The volume of fluid ingested for rehydration is essential in determining the restoration of euhydration because it must be in excess of the water lost since the individual was last euhydrated. The formulation of any ingested beverage is also important as this affects the rate at which the fluid is emptied from the stomach, absorbed in the small intestine, and hence assimilated into the body water pool. This review highlights the essential role of the gastrointestinal tract in the maintenance of hydration status.

INTRODUCTION

In everyday life, water is continually being lost in the expired breath and by insensible sweating; it is also lost intermittently, mainly in urine, feces, and sweat. Although these losses are, in themselves, relatively small in comparison with total body water content,² they are cumulative, and the body’s ability to function normally is measurably diminished both mentally² and physically³ by being hypohydrated by as little as 2% of body mass. Levels of dehydration >10% of body mass are potentially fatal.⁵ In humans, the pattern of fluid consumption is usually periodic and in excess of that lost since the last intake⁶; with thirst and habit being important factors in controlling intake and the kidneys playing an important role in regulating excretion.⁷

FACTORS AFFECTING THE ASSIMILATION OF INGESTED BEVERAGES INTO THE WATER POOLS

The absorption of water and solutes occurs predominantly in the small intestine⁷; therefore, the rates of gastric emptying and intestinal absorption, delivery of the absorbed components to the circulation, and excretion of ingested beverages are integral factors in determining the effectiveness of a beverage for hydrating an individual. The efficacy of any solution to rehydrate is critically dependent on both the volume and formulation of the beverage. While the amount of fluid ingested will ultimately determine how well the individual is hydrated, the constituent solutes of the beverage markedly affect the rate at which the beverage enters the body pool,⁸ the duration of fluid retention,⁹–¹³ maintenance of the stimulus to drink,¹¹,¹² and restoration of electrolyte and substrate deficits.⁵,¹¹,¹⁴ While consumption of many beverages occurs for pleasure or from habit,⁶,¹⁵ the resultant intake of fluids will cause their water content to enter the body water pool following ingestion. How quickly this occurs is dependent on many factors, of which the 3 main elements are the rate of gastric emptying, the rate of intestinal absorption of the ingested beverage, and the speed at which the absorbed water enters the water pools.⁸,¹¹

ROLE OF THE GASTROINTESTINAL TRACT IN REGULATING WATER ABSORPTION

Formulation, palatability, and voluntary ingestion of beverages

Beverages range from distilled water, which contains only trace amounts of solutes, to liquid meals, which contain all the macronutrients, micronutrients, vitamins, and minerals required for normal nutrition. While there are various benefits to supplying nutrients in liquid rather than in solid form, the main advantage
lies in the faster absorption of fluids. The presence of nutrients such as carbohydrates, fats, and proteins in beverages not only supplies energy, it also affects the solutions’ organoleptic properties and their rate of absorption in the small intestine. Carbohydrates are the most common energy source included in commercial beverages, presumably because they are an adjunct to the flavorings used to encourage voluntary fluid consumption. It must also be recognized that the ingestion of beverages is very often associated with the consumption of food, and it is the global solute mixture in the chyme that affects the rate of intestinal absorption.

Although humans appear to enjoy the taste of sodium chloride, the human appetite for salt is appreciably lower than that of many animals. In addition, relatively high concentrations of sodium chloride are discerned as being bitter and may cause nausea. Following exercise-induced dehydration, the thirst response increases, but ingestion of electrolyte-free beverages can inhibit this response by lowering blood osmolality and may result in insufficient voluntary fluid intake to meet the water deficit–related rapid fall in plasma osmolality. Conversely, the reduction in the volume-dependent dipogenic stimulus that develops when fluids with a high sodium chloride content are ingested is an important factor in limiting ad libitum fluid intake during rehydration. Nevertheless, inclusion of electrolytes in rehydration beverages promotes retention of the fluid ingested. When hypohydrated individuals consume prescribed volumes (amounting to 150% of their sweat loss) of solutions containing relatively high (52–100 mmol/L) concentrations of sodium chloride, restoration of euhydration is prolonged compared with that which occurs when low-salt beverages are consumed. Because sodium is the main electrolyte in extracellular fluid, it is closely involved in the homeostatic control of body water. Consequently, many of the sensory signals and mechanisms that control water intake also influence sodium intake. Potassium, the main osmotically active cation in the intracellular space, does not play as pivotal a role as sodium in the maintenance of water balance.

