Pinocytosis

Fluid-phase endocytosis or pinocytosis is the engulfment of small droplets of extracellular fluid by membrane vesicles. The cell will internalize material regardless of its metabolic importance to that cell. The efficiency of this process is low. The fat-soluble vitamins A, D, E and K are absorbed via pinocytosis.

Receptor-mediated endocytosis

Many cells within the body have receptors on their cell surfaces that are capable of binding with suitable ligands to form ligand-receptor complexes. These complexes cluster on the cell surface and then invaginate and break off from the membrane to form coated vesicles. The binding process between the ligand and the receptor on the cell surface is thought to trigger a conformational change in the membrane to allow this process to occur. Once within the cytoplasm of the cell, the coated vesicles rapidly lose their coat and the resulting uncoated vesicles will promptly deliver their contents to early endosomes. Within the endosomes, the ligands usually dissociate from their receptors, many of which are then recycled to the plasma membrane. The dissociated ligands and solutes are next delivered to prelysosomes and finally to lysosomes, the end-stage of the endocytic pathway. Lysosomes are spherical or oval cell organelles surrounded by a single membrane. They contain digestive enzymes which break down bacteria and large molecules, such as proteins, polysaccharides and nucleic acids, which have entered the cell via endocytosis.

Phagocytosis

Phagocytosis can be defined as the engulfment by the cell membrane of particles larger than 500 nm. This process is important for the absorption of polio and other vaccines from the gastrointestinal tract.

Transcytosis

Transcytosis is the process by which the material internalized by the membrane domain is transported through the cell and secreted on the opposite side.

Paracellular pathway

The paracellular pathway differs from all the other absorption pathways as it is the transport of materials in the aqueous pores between the cells rather than across them. The cells are joined together via closely fitting tight junctions on their apical side. The intercellular spaces occupy only about 0.01% of the total surface area of the epithelium. The tightness of these junctions can vary considerably between different epithelia in the body. In general, absorptive epithelia, such as that of the small intestine, tend to be leakier than other epithelia. The paracellular pathway decreases in importance down the length of the gastrointestinal tract and as the number and size of pores between the epithelial cells decrease.

The paracellular route of absorption is important for the transport of ions such as calcium and for the transport of sugars, amino acids and peptides at concentrations above the capacity of their carriers. Small hydrophilic charged drugs that do not distribute into cell membranes cross the gastrointestinal epithelium via the paracellular pathway. The molecular weight cut-off for the paracellular route is usually considered to be 200 Da, although some larger drugs have been shown to be absorbed via this route.

The paracellular pathway can be divided into convective (‘solvent drag’) and diffusive components. The convective component is the rate at which the compound is carried across the epithelium via the water flux.

In celiac disease there is an increase in intestinal permeability due to a ‘loosening’ of the tight junctions. An approach to improving the absorption of poorly permeable drugs is aimed at making the intestine more ‘leaky’ by opening up the tight junctions.

Efflux of drugs from the intestine

Efflux proteins or transporters that expel specific drugs back into the lumen of the gastrointestinal tract after they have been absorbed, can play a key role on the bioavailability of drugs. One of the key counter-transport proteins is P-glycoprotein. P-glycoprotein is expressed at high levels on the apical surface of columnar cells (brush border membrane) in the jejunum. It is also present on the surface of many other epithelia and endothelia in the body, and on the surface of tumour cells. P-glycoprotein expression tends to be significantly higher in the small intestine than colon. P-glycoproteins were discovered because of their ability to cause multidrug resistance in tumour cells by preventing the intracellular accumulation of many cytotoxic cancer drugs by pumping the drugs back out of the tumours. Certain drugs with wide