluids and electrolytes

1. Fluids

- Used in the preparation and administration of parenteral products **include** sterile water and sodium chloride, dextrose, and Ringer's solution, all of which have multiple uses.
- These fluids serve as **vehicles** in IV admixtures, providing a mean for reconstituting sterile powders.
- They serve as the basic for correcting body fluid and electrolyte disturbances and provide a caloric source in parenteral nutrition.

B. IV fluids and electrolytes

- **a. Dextrose (D-glucose) solutions** are the most frequently used glucose solution in parenteral preparation.

- **(1) Uses**
  - Generally, a solution of dextrose 5% in water (d5w) is used as a **vehicle** in IV admixtures.
  - D5W may also serve as a **hydrating solution**.
  - In higher concentration (e.g., a 10% solution in water), dextrose provides a source of **carbohydrates in parenteral nutrition solutions(TPN)**

B. IV fluids and electrolytes

- **(2) Considerations.** Because the pH of D5W ranges from 3.5-6.5, instability may result if it is combined with an acid-sensitive drug.

  (a) Dextrose concentrations greater than 15% must be administered through **a central vein**.

  (b) Dextrose solutions should be used **cautiously in patients with diabetes mellitus.**

B. IV fluids and electrolytes

- **b. Sodium chloride**
  - Usually is given as a 0.9% solution. **Because** it is isotonic with blood, this solution is called **normal saline solution (NSS).**
  - A solution of 0.45% sodium chloride is termed **half-normal saline.**
  - A solution of 0.225% sodium chloride is termed **quarter-normal saline.**

B. IV fluids and electrolytes

- **(1) Sodium chloride for injection**
  - which is a solution of 0.9% sodium chloride, is used as **vehicle** in IV admixture and for fluid and electrolyte replacement.
  - In **smaller** volumes, it is suitable for the **reconstitution of various medications.**

- **(2) Bacteriostatic sodium chloride for injection**
  - Which is also a 0.9% solution, is intended slowely for multiple reconstitution.
  - It contains an **agent that inhibits bacterial growth** (e.g., benzyl alcohol, propylparaben, methylparaben), **which allows for its use in multiple-dose preparations.**

B. IV fluids and electrolytes

- **c. Water**
  - Are used **for reconstitution** and for dilution of such IV solutions as dextrose and sodium chloride.
  - Waters suitable for parenteral preparations **include** sterile water for injection and bacteriostatic water for injection.

- **d. Ringer's solutions**
  - Which are appropriate for **fluid and electrolyte replacement**, commonly are administered to **postsurgical** patients.

B. IV fluids and electrolytes

- **(1) Lactated Ringer's injection** (i.e., Hartmann's solution, Ringer's lactate solution) contains sodium lactate, sodium chloride, potassium chloride, and calcium chloride. Frequently, it is combined with dextrose (e.g., as 5% dextrose in lactated Ringer's injection).
- **(2) Ringer's injection** differs from lactated Ringer's injection in that it **does not contain sodium lactate** and has slightly different concentration of sodium chloride and calcium chloride. Like lactated Ringer's injection, it may be combined in solution with dextrose.

B. IV fluids and electrolytes

2. Electrolyte preparations.

- With ions present in both intracellular and extracellular fluid, electrolytes are crucial for various biological processes.

- Surgical and medical patients who cannot take food by mouth or who need nutritional supplementation require the addition of electrolytes in hydrating solutions or parenteral nutrition solutions.

2. Electrolyte preparations.

A. Cations are **positively** charged electrolytes.

(1) Sodium is the chief extracellular cation.

- **(a) Importance.** Sodium plays a Key role in interstitial osmotic pressure, tissue hydration, acid-base balance, nerve-impulse transmission, and muscle contraction.

- **(b) Parenteral sodium preparations** include sodium chloride, sodium acetate, and sodium phosphate.

2. Electrolyte preparations.

(2) Potassium is the chief intracellular cation.

- **(a) Importance** Potassium participates in carbohydrate metabolism, protein synthesis, muscle contraction (especially of cardiac muscle), and neuromuscular excitability.

- **(b) Parenteral potassium preparations** include potassium acetate, potassium chloride, and potassium phosphate.

2. Electrolyte preparations.

(3) Calcium

- **(a) Importance.** Calcium is essential to nerve-impulse transmission, muscle contraction, cardiac function, bone formation, and capillary and cell membrane permeability.

