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Xenobiotics Translocation [Absorption; Distribution; Biotransformation and Excretion]

SYNOPSIS

Introduction, Translocation, Mechanism of xenobiotics transfer, Distribution of xenobiotics, Storage depots, Biotransformation, Excretion of xenobiotics, Deposition of xenobiotics, Membranous barriers.

Introduction

Xenobiotics are the environmental chemicals. It is a term derived from the Greek word — *xenon* = a stranger + *bios* = life i.e., stranger to life. The salient xenobiotics of concern to human health and environment are listed in Table 14.1 :

Table 14.1 : Xenobiotics of Concern to Human Health and Environment

Products	*Examples*	
Synthetic compounds of use	Foods additives, Biocides, Pesticides, Dyes, Explosives, Detergents, Polymers, Intermediates etc.	
Inadvertently formed waste and byproducts	Industrial waste water, automobile exhaust, products of incinerations, chlorination drinking water	CO, SO_x, NO_x metals, PAH, NH_3, Chloroform, Hydrocarbons, Chlorophenols, Chloroform, Particulate matter
Environmental transformation products of xenobiotic (Industrial) compounds	DPE, photomirex, 2, 4-dichlorophenol, 3,4 — dichloroaniline, benzo (a) pyrene, quinines	

The metabolism of xenobiotics provides a basic knowledge to the understanding of pharmacology, toxicology, cancer research, drug addiction. All these areas involve exposure to xenobiotics.

Translocation

The biological system may be exposed to the high amounts/concentration of xenobiotics, but if the concentration at the specific sites remain low due to any reason viz., defensive mechanism, there appears little or no effect. In order to produce a measurable effect, a xenobiotic must be transported from the site of exposure to the specific sites of action. The process of *transport of xenobiotics* (toxicants) from the site of their application to the specific site of action or more diffused sites of action is designated as translocation of xenobiotics. In other words, dynamics of movement of xenobiotics in the living system from its penetration into the blood to its final elimination from the body is termed *translocation.* The factors which bring translocation are referred to as translocation factors including absorption, distribution, binding and excretion.

The process of translocation involves four principal steps :

1. Absorption from the site of action via skin or GIT or lungs.
2. Transport of xenobiotics by blood to —
   (a) The biotransformation sites, (b) Other tissues.
3. Accumulation of xenobiotics and their release into the blood.
4. Elimination from the body mainly through :
   (a) G.I.T. (b) Kidney

The entire process of translocation is represented in the Fig. 14.1. The major routes by which xenobiotics enter the body are skin, G.I.T. and lungs. Xenobiotics thus absorbed are eliminated from the circulation by metabolism and circulation. The quantification and determination of the time course of absorption, distribution, biotransformation and excretion of xenobiotics are referred to as toxicokinetics.

deleterious effects at one site or several sites in the body. Exceptions are caustic and corrosive agents (acids, bases, salts, oxidizers), which act topically. A toxicant absorbed into the blood stream through any barrier (described ahead) is distributed, at least to some extent, throughout the body, including the site where it produces damage. This site is often called the target organ or target tissue.

