

DELIVERY OF PROTEINS: ROUTES OF ADMINISTRATION

Lecture 6

Asra'a A. Abdul-Jalil

Ph.D. in Genetic Engineering and Biotechnology/university of Baghdad

Routes of administration

❖ Is the path by which a drug, fluid, poison or other substance is brought into contact with the body.

- **Factors affecting choice of route**

- ✓ Drug-related factors
- ✓ Patient related factors
- ✓ Therapeutic action

DELIVERY OF PROTEINS

- **The Parenteral Route of Administration**

defined as administration via those routes where a needle is used, including:

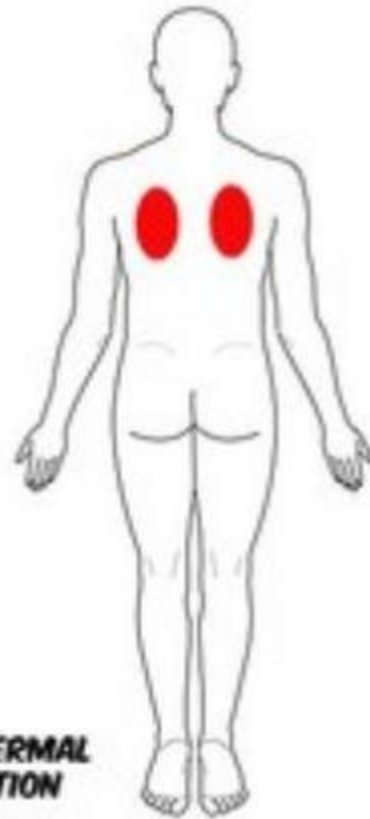
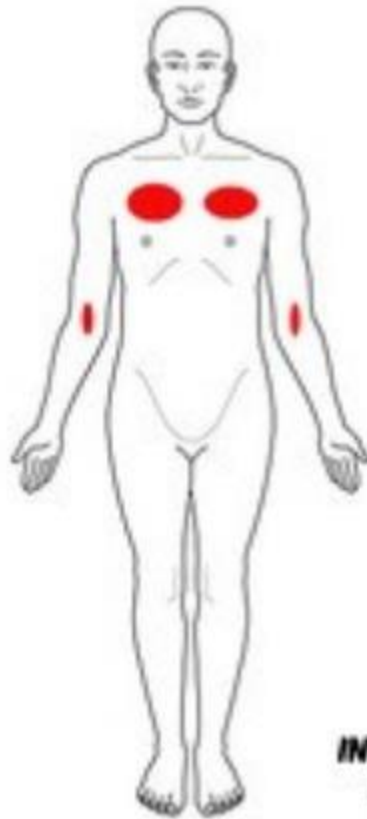
- intravenous (IV),
- intramuscular (IM),
- Subcutaneous (SC)
- intraperitoneal (IP) injections.

Table 1-1 Parenteral Routes

Route	Injection Site
Intravenous (IV)	Vein
Intramuscular (IM)	Muscle tissue
Intradermal (ID)	Dermis of the skin
Subcutaneous (subcut; SQ)	Subcutaneous tissue of the skin
Intrathecal (IT)	Subarachnoid space of the spinal cord
Epidural	Epidural space of the spinal cord
Intra-arterial	Artery
Intra-articular	Joint space
Intracardiac	Heart
Intraocular	Eye
Intraperitoneal	Peritoneal cavity

Intradermal or Intracutaneous

- to diagnose TB, identify allergens, administer local anesthetics
- * -drugs are absorb slowly from this site
- * -commonly used for ID injection are the **INNER ASPECT OF THE FOREARM (upper chest and upper back beneath the scapula)**
- * -drug's dosage contained in a small quantity of solution (0.01 to 0.1 ml)



