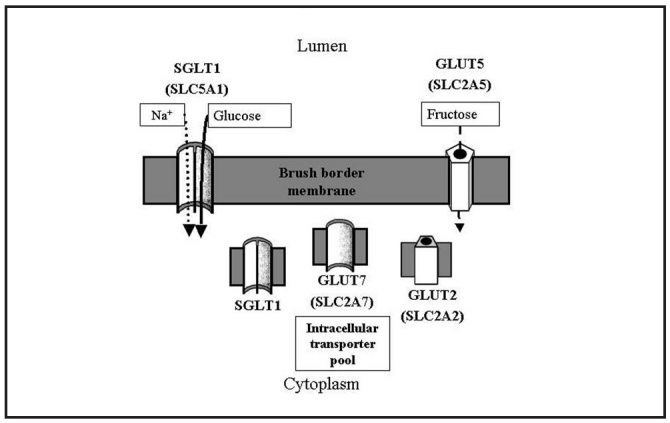

Figure 8-1A. Glucose and fructose are initially transported across the brush-border membrane via SGLT1, GLUT5. Additional transport capacity is retained within the enterocyte in the form of intracellular hexose transporters (SGLT1, GLUT7 and GLUT2).

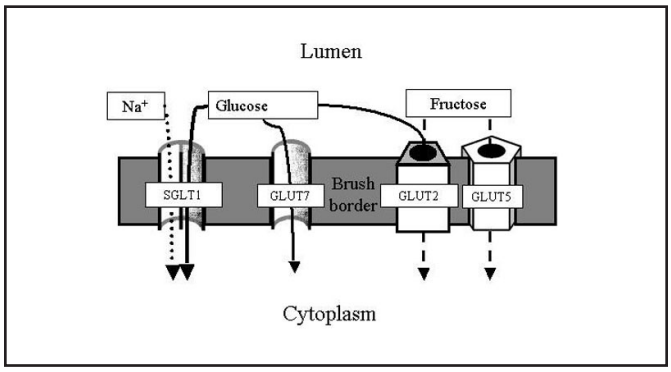

Figure 8-1B. Should the normal brush-border hexose transport mechanism (SGLT1 and GLUT5) become overwhelmed, SGLT1, GLUT2 and GLUT7 from a sub-apical intracellular store can be inserted into the brush border to increase epithelial hexose absorptive capacity by increasing the number of hexose transport proteins.

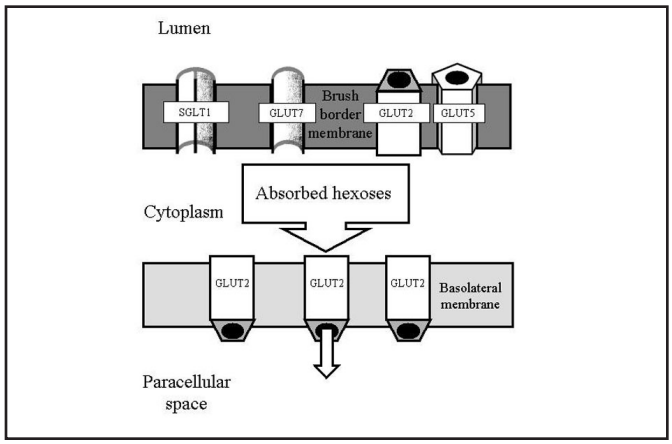

Figure 8-1C. Hexoses transported across the brush border and into the cytoplasm of the absorptive enterocyte are then transported across the basolateral membrane and into the paracellular space via the facilitative hexose transporter GLUT2.

An additional monosaccharide transport pathway stems from the interesting findings that GLUT2, the classic facilitative glucose transporter initially believed to be sequestered to the basolateral membrane, as well as a novel facilitative glucose-specific transporter GLUT7 (SLC2A7), can both be inserted into the brush border in response to high glucose loads in the lumen of the small intestine.[11,16,19] This model requires glucose to initially be transported by SGLT1, whose activity triggers protein kinase C (PKC) and mitogen-activating protein kinase (MAP-K), the end effect of which is the rapid insertion of GLUT2 into the brush border.[16] The rapid insertion of facilitative glucose (GLUT2 and GLUT7) and fructose (GLUT2) transport proteins in the apical brush border would then provide a pair of high-volume facilitative hexose transporters capable of handling the microclimate of high monosaccharide concentrated by brush-border dissacharidases.[16,19,20] Figure 8-1A-C illustrates the various carrier-mediated pathways which dietary monosaccharides can be transported across the absorptive enterocyte. Figure 8-2 illustrates the difference between specific carrier-mediated monosaccharide transport that occurs via absorptive enterocytes lining the upper villus region, as well as paracellular solvent drag between adjacent enterocytes.

Patients diagnosed with the rare genetic disorder known as Fanconi-Bickel disease demonstrate a defect in GLUT2 function. Accordingly, these patients present no classic basolateral hexose transport pathway. However, despite this defect, these patients can be managed with correct dietary manipulation. To this end, this condition has been studied and data indicates an alternative hexose delivery pathway wherein luminal glucose is transported into the cytoplasm via SGLT1. Subsequently, glucose is phosphorylated and transferred into the endoplasmic reticulum whereupon membrane-trafficking delivers glucose-containing vesicles to the basolateral membrane and hence delivered into the basolateral space.[20-23]

The crucial step in intestinal hexose transport remains sodium-coupled glucose transport through SGLT1. Following transport across the brush-border membrane, numerous signaling pathways, microclimate changes, and metabolic enzymes can act to regulate the rate of glucose hexose transport as well as the transfer of the absorbed hexoses into the basolateral space.[24-28]

Regulation of Monosaccharide Transport

Numerous studies have demonstrated an innate capacity for increased transport capacity in response to numerous stimuli.[17] Glucose itself has been shown to elicit rapid increases in active glucose transport mediated via SGLT1, as have other clinically relevant conditions such as prior exercise, forskolin treatment (and possibly other conditions that cause prolonged elevations in cyclic AMP), surgical anesthetics, heat shock injury, epinephrine, and various hormones such as epidermal growth factor and glucagon-like peptide-2 over a longer time.[27,29-40] In addition to expression patterns changing in accordance to circadian rhythm, changes in dietary intake of carbohydrates, leading to alterations in the luminal hexose load, have been