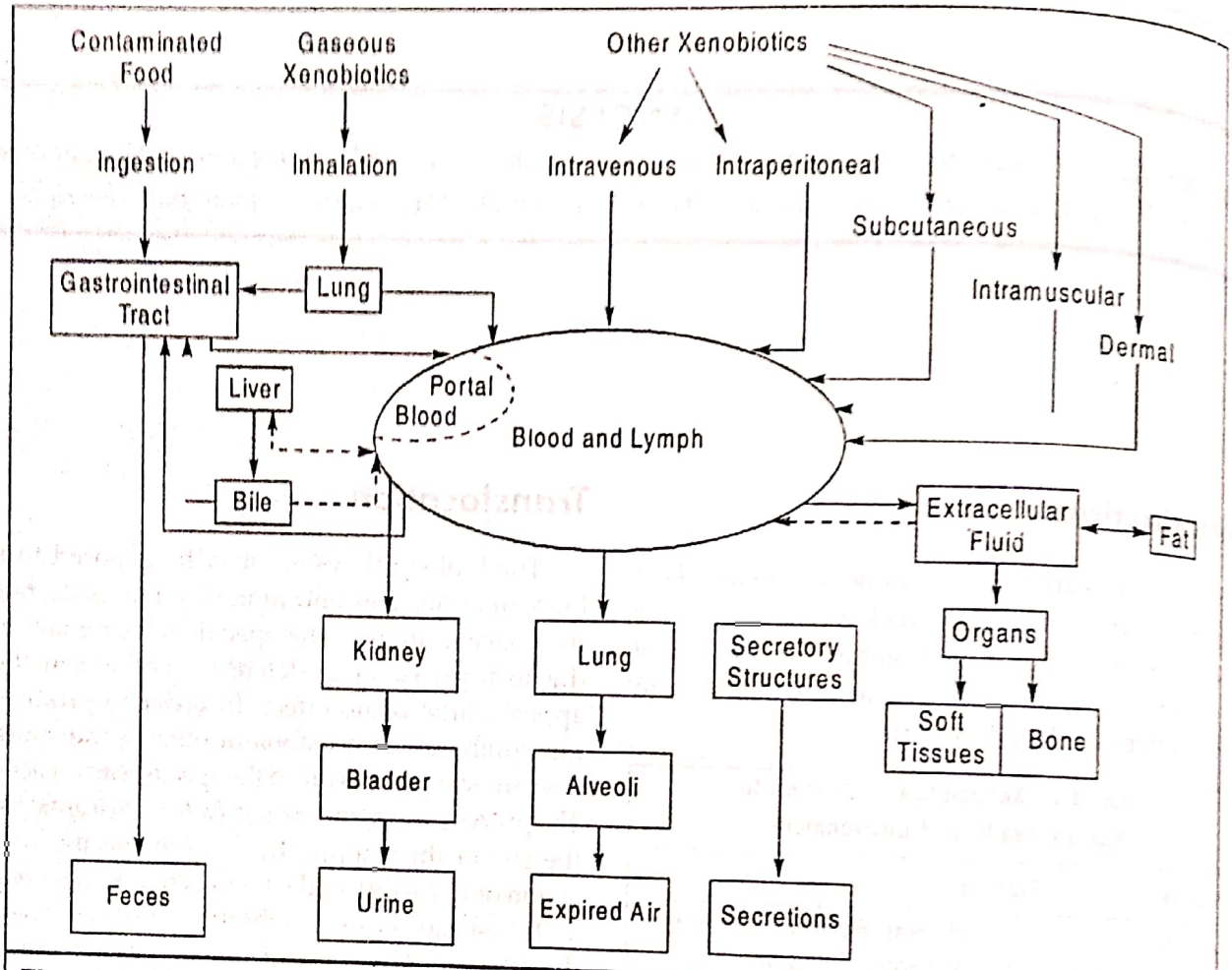

Fig. 14.1 : Routes of absorption, distribution, and excretion of xenobiotics (toxicants) in the body

Mechanism of Xenobiotic Transfer

Xenobiotics usually pass through a number of cells, such as the stratified epithelium of the skin, the thin cell layers of the lungs or G.I.T., the capillary endothelium, and the cells of target organ or tissue. The cell membrane (plasma membrane) surrounding all these cells are remarkably similar. It is approximately 100 A^0 thick with pores of size ranging from 4 to 40 A^0. The lipid layer of the plasma membrane is permeable to and readily penetrated by lipid soluble substances. In order to enter the animal and reach some target organ, any xenobiotic (toxicant) must penetrate one or more living membrane(s). The membranes form barriers through which toxicants have to cross to exert their

It is to be emphasized here that a xenobiotic may have one or several target organs, and, in turn, several xenobiotics may have same target organ. For example, benzene affects the hematopoietic system and CCl_4 injures the liver. Lead and mercury both damage the CNS, the kidneys, and the hematopoeitic system. Toxic agents in different ways may modify the permeability of plasma membrane. For instance, size, shape, degree of ionization, and lipid solubility of ionized and non-ionized forms of a xenobiotic (toxicant) are its important physiochemical properties that influence its passage across the plasma membrane.

A toxicant may pass through plasma membrane by one of the two general processes :