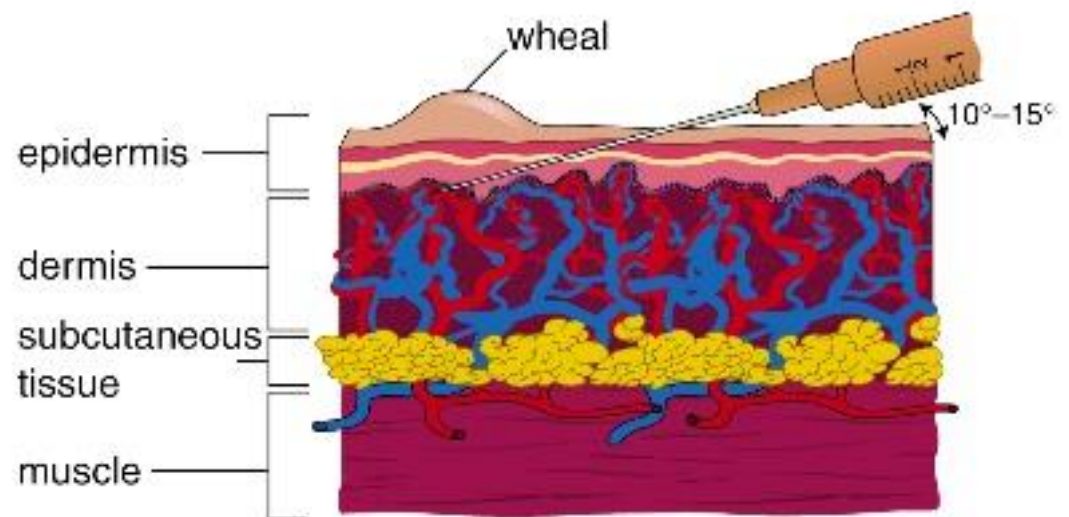
**INTRADERMAL
INJECTION**



Intradermal Injections

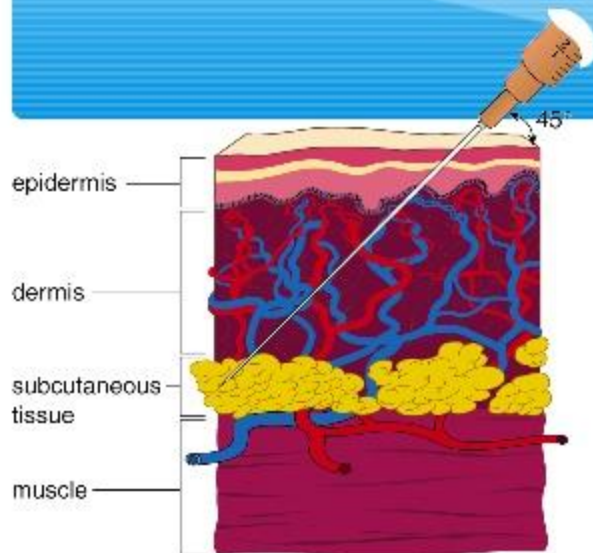
Given into capillary-rich layer just below epidermis for

- * local anesthesia
- * diagnostic tests
- * immunizations





Subcutaneous Injections



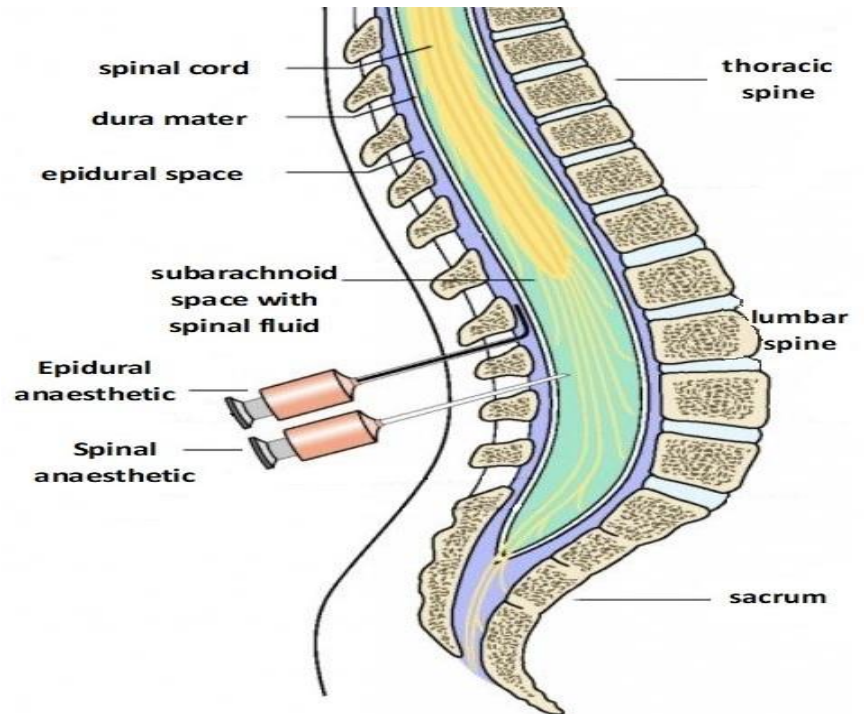
Given at a 45-degree angle

- * 25- or 26-gauge needle, 3/8 to 5/8 inch length
- * No more than 1.5 mL should be injected into the site
- * to avoid pressure on sensory nerves causing pain and discomfort

- **Intrathecal injection**

injection of a substance through the theca of the spinal cord into the subarachnoid space.

- Patients receiving intrathecal chemotherapy for metastatic malignancy.



The Parenteral Route of Administration

- The blood half-life of biotech products can vary over a wide range. For example, the circulation half-life of Tissue Plasminogen Activator tPA is a few minutes, while monoclonal antibodies (MAb) reportedly have half lives of a few days

The Parenteral Route of Administration

Obviously, one reason to develop modified proteins through site directed mutagenesis (*In vitro* mutagenesis) is to enhance circulation half-life.

