membrane of the kidney. Additionally, OAT-K1 and OAT-K2 are kidney-specific transporters structurally similar to OATP1. These transporters are sodium- and ATP-independent. Although it is assumed that these are efflux transport systems (lumen → urine), they may also be involved in luminal reabsorption.

Many compounds that are secreted by the organic anion secretory system are poorly lipophilic and therefore are not significantly reabsorbed by the kidney. However, there are weak acids (e.g., salicylates) that are sufficiently lipophilic to undergo tubular reabsorption. For these compounds, urine pH and urine flow rate will be expected to influence renal excretion.

6.4. Other Renal Transporters

6.4.1. Peptide Transporters

The kidney contains the peptide transporters, designated PEPT1 and PEPT2. In contrast to the low-affinity, high-capacity, intestinal oligopeptide transporter (PEPT1), PEPT2 is a high-affinity, low-capacity transporter. However, both transport systems are similar in terms of substrate specificity. Renal disposition of β-lactam antibiotics and ACE inhibitors involves PEPT2-mediated transport (61).

6.4.2. Nucleoside Transporters

The identification of nucleoside receptors (CNT1, CNT2) in the kidney suggests a role of these systems in the renal tubular transport of nucleosides and nucleoside analogs. However, the importance of this transport system as a clearance pathway for xenobiotics remains to be determined.

7. CENTRAL NERVOUS SYSTEM TRANSPORT

Unlike the other organ systems discussed in this chapter that function in drug clearance and bioavailability, the CNS is an important region for drug targeting. However, the movement of compounds from the systemic circulation into the CNS is limited by two general barriers: the BBB and the blood–cerebrospinal fluid barrier (BCSFB). The BBB, composed of brain capillary endothelial cells (BCECs), has traditionally been viewed as a lipoidal barrier with tight junctions between cells, rendering the BBB restrictive to CNS translocation of xenobiotics. The BCSFB consists of a single continuous layer of epithelial cells that line the endothelial cells of the choroids plexus (CNS1). The tight junctions of these epithelial cells form the BCSFB barrier.

Given the nature of the BBB and BCSFB, drug transport to the brain is a transcellular process, with lipophilicity being a primary determinant of the process. For a number of compounds, however, lipophilicity does not correlate with CNS penetration; that is, drug uptake across the BBB is lower than expected (40). On the basis of recent evidence, this discrepancy is