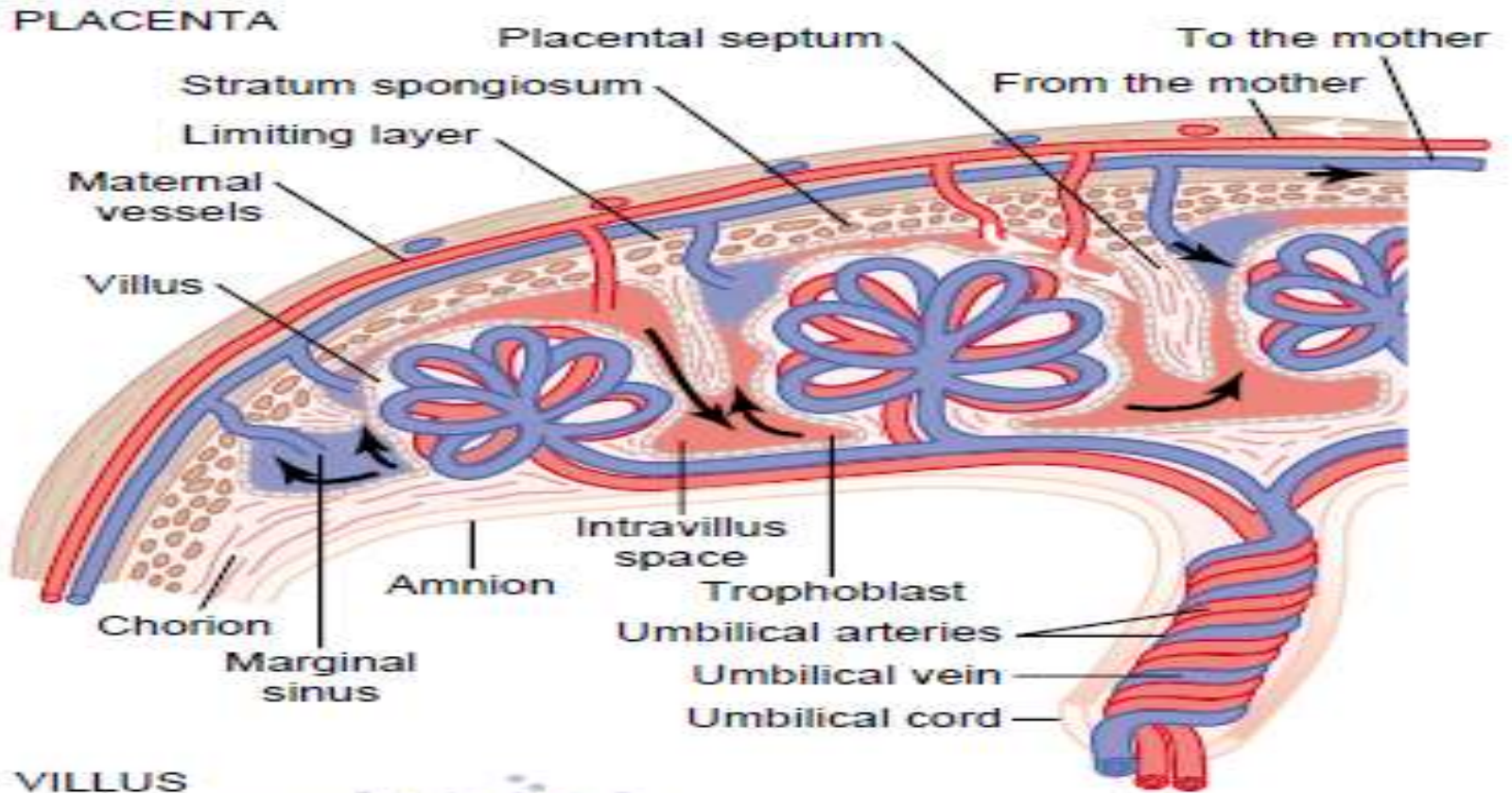


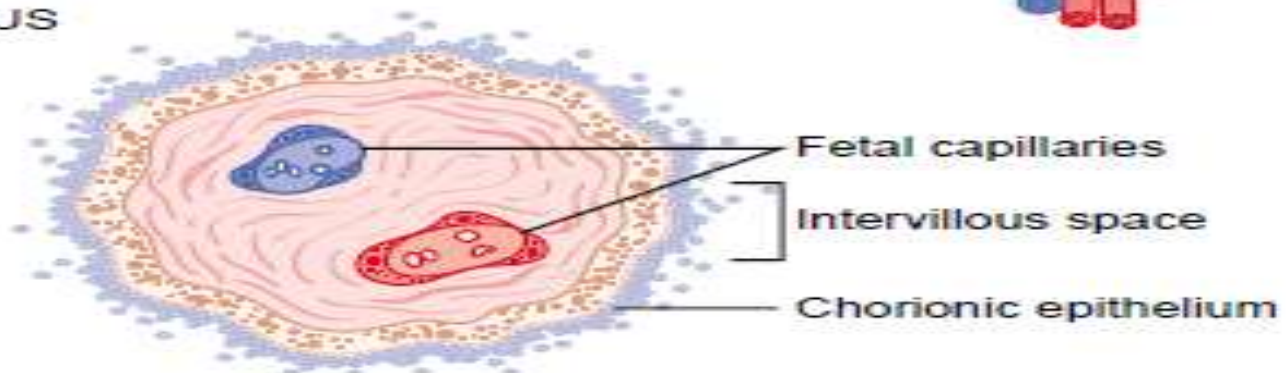
Barrier Function

- Fetal membrane has long been considered as a protective barrier to the fetus against noxious agents circulating in maternal blood.
- In general, substances of higher molecular weight of > 500 daltons can not cross it, but there are some exceptions. Antibodies and antigens can cross the placental barrier in both direction by process of endo & exo cytosis. It is facilitated by pinocytosis. The rate of drug transfer is increased in late pregnancy. Maternal viral, bacterial / protozoa infections can reach to fetus by crossing placental barrier. Similarly