The method provides a means of introducing specific nucleotide changes into a gene and leading to change in the type of amino acid.

A simple way to expand the mean residence time for short half-life proteins is to switch from IV to IM or SC administration.

One should realize that by doing that, changes in disposition may occur, with a significant impact on the therapeutic performance of the drug. These changes are related to:

(i) the prolonged residence time at the IM or SC site of injection compared to IV administration and the enhanced exposure to degradation reactions (peptidases) .

(ii) differences in disposition

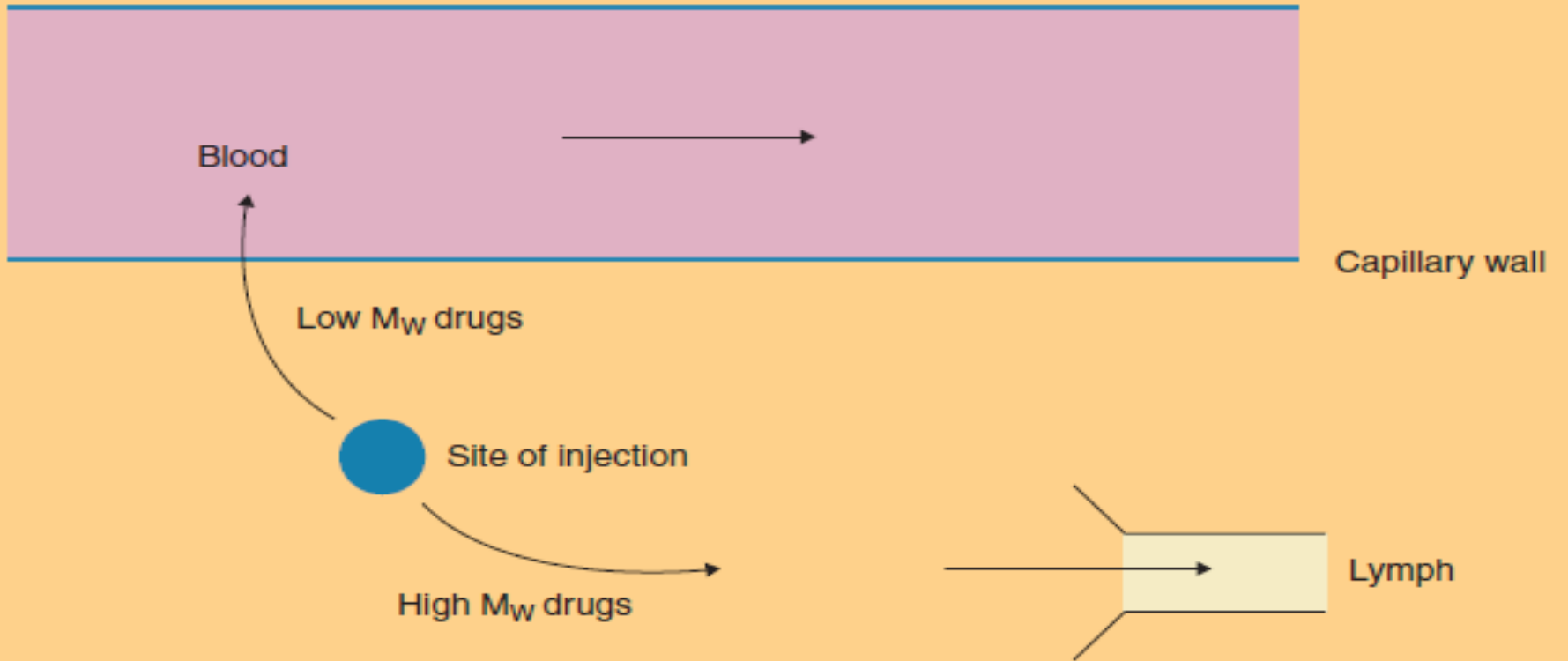
(i) the prolonged residence

- For instance, diabetics can become “insulin resistant” through high tissue peptidase activity, Other factors that can contribute to absorption variation are related to differences in exercise level of the muscle at the injection site and also massage and heat at the injection site. The state of the tissue, for instance the occurrence of pathological conditions, may be important as well.

(ii) differences in disposition:

Upon administration, the protein may be transported to the blood through the **lymphatics** or may enter the blood circulation through the **capillary** wall at the site of injection.

The fraction of the administered dose taking this lymphatic route is molecular weight dependent . Lymphatic transport takes time (hours) and uptake in the blood circulation is highly dependent on the injection site. On its way to the blood, the lymph passes through draining lymph nodes and contact is possible between lymph contents and cells of the immune system such as macrophages, B- and T-lymphocytes residing in the lymph nodes.



Routes of uptake of SC or IM injected drugs.