

Parenterals

- ▣ Parenterals refer to the injectable routes of administration
- ▣ The term (Parenteral) has its derivation from the Greek words para (beyond) and enteron (intestine) meaning outside of intestine.
- ▣ Parenteral preparations are either used alone or diluted
- ▣ Their general requirements are:
 1. safety
 2. Sterility
 3. Free from pyrogen
 4. Clarity
 5. Stability
 6. Isotonicity.

General requirements for Parenterals

1. **Safety:** The vehicle (solvent) in general is water (sterile water); but for poorly-soluble drugs another solvent is added like alcohol, glycol
 - ▣ so all of these additives must undergo safety test (means all should be not toxic).
 - ▣ Some additives are not safe (toxic) like benzyl alcohol, which is toxic and harmful especially for infants.
 - ▣ Also all the containing and closures should be not toxic and should be safe.

2. **Sterility:** very important, so the product and the container must be sterilized to prevent infection when there is injury, the method of sterility is similar to ophthalmic solution sterilization which includes moist heat (autoclave), dry heat, gases and filter aid.
3. **Free from pyrogen:** pyrogen is fever producing organic substances arising from microbial contamination; they are a lipo-polysaccharide of the cell wall of microorganism and endotoxins.

Pyrogen test

- ▣ A group of three rabbits are used for pyrogen; they should be healthy, mature and of the same weight and size.
- ▣ The initial temperature of each rabbit is recorded (any rabbit showing temperature more than 39°C should be excluded), then inject the sample into the ear vein of each rabbit.
- ▣ Measure the temperature after 30 min and then every hour.
- ▣ A positive result is when each rabbit shows an increase in temperature more than 0.6°C or the sum of temperature increase of the three rabbits exceeds 1.4°C .
- ▣ If only two of the three rabbits show an increase in temperature, Repeat the test using a group of five rabbits, and the test will be +ve if four of the five rabbits show an increase in temperature in the repeated test.

- 4. Clarity:** free from particles specially which have a diameter $7.5\ \mu$.
- ▣ Clarity test is done by taking parenteral solution and observe it at strong beam of light and the product will be observed for any foreign particle.
- 5. Stability:** This is a standard requirement for all products not only for parenterals so the product should be stored at several temperatures for specific period of time then analyzed. They should not loss any amount of active constituents.should not loss its therapeutic activity
- 6. Isotonicity:** Parenteral products should be isotonic with body fluids so should not change the morphology of RBCs (no shrinkage or hemolysis).

Types of parenterals

- ▣ According to route of administration parenterals are classified into:
 1. **Intravenous (i.v)**: injected directly into vein (major or peripheral vein)
 2. **Intramuscular (i.m)**: injected directly into skeletal muscle (pelvic or arm).
 3. **Subcutaneous (s.c)**: this is injected into alveolar region beneath the layer of the skin.
 4. **Intra dermal (i.d)**: injected between layers of the skin.
 5. **Intra spinal (i.s)**: injected into spinal canal.
 6. **Intra arterial (i.a)**: injected directly into artery.
- ▣ Drugs may be injected almost any organ or area of body including joints (intra articular), a joint-fluid area (intra synovial), the spinal column (intra spinal), into spinal fluid (intrathecal), arteries (intra arterial) and in an emergency, even into the heart (intra cardiac).

The volume of injections for different types of injection is varying

Intravenous

Injected directly into a vein (major or peripheral vein)

Volume unlimited volume (infusion)

Intramuscular

Injected directly into skeletal muscle (pelvic)

Volume (2-5 ml)

Subcutaneous

Injected directly into alveolar region beneath the layer of the skin

Volume (2 ml)

Intradermal

Injected between the layer of the skin

Volume (0.2 ml)

Intraspinal

Injected into spinal canal

Volume (up to 10 ml)

Advantages and disadvantages of (intravenous route of injection)

Advantages

1. Has very rapid response, since drug go directly to blood.
2. Has a great intensity of response, because there is no loss of drug.
3. It is less irritant and
4. Has a great stability with some drugs compared to intramuscular.
5. It can be used for large volume fluids.

Disadvantages

1. Restricted to solution.
2. It may cause haemolysis but can avoid by slow injection.
3. The drug cannot be recover, if anything injected accidentally, it is difficult to get rid of it.

Types of injections (intramuscular)

1. It is easier than IV
2. It can be used for solutions, suspensions, and emulsions.
3. The drug will stay in muscle and diffuse slowly so it has slower onset of action.
4. Prolong action.
5. The absorption from this route depend on the release of drug and blood flow.
6. Salt form of the drug absorb faster than free drug.