**Gastric emptying of fluids**

Ingested fluids are not immediately available for assimilation into the body. They are initially stored in the stomach, and there is little net absorption of water or solute across the gastric mucosa. Any delay in gastric emptying is detrimental to the effectiveness of a beverage in situations where the constituents of the beverage are urgently needed by the body. In other circumstances, a beverage that slowly empties would delay the integration of its water content into the body water pool and, hence, slow urine production might be preferred.

A variety of methods have been used to measure gastric emptying of liquids in humans, and all have some advantages and disadvantages. While most claim that they have been validated, this generally means they have been compared with another “standard” method, usually scintigraphy, and that both have shown some measure of agreement in assessment. Typically, the comparison between methodologies has been assessed using correlation coefficients, with r values ≥0.60 being accepted as indicators of reasonably good agreement and, hence, validity. Much of the variance seen between these techniques is undoubtedly due to the large between-subject variability (~30%) seen among techniques, while within-subject variability is on the order of <10%. This would suggest that most techniques can be used to give an estimate of gastric emptying rates of various solutions, but that power analysis indicates that for a sample size of 8 individuals, there is an 80% chance of identifying a real difference in gastric emptying rates only when the emptying characteristics of the beverages differ by ≥30%. For a sample size of 10 individuals, the difference must be ≥27%.

The double sampling aspiration method, although subject to the same approximately 30% intersubject variance, has the advantage of being able to provide the following estimates: the change in emptying rate over time, the volume of gastric secretions and their effect on total volume, and the content of liquid in the stomach; endpoint gastric fluid volumes can be verified both by aspiration and by dye dilution. This technique can be used with individuals who are seated, standing, or exercising in a variety of modes and intensities. The disadvantages are that relatively large initial test volumes (usually between 400 and 600 mL) are ingested and that not all individuals can tolerate the aspiration tube.

**Factors affecting gastric emptying**

It is thought that the rate of gastric emptying is the main limiting factor in the assimilation of ingested fluids. Because of the complexity of the mechanisms that control the gastric emptying process, it is not surprising that there is considerable interindividual variation in emptying rates. However, most individuals do appear to be relatively consistent in the rate at which they empty the same solution on different occasions. Many factors have been shown to influence the rate of gastric emptying of solutions.

Apart from the receptors that respond to the volume of the stomach, the majority of receptors that regulate gastric emptying are found in the duodenum and ileum. These receptors appear to function primarily by initiating neural and hormonal responses that modify gastric and duodenal muscular
tone and the frequency of contraction. The position of the receptors in the small intestine suggests their main function is to inhibit gastric emptying and, thus, prevent the absorptive capacity of the intestine from being overwhelmed. Most of this information is derived from studies on resting individuals that used either single-time-point or serial-time-point aspiration techniques.

The various factors that affect the rate of gastric emptying of ingested fluids are summarized in Table 1 and described below.

### Gastric volume as a regulator of gastric emptying

The negative exponential nature of the gastric emptying curve indicates the importance of the volume of the stomach in controlling the rate of emptying (Figure 1). Because the stomach acts as a reservoir, it must be able to distend to accommodate the ingestate while maintaining a relatively low intragastric pressure. It is the slow, sustained contractions sweeping from the proximal to the distal regions of the stomach that mainly influence the pressure in the antral area of the stomach, and these remain unaffected by the muscle tone of the upper portion of the stomach. Increasing the pressure in the antral region increases the rate of gastric emptying of fluids. Increasing the volume of the gastric contents stimulates the activity of the stretch receptors in the gastric mucosa; this, in turn, raises the intragastric pressure and promotes faster emptying.

It is the total volume in the stomach that is important, which includes the volume of beverage ingested plus the volume of gastric secretions and swallowed saliva. Research has demonstrated that repeated ingestion of test solutions will maintain a high gastric volume and result in faster rates of gastric emptying than would have been expected from the contents of the beverages. Following ingestion of a single bolus of a liquid, there is an initial fast phase of gastric emptying when the volume in the stomach is at its greatest. The emptying rate then becomes progressively slower as the volume in the stomach decreases. This means a constant fraction of the volume in the stomach empties per unit time. By refilling the stomach at intervals, the volume in the stomach can be kept high and rates of gastric emptying equivalent to that of the initial phase can be maintained for prolonged periods (Figure 2).