Any drug taken by women during pregnancy can cross the placental barrier in variable concentration and may have deleterious effect on fetus

Placental Circulation



VILLUS



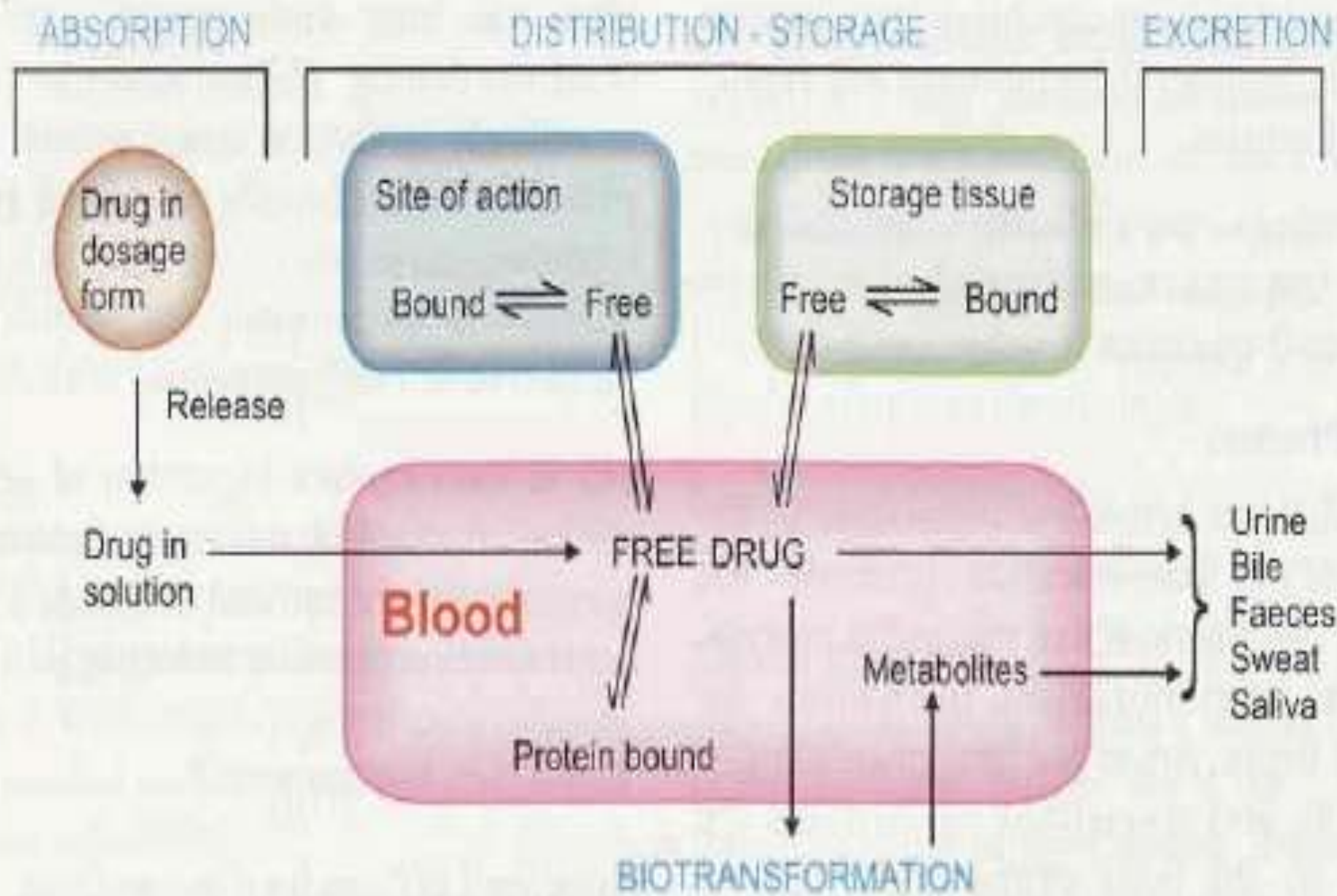


Fig. 2.1: Schematic depiction of pharmacokinetic processes

Factors for Placental Transfer From Mother to Fetus

A. SUBSTANCE Properties →

1. Molecular weight : Lower the MW more is transfer .
2. Lipid solubility: Lipophilic substances diffuse rapidly.
- 3 . Ionization : non ionized form crosses lipid membrane freely.
- 4 . pH of blood favours ionization of many drugs delays diffusion .
5. Protein binding.
6. Spatial configuration

