The fate of administered radiopharmaceuticals

The biologic fate of administered radiopharmaceutical is depicted in Figure 5.1 and depends mostly on distribution and elimination because most radiopharmaceuticals are administered by intravenous injection. Absorption plays a minimal role and affects only those few procedures in which radiopharmaceuticals are given intradermally (lymphoscintigraphy), orally (thyroid uptake), intrathecally (cisternography) and by inhalation (ventilation). Both distribution and elimination are influenced by blood flow, capillary permeability, intracellular interaction and degree of binding to blood components. The residence time in the organ is in turn influenced by any biotransformation that occurs intracellularly. Other factors such as the quality of the radiopharmaceutical and the health status of the patient also affect the distribution and elimination of the administered radiopharmaceutical.

A time course of the distribution and elimination of an intravenously injected radiopharmaceutical is shown in Figure 5.2. Qualitatively, it is possible to deduce that the radiopharmaceutical has a long residence (curve A) or fast transit time (curve B), as exemplified by $^{99m}Tc$-MDP, $^{99m}Tc$-l, $^{99m}Tc$-d, $^{99m}Tc$-HMPAO and $^{99m}Tc$-sestamibi for curve A or $^{99m}Tc$-IDA, $^{99m}Tc$-teboroxime and $^{99m}Tc$-MAG3 for curve B. Quantitatively, pharmacokinetic parameters such as rates of extraction, elimination and volumes of distribution can be calculated and used to answer the following questions:

- How much of the radiopharmaceutical is in the target organ(s) at various times after its administration?
- How quickly is the radiopharmaceutical excreted by each excretory organ (kidney/liver)?

Figure 5.1 Routes of administration, distribution and elimination of radiopharmaceuticals (modified from [1]). ECF, extracellular fluid; GIT, gastrointestinal tract; GB, gallbladder.
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Figure 5.2 The uptake of radiopharmaceuticals in and elimination from the target organ(s). Curve A represents radiopharmaceuticals with long residence time, while curve B represents those with fast transit time through the target organ(s).

To describe the distribution and elimination of the intravenously injected radiopharmaceutical adequately, a brief description of membrane transport systems is helpful.

MEMBRANE TRANSPORT SYSTEMS

There are two basic transport systems: passive and specialized.

PASSIVE TRANSPORT SYSTEMS

Passive transport does not involve expenditure of energy and there are two types: diffusion and filtration.

Diffusion

Small hydrophilic molecules such as \(^{99m}\text{TcO}_4^-\) pass across lipid membranes through aqueous channels or pores, whereas the lipophilic radiopharmaceuticals such as \(^{99m}\text{Tc}-d,l\)-HMPAO pass through the lipid bilayer. The rate of transfer across the cell membrane is dependent on the lipid solubility of the radiopharmaceutical, as measured by lipid–water partition coefficient. If the lipophilic radiopharmaceutical exists in both ionized and non-ionized form, it is the non-ionized form or neutral molecule that crosses the membrane. For example, newly prepared \(^{99m}\text{Tc}-d\), \(l\)-HMPAO is neutral and upon injection can cross the blood–brain barrier and enter the central nervous system; however, when it is left standing for more than 30 mins after preparation, there is an increase, in the amount of the ionized form, which does not cross the blood brain-barrier [2]. Therefore, preparations of \(^{99m}\text{Tc}-d\), \(l\)-HMPAO should not be used after 30 mins.

Filtration

When water flows in bulk across a porous membrane, it carries solutes that are small enough to pass through pores. These pores have a relatively small diameter (4 nm), and therefore only radiopharmaceuticals with small molecular weight of approximately 100–200 can pass through them. However, in the glomeruli of the kidney, where the pores are much larger (70 nm), hydrophilic radiopharmaceuticals with a molecular weight less than that of albumin (60 000) can pass through and be filtered. These radiopharmaceuticals include \(^{99m}\text{Tc}-\text{DTPA}\), \(^{99m}\text{Tc}-\text{glucoheptonate}\), \(^{99m}\text{Tc}-\text{phosphorus complexes}\) and metabolized \(^{99m}\text{Tc}\text{I}, \text{I-ECD}\).

SPECIALIZED TRANSPORT SYSTEMS

Active transport, facilitated transport and phagocytosis are described as specialized transport systems.

Active transport

This describes a transport system characterized by movement of substances across elec-