### Energy density as a regulator of gastric emptying

Plain water empties rapidly from the stomach, while increasing the energy content of ingested solutions slows
the rate of gastric emptying. Surprisingly, the rate of gastric emptying is regulated such that approximately isoenergetic amounts of carbohydrates, proteins, fats, and alcohol are delivered into the duodenum. It is widely accepted that the receptors that respond to energy density lie outside the stomach; however, it is not known whether they are positioned on the luminal or serosal side of the small intestine or whether they respond to the same stimulus for each nutrient. While hyperglycemia can slow gastric emptying and hypoglycemia can accelerate the emptying of nutrient solutions, no hormone or gastrointestinal peptide has yet been identified as the unequivocal regulator of gastric emptying of energy sources.

The main nutrient source in most beverages is carbohydrate, and the majority of studies that examined the effects of energy content on gastric emptying used carbohydrate solutions. It is now well recognized that solutions with a carbohydrate content of ≤2.5% empty from the stomach at essentially the same rate as that of equal volumes of water, and most studies have shown that carbohydrate levels ≥6% unequivocally slow emptying. Even glucose concentrations of 4%–5% produce small but significant slowing of gastric emptying. Some studies have found no difference in the gastric emptying rate of water and carbohydrate solutions of up to 10%; however, most of this disparity is probably due to individual study design and participant population. Increasing the carbohydrate content of solutions slows the rate of emptying in proportion to the energy density, but it results in faster rates of carbohydrate delivery to the duodenum.

Osmolality as a regulator of gastric emptying

While it is clear that osmolality is a major controlling factor for solutions with no nutrient content, this is not the case for fluids that contain energy. Substitution of glucose polymers for glucose monomer can be used to reduce the osmolality of the solution while maintaining the total carbohydrate content. Several studies have examined the effect of replacing glucose monomer with polymers on gastric emptying, but the findings are not consistent. Most investigations have found little or no difference in gastric emptying of isoenergetic solutions of glucose monomers compared with glucose polymers, despite the often large differences in osmolality. This lack of difference implies that hydrolysis of the polymers occurs before reaching the small intestinal osmoreceptors. Therefore, the osmolality of the isoenergetic solutions are, in fact, equal at the point at which they come in contact with the regulating osmoreceptors. In one study, a 15% glucose polymer solution was found to empty faster than a 15% glucose monomer solution, but there was no difference in the emptying rates of 5% and 10% solutions of glucose monomer and polymer, respectively. Furthermore, the differences in gastric emptying could not be explained solely by the differences in the initial osmolality of the solutions. The addition of salts with a combined osmolality of ≤336 mosmol/kg to a 15% glucose polymer solution with an initial osmolality of 114 mosmol/kg did not significantly affect gastric emptying compared with the glucose polymer solution without electrolytes. Consensus opinion at present is that the energy density of a solution exerts a greater effect than osmolality in the regulation of gastric emptying and that the substitution of glucose polymer for monomer may slightly increase the rate of gastric emptying, but only at high energy densities.

Beverage temperature as a regulator of gastric emptying

Nerve conduction and muscle motility are both sensitive to changes in temperature, which implies that gastric emptying may be affected by the temperature of an ingested beverage. Several studies have shown that beverage temperature can slightly affect the gastric emptying rate, but only for about 10 min post-ingestion. The intragastric temperature appears to rapidly return to normal core levels, and the beverage temperature has little effect on overall rates of gastric emptying. The rate of recovery of intragastric temperature depends on the temperature of the beverage, the volume consumed, and the thermal capacity of the solution.
**Beverage pH as a regulator of gastric emptying**

The pH within the stomach is strongly acidic; as the chyme moves into and along the proximal small intestine, the acid is neutralized by the duodenal and pancreatic secretions. In a series of experiments, Hunt and Knox demonstrated that it was not the pH of the fluid that affected the rate of gastric emptying but the concentration and type of acids present. Low-molecular-weight acids were associated with greater inhibition of gastric emptying than high-molecular-weight acids. The type and concentration of acids commonly used in beverages are not thought to influence gastric emptying to a measurable extent.

