12. Ion transporters in cellular physiology

Questions

- In what ways do membrane transporters contribute to the regulation of pH, cell volume and nutrient uptake?
- How does the action of diuretic drugs in kidney tubules modify urine output ?
- How does anion exchange activity contribute to O_2 loading and delivery by erythrocytes?

Ion transporters maintain ionic concentration gradients and regulate cell pH (Fig. 3.12.1) and volume (Fig. 3.12.2).

Regulation of pH

When the short-term buffering capacity (PO_4^{3-}, HCO_3^- and protein) of a cell is exceeded, pH is controlled by the transport of H^+ and HCO_3^- across the plasma membrane. Most cells possess both Na^+–H^+ exchangers (NHE) and anion exchangers, which extrude H^+ and HCO_3^- from the cell, respectively. Cell acidification activates NHE in most cells and Na^+–Cl^-–HCO_3^-–H^+ counter-transporters and Na^+–HCO_3^- cotransporters, where present. All are driven by inward movement of Na^+, hence Na^+/K^+-ATPase activity is crucial. Cell alkalinization is normally

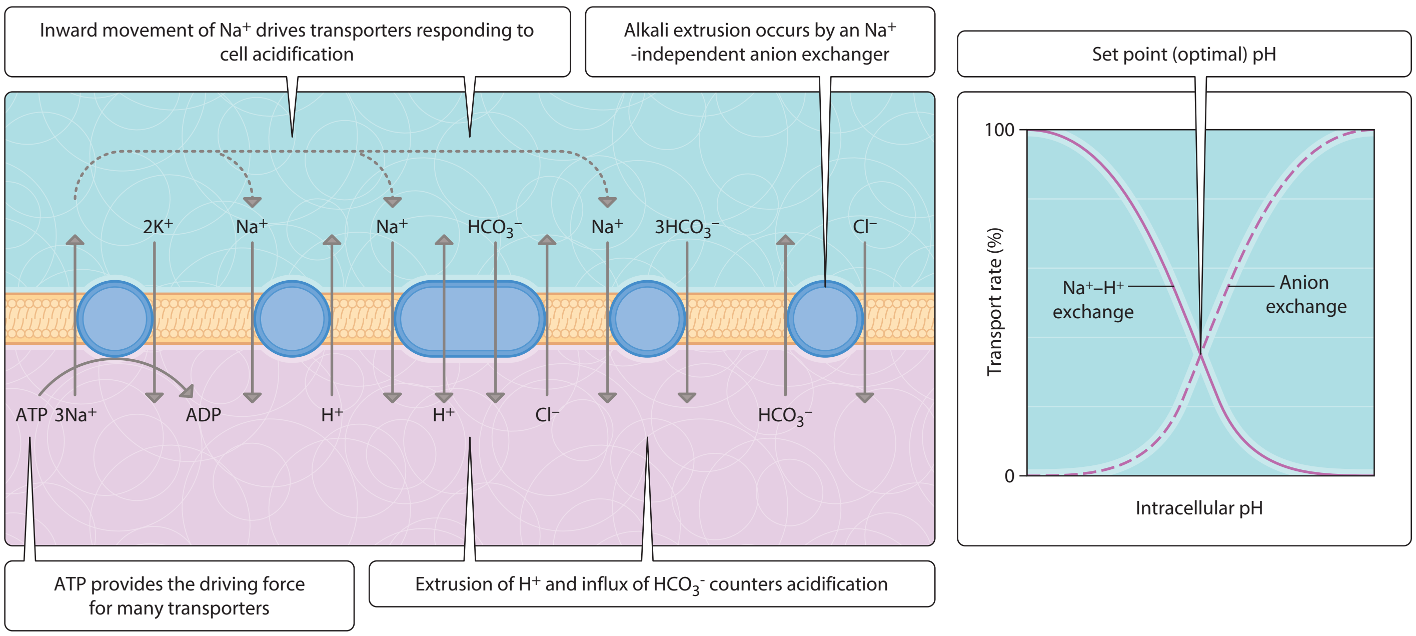

Fig. 3.12.1 Ion transporters in the regulation of pH.