Types of injections (intramuscular)

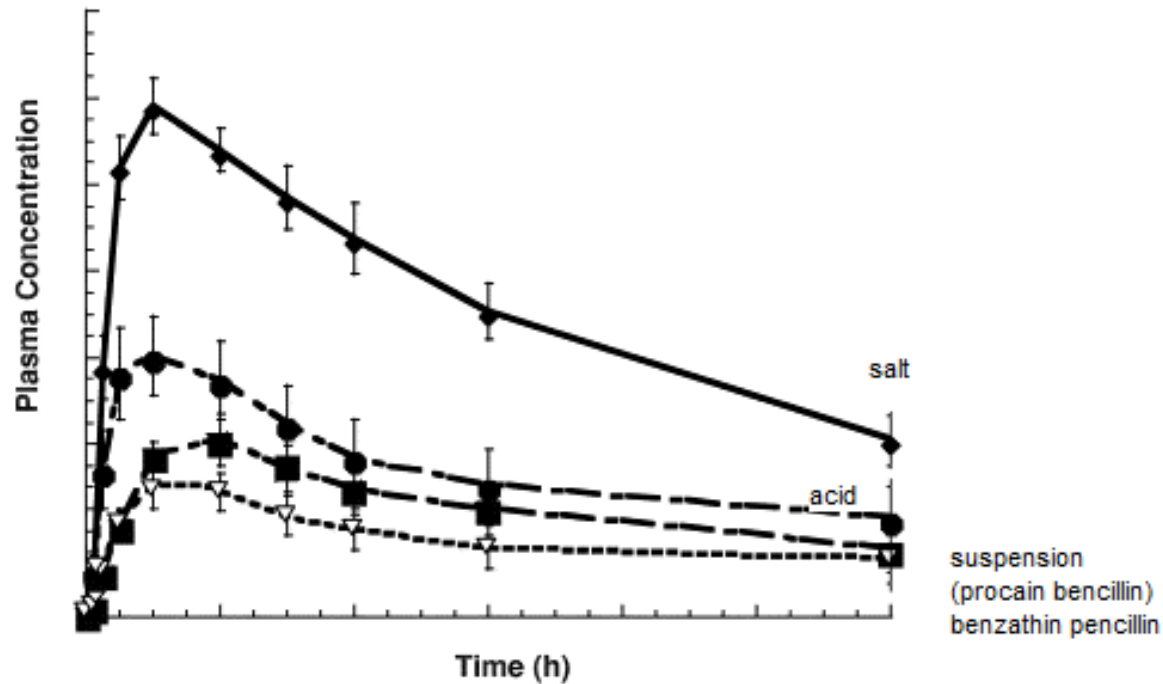


Figure 1. Plasma concentration time curve of different Ampicillin preparations

Depending on the type of preparation employed absorption may be in the following sequence: solution > aqueous suspension > oily solution > oily suspension > oily suspension with thickening agent.

Types of injections (subcutaneous)

1. It has slow onset
 2. It is simple to administered
 3. Absorption from this route of injection is affected by concentration, Solubility and blood flow
 - Example of drug given by this route is insulin of two types
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1. Soluble insulin show fast absorption but short duration of action
 2. Insoluble type protamine zinc insulin, which has slow response or onset but prolong action

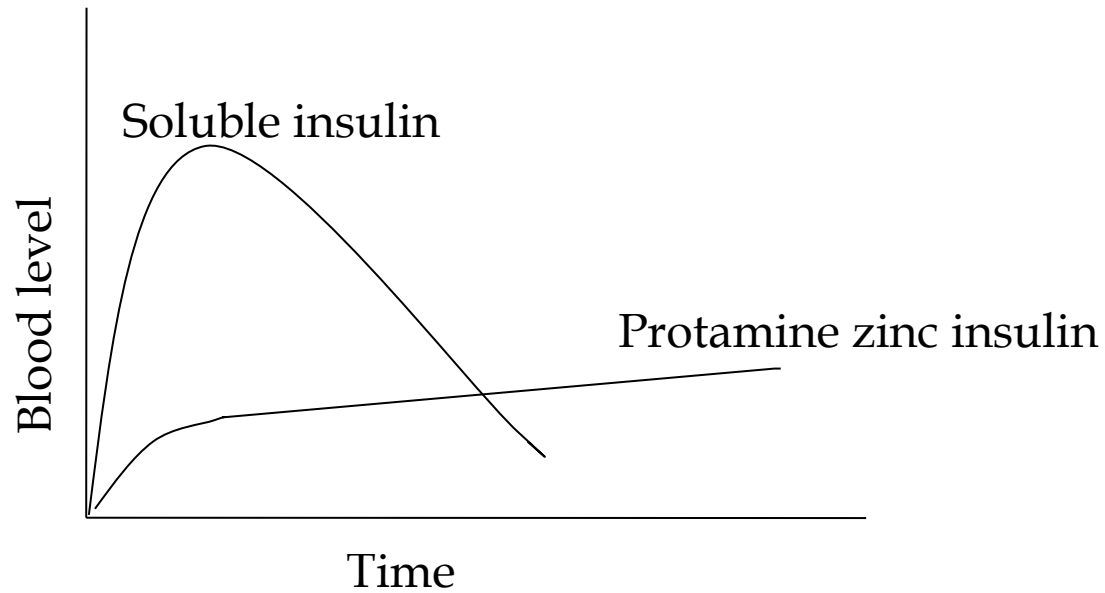


Figure 2. Plasma concentration time curve of two different types of insulin

Types of injections (intradermal)

1. It has local distribution
2. Its absorption is slow
3. It is used for vaccines and for diagnostic test

Types of injections (intraarterial)

1. Need surgical operation
2. It is used for targeting a drug into organ for diagnostic test and
3. Anti-neoplastic drugs

To prolong the duration of action of local anesthetic, epinephrine is mixed with the local anesthetic. Epinephrine is vasoconstrictor reduce blood flow and the absorption of the local anesthetic after intramuscular injection, thus prolong its duration as shown in Figure 3.