**Beverage carbonation as a regulator of gastric emptying**

Many commercial beverages are carbonated to varying degrees. An early study suggested that carbonation of beverages enhances gastric emptying due to the increase in intragastric pressure caused by the release of carbon dioxide from the beverage. The technique used in that study is now thought to be qualitative at best and probably inappropriate for measuring the emptying rate of beverages. While ad libitum ingestion of carbonated beverages during running exercise tends to be less than that of a noncarbonated beverage, the differences are small and not always apparent. Several studies have shown that carbonation has little effect on gastric emptying at rest or during exercise. However, the majority of studies that investigated the effect of carbonation on gastric emptying used single endpoint measurement, which is liable to miss subtle differences in emptying rates. The lack of an effect of carbonation on gastric emptying is likely due to either the carbon dioxide being rapidly removed by eructation or the compressibility of the gas, making it ineffective in stimulating the stretch receptors.

**EXERCISE AS A REGULATOR OF GASTRIC EMPTYING**

Several mechanisms have been proposed whereby exercise intensity may affect gastric emptying, but there is little evidence to suggest which of these factors plays the major role. When discussing the possible effects of exercise on gastric emptying, the mode, intensity, and duration of the exercise are of fundamental importance. A number of studies have confirmed the findings of Costill and Saltin that steady-state cycle exercise at an intensity below about 70% of an individual’s VO_{2max} has little effect on gastric emptying; increasing the intensity above this level produces progressive, significant slowing of the emptying rates of ingested fluids. To date, the gastric emptying characteristics of elite endurance athletes exercising at their race intensity have not systematically been investigated. The majority of studies that have examined the effect of prolonged moderate exercise of up to 3 h on gastric emptying have been carried out on recreationally active individuals, and they have shown that high gastric emptying rates can be sustained during this type of exercise even in the heat. Other studies, however, have indicated that both hydration and hyperthermia can slow gastric emptying.

Upright exercise undertaken between 28% and 70% of VO_{2max} has been demonstrated to stimulate gastric emptying compared with rest, but emptying was slower when running at 75% VO_{2max}. Other researchers, however, have found little effect during running at moderate exercise levels compared with rest. The differences in findings among studies may be due to the beverages used or the study protocols. There appears to be no significant difference in gastric emptying between cycling and running exercise.

At high exercise intensities known to inhibit gastric emptying, the duration is usually too short for any benefit to be derived from the fluid ingested during the exercise. During most sports and other forms of physical activity, however, the period spent exercising is prolonged while the exercise is intermittent and the intensity is varied. Many of the factors that have been shown to induce fatigue during prolonged constant-intensity exercise have the same effect on intermittent exercise of sufficient duration. It has been assumed, however, that in most forms of intermittent exercise, the time spent at relatively low levels of activity is sufficient to allow appropriate amounts of any ingested beverage to be emptied and absorbed.

It has been shown in a series of studies that intermittent, variable-intensity exercise significantly slows gastric emptying, even when the overall energy expenditure is not much greater than that of steady-state exercise, which had no measurable effect on emptying. Overall, these studies demonstrated that intermittent, variable-intensity exercise significantly slows gastric emptying of fluids, but that ingestion of dilute carbohydrate-electrolyte solutions (CESs) can still enhance exercise performance and capacity as enough carbohydrate can be absorbed to be effective.

**INTESTINAL ABSORPTION**

The structure and functional architecture of the small intestine is adapted for absorption while presenting a barrier to potential noxious chemicals and organisms.
The major barrier for transport across the intestinal mucosa is the phospholipid bilayer of the enterocytes of the villi and the intercellular junctions between those cells. Lipid-soluble solutes can readily permeate cell membranes, are translocated through the cell, and pass across the basal membrane on the serosal side into the lymphatics or portal vein. Water and water-soluble solutes require different mechanisms to cross the intestinal mucosa. Embedded in the brush-border membrane of the enterocytes are various transport carriers with different degrees of specificity. These transport carriers unidirectionally translocate carbohydrate monomers, amino acids, dipeptides, and tripeptides from the luminal surface into a cell’s cytoplasm. This transport is often linked with sodium uptake, which plays a pivotal role in the absorption of many organic and inorganic solutes; as an osmotically active transportable solute, it has a major influence on water absorption. The current concept of net water movement across the intestinal wall is that water flux is passive and dependent on osmotic, hydrostatic, and filtration pressures. Water absorption from the intestine is considered to be a passive consequence of solute absorption, resulting from local osmotic gradients that promote net uptake of water from the lumen across the intestinal mucosa.