- **(b) Parenteral calcium preparations** include calcium chloride, calcium gluconate, and calcium gluceptate.

2. Electrolyte preparations.

(4) Magnesium

- **(a) Importance.** Magnesium plays a vital part in enzyme activities, neuromuscular transmission, and muscle excitability.

- **(b) Parenteral preparation.** Magnesium is given parenterally as magnesium sulfate.

2. Electrolyte preparations.

- **B. Anions** are negatively charged electrolytes.

1. **Chloride** is the major **extracellular** anion.

- **(a) Importance.** Along with sodium, it regulates interstitial osmotic pressure and helps to control blood pH.

- **(b) Parenteral Chloride preparations** include calcium chloride, potassium chloride, and sodium chloride.

2. Electrolyte preparations.

(2) Phosphate is the major **intracellular** anion.

- **(a) Importance.** Phosphate is critical to various enzyme activities. It also influences calcium levels and acts as a buffer to prevent marked changes in acid-base balance.

- **(b) Parenteral Phosphate Preparations** include potassium phosphate and sodium phosphate.

2. Electrolyte preparations.

(3) Acetate

- **(a) Importance.** Acetate is a Bicarbonate precursor that may used to provide alkali to assist in the preservation of plasma pH.

- **(b) Parenteral acetate preparations** include potassium acetate and sodium acetate.

C. Parenteral antibiotic preparations

- Are available as sterile unreconstituted powders, which must be reconstituted with sterile water, normal saline, or d5w, or as a sterile, ready-to-use liquid parenteral

C. Parenteral antibiotic preparations

- **1. Administration methods.** Parenteral antibiotics may be given intermittently by direct IV injection, short-term infusion, intramuscular injection, or intrathecal injection.
- **2. Uses.** Parenteral antibiotics are used to treat infections that are serious and require high antibiotic blood levels or when the gastrointestinal tract is contraindicated, such as in ileus.
- **3. Dosing frequencies** of parenteral antibiotics vary from once daily to as often as every 2 hours, depending on the kinetics of the drug, seriousness of the infection, the site of infection, and the patients disease or organ status (e.g., renal disease)

D. Parenteral antineoplastic agents.

- Studies suggest that these medications may be toxic to the personnel who prepare and administer them.
- The evidence is not conclusive, which necessitates special precautions to ensure safety and minimize risks.
- In response to concerns, the occupational safety and health Administration (OSHA) has published a technical manual, "Controlling Occupational Exposure to Hazardous Drugs" Every facility must have a written plan that include drug preparation precautions, storage, transport, personal protective equipment (gloves, gowns, masks), work equipment, waste disposal, spill management , and personnel medical surveillance,

D. Parenteral antineoplastic agents.

- **1. Administration methods.** Parenteral antineoplastic may be given by direct IV injection, short-term infusion, or long-term infusion. Some are administered by a non-IV route, such as **the subcutaneous, intramuscular, intra-arterial, or intrathecal routes**.

- **2. Safe antineoplastic handling guidelines.** All pharmacy and nursing personnel who prepare or administer antineoplastics should receive special training in the following guidelines to reduce the risk of exposure to these drugs.

D. Parenteral antineoplastic agents.

- **a.** A **vertical laminar flow hood** Should be used during drug preparation, with exhaust directed to the outside.
- **b.** All syringes and IV tubing should have **Luer-Lok Fittings**
- **c. Clothing.** Personnel should wear personal protective equipment including closed-front cuffed surgical gowns and double-layered latex surgeon's gloves.
- **d. Negative-pressure technique** should be used during withdrawal of medication from vials. This will prevent pressure from building up inside the vial and causing the drug to spray around the needle.

D. Parenteral antineoplastic agents.

- **e. Final dosage adjustment** should be made into the vial, ampule, or directly into an absorbent gauze pad.

- **f. Priming equipment.** Special care should be taken when IV administration sets are primed. The IV tubing should be primed before adding the drug, or the tubing can be primed with drug-free fluid before connecting it to the chemotherapy drug container. If these are not available, primed the tubing into sterile gauze in a sealable plastic bag.