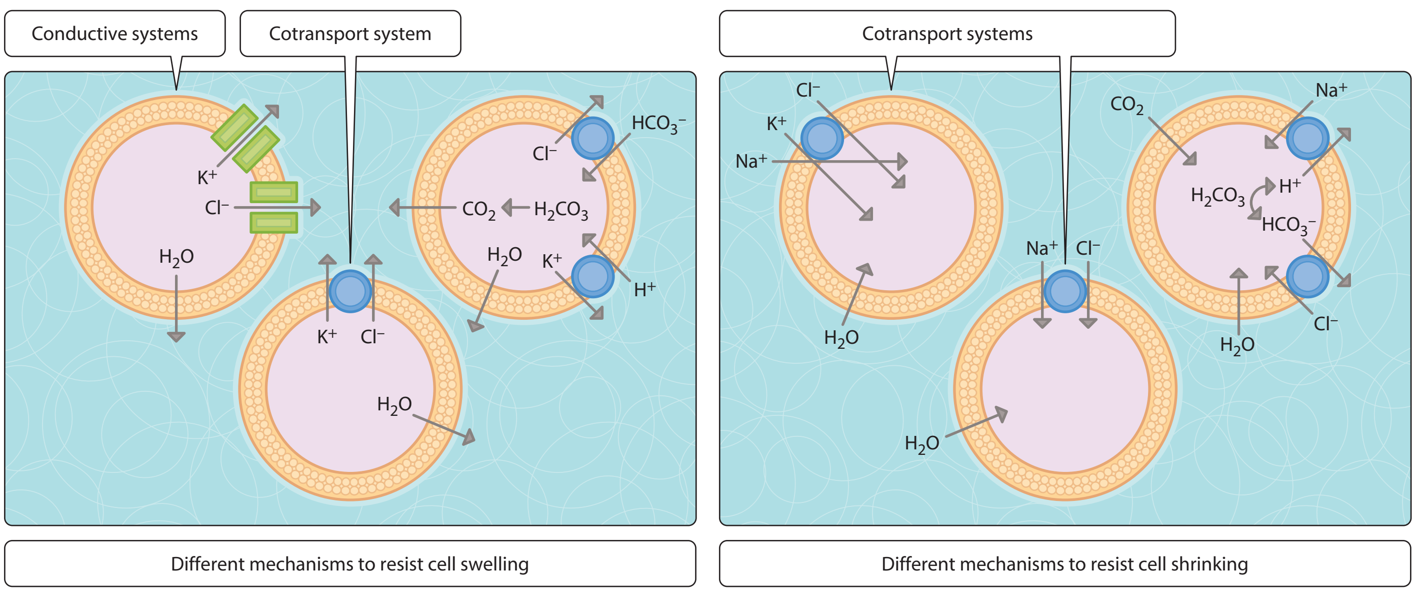

Fig. 3.12.2 Ion transporters in the regulation of cell volume.

controlled by the extrusion of HCO_3^- by Na^+-independent anion exchangers.

Volume regulation

Cell volume changes are mediated by the movement of water across membranes in response to modifications in osmotic strength. Osmotic gradients are altered by the movement of ions (Na^+, K^+ and/or Cl^-) or osmotically active compounds, such as sugars. Na^+/K^+-ATPase maintains a low intracellular Na^+ and provides the driving force for the passive diffusion of K^+or Cl^- in response to cell swelling and the Na^+–K^+–$2Cl^-$ cotransport system in response to cell shrinking, and/or the concerted action of proton and anion exchangers. In some cells, it appears that swelling-operated channels for efflux of organic solutes may exist (e.g. myoinositol, in the brain, or amino acids).

Transport of small molecules

Transporters that mediate facilitated diffusion of small solute molecules (e.g. glucose and amino acids) are often present in cell membranes. Where transport is in the same direction as the concentration gradient for the solute molecule, facilitated diffusion occurs (e.g. glucose uptake into adipose tissue, brain, liver and skeletal muscle). Rapid metabolism of glucose in the cell prevents slowing of uptake. Stimulation of glucose uptake by insulin in tissues such as adipose tissue and skeletal muscle occurs by the recruitment of glucose transporters, stored in vesicles, to the plasma membrane.

In both the intestine and kidney, solute molecules are actively transported coupled to Na^+ movement (Fig. 3.12.3). In red blood cells, anion exchange contributes both to transport of O_2 and CO_2 and to buffering in the circulation (Fig. 3.12.4).