MEASUREMENT OF INTESTINAL ABSORPTION

Many methods have been described to study intestinal absorption in animals and humans. Both in vitro and in vivo techniques have been used in intestinal studies. Generally, studies that use the steady-state intubation method have been the most productive. All intubation methods require the participant to pass an oral tube into the intestinal region of interest to allow fluid and solute absorption to be measured over a prescribed length of the tract. Absorption is measured as the difference between the amount of test substance introduced into the intestinal segment and the amount that is subsequently recovered further down the lumen. The use of nonabsorbable markers allows studies to be made without quantitative recovery of all luminal contents. The results are expressed per unit length of intestine perfused (cm) per unit time (h).

There is fairly large between-subject variability in intestinal water and solute absorption, but intrasubject variability is much smaller. In one study in which 6 individuals were perfused with the same CES 7 times, the intersubject range for water absorption using the steady-state perfusion technique was 2.6–7.2 mL/cm/h with a coefficient of variance (cv) of 22%, but the within-subject variability had a minimum cv of 3% and a maximum of 12%. The steady-state perfusion method has been used to study mechanisms of water absorption and solute exchange throughout the intestine both at rest and during exercise. The method is limited by the requirement to minimize the radiation dose given during fluoroscopic positioning of the perfusion set in the intestine and by the ability of individuals to successfully pass the perfusion set into their intestine and to tolerate its presence in their gastrointestinal tract, particularly during exercise. This technique has also been criticized because steady-state conditions are unlikely to be normally maintained in the small intestine for extended periods following ingestion of beverages and that the high rates of perfusion (5–20 mL/min) used to establish steady-state usually only occur in the initial stages of gastric emptying after swallowing 500–600 mL of fluids. Nevertheless, to date, the perfusion model has been used to establish our understanding of many of the parameters that regulate intestinal absorption.

REGIONAL DIFFERENCES IN INTESTINAL FUNCTION

The stomach contents delivered to the duodenum are rapidly brought into osmotic equilibrium with the circulating plasma. This appears to be brought about by bidirectional movement of water and electrolytes across the intestinal lumen along osmotic and electrochemical gradients. The proximal small intestine is relatively permeable to water and electrolytes, and movement in either direction across the mucosa is dependent on the prevailing gradient for the specific molecules. The ileum is less permeable to water and electrolytes, and the colon is less permeable than the ileum.

One study investigated fluid absorption from different segments of the upper small intestine (total length of perfused gut was 75 cm) during cycle exercise. In this steady-state study, water absorption was fastest from the first 25 cm of intestine perfused (duodenum), followed by the adjacent 25 cm of the proximal jejunum, with the slowest water uptake from the next 25-cm segment of the perfused jejunum. Water flux was different from perfused plain water and a CES, with uptake being faster from plain water in the duodenum but slower than that of the CES in the first part of the jejunum. Total solute absorption (carbohydrate and electrolytes) was not significantly different between segments for a given solution or between solutions for a given segment.

In the human jejunum, net sodium absorption occurs only when the sodium chloride concentration of an isotonic solution is ≥127 mmol/L, with net efflux of sodium occurring into the lumen at lower concentrations. In the ileum, however, sodium is absorbed when...
the luminal concentration is ≥115 mmol/L. The addition of relatively small amounts of actively transported sugars enhanced sodium uptake by the jejunal but not by the ileal mucosa. In the jejunum, absorption of chloride appears to be determined by water and sodium transport rather than by a specific transport mechanism. In the ileum, however, chloride is actively absorbed even against strong chemical gradients by a linked anion-exchange mechanism, with chloride being exchanged for bicarbonate. This exchange mechanism does not operate in the jejunum, which is the predominant site of both chloride and bicarbonate absorption.

**ABSORPTIVE MECHANISMS**

Two transcellular routes and 1 intercellular route have been proposed to explain the absorption of water and hydrophilic solutes across the intestinal mucosa of the proximal small intestine. One transcellular route is via aquaporins that penetrate the enterocyte membrane. Because the inner surface of these aquaporins carries an electrical charge, both the 3-dimensional size and the charge of the molecule will influence the effective permeability. These aquaporins are known to be important routes that allow water and electrolytes to cross the mucosal barrier by osmotic and hydrostatic gradients and by diffusion along electrochemical gradients. The comparatively large physical size of monosaccharides and amino acids prevents their access via this route. Aquaporins comprise a family of highly efficient water-transporting membrane proteins that span the cell membrane of a variety of different cells throughout the body. Aquaporin-10 appears to be expressed exclusively in the duodenum and jejunum, with the highest expression in absorptive enterocytes at the tips of villi in the jejunum. One isofrom is also permeated by neutral solutes such as urea and glycerol, but not adenosine, while the other isofrom appears to transport only water.