B. Maternal Properties →

1. drug concentration in maternal blood – higher concentration – more is diffusion.
2. Uterine blood flow
3. Concentration gradient on either side of placental membrane.

C. Placental properties →

1. Lipid membrane of placenta enhances transfer of lipophilic substances.
2. Total surface area of placental membrane .
3. Functional integrity and thickness of placental barrier.

Mechanism Involved in placental Transfer

- 1, Simple Diffusion: O₂ & CO₂ transfer take place by simple diffusion . Partial pressure gradient across placental barrier is the driving force. O₂ supply to fetus is at the rate of 8ml / Kg / min and this is achieved with cord blood flow of 165-330 ml/ min .Excretion of urea, uric acid ,creatinine.
- Facilitated Diffusion: (transporter mediated using transporter protein in syncytiotrophoblast., glucose with the help of transporter protein (GLUT I) , glucose transfer increases more when maternal blood glucose is low.
- Active Transfer: Against pressure gradient, energy ATPases mediated ,

Mechanism involved in placental transfer -----

- Endocytosis: Invagination of cell membrane to form intra cellular vesicle which contain the extra cellular molecule. IgG immunoglobulin is taken up by endocytosis from maternal circulation
- Exocytosis: Release of molecule with in the vesicle to the extra cellular space ---IgG immunoglobulin are transferred to fetus from placenta by exocytosis.
- Leakage: break in placental membrane –Foetal RBC leak into maternal circulation.

Other functions of Placenta

- Transfer of nutrients and waste products between mother and fetus ; Hence it attributes to –1. respiration, 2.excretion 3. nutrition.
- Endocrine function-- placenta is an endocrine gland ., secrets –HCG , Steroids and peptide hormones.
- Immunological function.
- Blood Barrier.

Nutritive Function

- Fetus obtains its nutrients from mother., when mother's diet is inadequate , then only depletion of maternal tissue storage occur.

Glucose → The principle source of energy is transferred by Facilitated diffusion . There are transporter proteins (GLUT I) for this mode of diffusion. Glucose transfer to fetus is not linear ., it decreases when mother glucose concentration increases. Fetal blood glucose level is lower than that of mother indicating rapid utilization by fetus.

Nutritive function--

- Lipids → Triglycerides and fatty acids are directly transferred to fetus in early pregnancy but probably synthesized by fetus itself in late pregnancy. Essential fatty acids are transferred more than non essential fatty acids. Cholesterol is able to transfer directly. Thus lipids have dual origin.
- Amino acids → They are transferred by active transfer, energy requiring mechanism (ATPS Enzyme). Amino acid concentration in fetal blood is more than maternal. Gig cross by endocytosis. Fetal proteins are synthesized from transferred amino acids, their concentration is lower than mother.

A

Nutritive Function----

- Water and Electrolytes → Na, K, Ca transferred by simple diffusion., Ca, P and Fe are transferred by active transfer with the help of transporter proteins against a concentration gradient. Their concentration is higher than maternal. Water soluble vitamins are transferred rapidly by active transport while fat soluble vitamins are transferred slowly.

Nutritive function---

- Hormones → Insulin, steroids from adrenals, thyroid, HCG, placental Lactogen, cross the placenta very slowly. Neither parathormone nor calcitonin cross the placenta. Placenta also produce TSH and Growth Hormone.

Enzymatic Function

- Numerous enzymes are mentioned in placenta ., few of them are---
- 1. Diamine oxidase which inactivates circulatory pressure amines.
- 2. Oxytocinase --- neutralises the oxytocin .
- Phospholipase A2-- synthesises arachidonic acid precursor of PGs.

Immunological function

- Fetus and placenta have partial parental antigens foreign to mother in spite of this, fetus is not rejected. Placenta offers immunological protection,
- Placental hormones, proteins (SP₁) early pregnancy factor (EPF) PAPP-A, Steroid, HCG have got some immune suppressive effect.
- Villous trophoblast do not express HLA Class 1 or class 2 molecules.
- There is shift of maternal response from cell mediated (T helper 1) to hormonal (T helper 2) immunity.
- Decidual Natural Killer (NK) cells and extravascular trophoblast HLA class I molecules interact, the cytokines just derived will regulate the invasion of extravascular trophoblast in spiral arteries, which are converted into low resistance, high conductance utero placental vessels.