D. Parenteral antineoplastic agents.

- **g.** Proper procedures should be followed for **disposal** of materials used in the preparation and administration of antineoplastic .
- **(1) Needles** should not be clipped or recapped.
- **(2) Preparations** should be discarded in containers that are puncture-proof, leak-proof, and properly labeled.
- **(3) Hazardous waste.** There is no completely acceptable method for disposing of hazardous waste. High-temperature incineration may be the preferred method. These materials may also be buried in an EPA-licensed hazardous waste dump or chemically deactivated.

D. Parenteral antineoplastic agents.

- **h.** After removal of gloves, personnel should **wash hands** thoroughly.

- **i.** Personnel and equipment involved in the preparation and administration of antineoplastic agents should be **monitored** routinely.

D. Parenteral antineoplastic agents.

- **3. Patients problems.** Infusion **phlebitis and extravasation** are the most serious problems that may occur during the administration of parenteral antineoplastics.

D. Parenteral antineoplastic agents.

- **a. Infusion phlebitis** (inflammation of a vein)
  - Is characterized by pain, swelling, heat sensation, and redness at the infusion site.
  - Drug dilution and filtration **can eliminate or minimize the risk of phlebitis.**

- **b. Extravasation** (infiltration of a drug into subcutaneous tissues surrounding the vein) measures must be taken immediately if extravasation occurs.

Measures must be taken immediately if extravasation occurs.

- **(1)** Depending on the drug involved, emergency measures may include:
  - stopping the infusion,
  - Injecting hydrocortisone or another anti-inflammatory agent directly into the affected area,
  - Injecting an anti-dote (if available),
  - Applying a cold compress (to facilitate a drug-anti-dote reaction).

- **(2)** A warm compress may then be applied to increase the flow of blood, and thus the vesicant, away from damaged tissue.

E. Parenteral biotechnology products

- Are created by the application of recombinant technology to the generation of therapeutic agent, **such as** monoclonal antibodies, various vaccines, and colony-stimulating factors.
- **1. Uses** of these agents include:
  - Cancer therapy,
  - Infections,
  - Transplant rejection,
  - Rheumatoid arthritis, inflammatory bowel disease, respiratory disease, and malaria as well as vaccines against cancer, HIV infection, and hepatitis B.

E. Parenteral biotechnology products

- **2. Characteristics.** Protein and peptide biotechnology drugs have a shorter half-life, often require special storage such as refrigeration or freezing, and must be not shaken vigorously to avoid destroying the protein molecules .

- **3. Administration.** Many biotechnology products require reconstitution with sterile water or normal saline and may be parenterally administered by direct IV injection or infusion, or by intramuscular or subcutaneous injection.

IRRIGATING SOLUTIONS.

- Although these sterile products are manufactured by the same standards used to process IV preparations, they are **not intended for infusion into the venous system.**
- Labeling differences between irrigation solutions and injections are specified in the *United States Pharmacopeia* (USP) and reflect differences in acceptable particular matter levels, volume of solution available for use, and the container design.

IRRIGATING SOLUTIONS.

- **A .Topical administration.** Irrigating solutions for topical use are packaged in pour bottles so that they can be applied directly onto the desired area. These solutions are intended for such purposes **as irrigating wounds , moistening dressings, and cleaning surgical instruments.**

IRRIGATING SOLUTIONS.

- **B. Infusion of irrigating solutions.** This procedure, using an administration set attached to a Foley catheter, is commonly used for many surgical patients. **Surgeons performing urological procedures often use irrigating solutions to perfuse tissues in order to maintain the integrity of the surgical field**, remove blood, and provide a clear field of view. To decrease the risk of infection, 1 mL of Neosporin G.U. Irrigant, an antibiotic preparation, often is added to these solutions.

IRRIGATING SOLUTIONS.

- **C. Dialysis.** Dialysates are irrigating solutions used in the dialysis of patients with such disorders as renal failure, poisoning , and electrolytes disturbances. These products **remove waste materials, serum electrolytes, and toxic products from the body.**

IRRIGATING SOLUTIONS.

- **1.** In **peritoneal dialysis,** a hypertonic dialysate , which contains dextrose and electrolytes, remove harmful substances by osmosis and diffusion. After a specified period of time, the solution is drained. **Antibiotics and heparin may be added to the dialysate.**
- **2.** In **hemodialysis,** the patient's blood is transfused through a dialyzing membrane unit that removes the harmful substance from the patient's vascular system. After passing through the dialyzer, the blood reenters the body through a vein.