The second transcellular route involves the carrier-mediated transporter systems that are embedded in the brush-border membrane of the enterocytes. Carrier transport is specific to individual molecules or to a group of similar molecules. For example, the carrier mechanism that transports glucose (sodium-dependent glucose transporter [SGLT]) is equally effective in transporting galactose but is not involved in the transport of fructose or lactose. There are families of carrier mechanisms that have different specificities for neutral, acidic, and branched-chain amino acids and for small peptides. Movement of solute against an electrical or concentration gradient requires energy; active transporters are carrier-mediated systems that are energy dependent and capable of moving solute against a concentration gradient. Active transporters use the electrochemical potential gradient of a cotransported cation, which is usually sodium, to supply the required energy. Therefore, they are ultimately dependent on the activity of the sodium–potassium–ATPase pump located in the basolateral membrane of the enterocytes. Other carriers, termed facilitated transporters, are driven by concentration differences that favor absorption of a specific solute; however, the carrier mechanism increases the rate of transport compared with simple diffusion. Facilitated transporters are energy and sodium independent but they are less efficient, especially at relatively low solute concentrations, than the active transporters. While glucose is mainly absorbed when it is actively cotransported with sodium by the transporter SGLT1, the facilitated transporter GLUT5 absorbs fructose. In addition to the brush-border transporter systems, there are a number of electrically neutral ion-exchange mechanisms and ion-cotransport systems sited in the enterocyte membrane. In the jejunum, sodium and chloride are transported into the enterocyte via a dual-coupled antiport system that involves hydrogen and bicarbonate ions. In the ileum, chloride enters the enterocyte in exchange for bicarbonate.

The intercellular route occurs through the tight junctions between the enterocytes at the luminal side of the lateral edge of the cells. Below this junction, the lateral membranes diverge to form the intracellular lateral space that opens into the interstitial space of the villus core. The perijunctional actomyosin ring of the intestinal tight junctions can be activated to increase or decrease the permeability of the intercellular junction. Initiation of any of the active transporters causes the tight junctions to become more permeable to water and solute.

Water absorption from isotonic luminal fluid is mainly a passive consequence of solute absorption that establishes a local osmotic gradient that promotes the net uptake of water from the intestine. A number of different models have been proposed that couple solute and water absorption in the absence of, or against, moderate osmotic gradients. In each paradigm, active uptake of nutrients and/or sodium initiates an osmotic gradient, which causes an increase in the lumen-to-mucosa water flux. It has been clearly established that the intestinal absorption of solutes such as glucose promote net water uptake, which in turn increases the nonselective transport of additional solute from the intestinal lumen.

**FACTORS THAT AFFECT INTESTINAL ABSORPTION**

Most studies that have investigated the factors that affect intestinal absorption in humans have used steady-state perfusion methods in a segment of intestine.
Absorption of solute by active and passive means promotes water absorption\textsuperscript{6,71,74,75,79} and the flow of water through the tight junction can act as a conduit, conveying a heterogeneous sample of the intestinal contents across the intestinal mucosa by solvent drag.\textsuperscript{89,91} Therefore, absorption of both water and solute are closely related, and each can assist the absorption of the other.\textsuperscript{6,26} The factors that affect the rate of intestinal absorption of water from ingested beverages are summarized in Table 2.

**Effect of intestinal flow rate on absorption**

Because the normal pattern of gastric emptying of solutions is not linear, the flow rate through the intestine is variable. In the steady-state perfusion method, although the rates of perfusion used (5–15 mL/min) are similar to normal gastric emptying rates of liquids in humans, the flow rate is held constant. It is possible for individuals to ingest beverages at a frequency and volume that maintains relatively constant rates of gastric emptying, which can be used to calculate fluid and solute flux in the proximal small intestine. However,\textsuperscript{92} this is not a usual occurrence in life. Studies have shown that increasing the perfusion rate in the intestinal segment produces greater absorption of water and solute; however, this appears to be due to the increase in the absolute solute load in the lumen rather than the greater fluid volume.\textsuperscript{93}