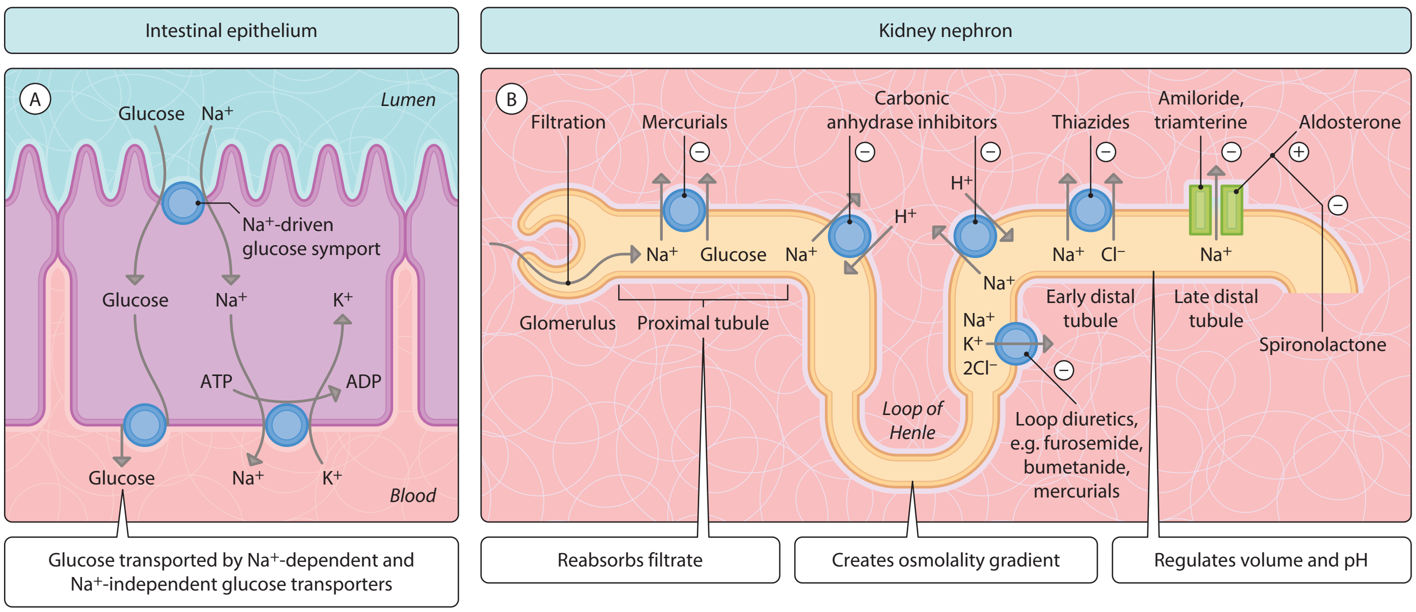

Fig. 3.12.3 Glucose uptake in the gut (A), and sodium reabsorption in the kidney (B).

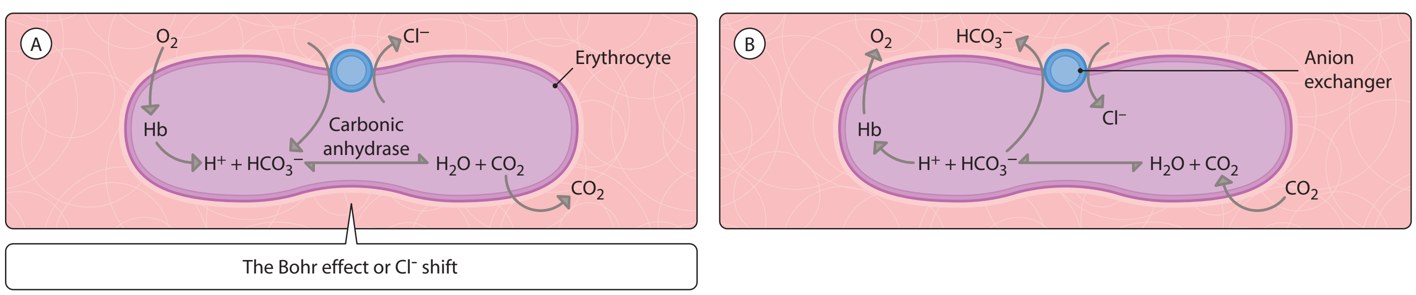

Fig. 3.12.4 Anion exchange in red blood cells. (A) Pulmonary capillaries; (B) capillaries in active metabolizing tissue. Hb, haemoglobin.