**Effects of nutrient type and concentration on intestinal absorption**

The major nutrient source in most beverages is carbohydrate in the form of sucrose, glucose monomer, maltodextrins, fructose, or cornstarch. Several studies have shown that the rate of glucose absorption in the human jejunum appears to plateau as the glucose monomer content in the lumen approaches about 200 mmol/L.\textsuperscript{71,93} Although greater glucose monomer concentrations are associated with luminal hypertonicity and reductions in water absorption, rates of glucose absorption still tend to increase, at least up to a glucose concentration of around 555 mmol/L.\textsuperscript{91} It is thought that the majority of glucose absorption up to the 200-mmol/L concentration is due to the SGLT1, which becomes fully saturated above this concentration. Thereafter, the more gradual increase in glucose absorption is caused by diffusion down the concentration gradient and/or by solvent drag.\textsuperscript{91} Although glucose absorption tends to increase with increasing luminal concentration, the main effect on glucose and water absorption occurs with perfusion solutions that have a glucose content of approximately 200 mmol/L (i.e., 3.6% glucose w/v).

The substitution of disaccharides or maltodextrins for equimolar amounts of glucose monomers has been reported to increase glucose absorption.\textsuperscript{76,94} While most hypotheses have stressed that this effect is due to an improved rate of binding between SGLT1 and the hydrolysis products of maltodextrins, others have suggested that membrane-bound digestion results in a high local concentration of glucose monomer from which nonspecific paracellular absorption occurs. However, it is not a universal finding that glucose absorption is faster from maltodextrins than from equivalent concentrations of glucose monomers.\textsuperscript{68,95} Because solutions containing maltodextrins have a lower osmolality than those of equivalent amounts of glucose monomer, water uptake is usually reported as being faster from the

---

**Table 2** Summary of the factors that affect the rate of intestinal absorption of water from ingested beverages

<table>
<thead>
<tr>
<th>Factor</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric emptying rate</td>
<td>Fast rates of emptying increase intestinal absorption</td>
</tr>
<tr>
<td>Osmolality</td>
<td>Water absorption rates are faster from moderately hypotonic beverages (200–260 mosmol/kg), but in the duodenum marked hypertonicity may be more effective; hypertonicity retards water absorption</td>
</tr>
<tr>
<td>Carbohydrate content</td>
<td>Active cotransport of glucose and sodium facilitates the absorption of glucose and promotes osmotic gradients that support water absorption; facilitated transport of fructose is slower and is less effective in supporting water uptake; high concentrations of maltodextrins may assist absorption by producing relatively lower beverage osmolality than would occur with the same glucose monomer content</td>
</tr>
<tr>
<td>Other actively transported solutes</td>
<td>Actively transported amino acids, peptides, and organic acids that are linked with sodium absorption promote intestinal water uptake</td>
</tr>
<tr>
<td>Sodium concentration</td>
<td>Intestinal sodium absorption is closely linked with water transport, but it is not clear if it is required in rehydration beverages, as sodium from the blood rapidly effluxes into lumen; no other ion has been shown to be as crucial for water absorption</td>
</tr>
<tr>
<td>pH</td>
<td>It is unlikely that commercial beverage formulations will affect the pH buffering capacity of the intestine; an acidosis appears to enhance water and sodium absorption but not that of glucose</td>
</tr>
<tr>
<td>Temperature</td>
<td>Because the stomach rapidly equilibrates the temperature of beverages, it is predictable that the luminal contents are always at body temperature</td>
</tr>
<tr>
<td>Exercise</td>
<td>Steady-state exercise levels below 70% VO\textsubscript{2}max have little effect on intestinal absorption of carbohydrate solutions; however, exercise-induced changes in perfusion of the capillary bed may interfere with isotopic water tracers measured in the blood</td>
</tr>
</tbody>
</table>
Effect of intestinal osmolality on absorption

In a fasted individual, the normal osmolality of the luminal contents of the small intestine is usually between 270 and 290 mosmol/kg, which is approximately isotonic with human serum. Following ingestion of food and/or beverages, the osmolality of the duodenum and jejunum changes in accordance with the osmolality of the gastric contents and the rate at which those contents are emptied into the small intestine. Thereafter, luminal osmolality is eventually returned to isotonicity due to the bidirectional movement of water and electrolytes across the proximal intestine. After the luminal contents have been made isotonic, they remain so during the remaining process of absorption.

The time required to achieve isotonicity varies with the osmolality and nutrient load of the gastric efflux. For example, water is rapidly made isotonic within the duodenum and proximal jejunum by the influx of electrolytes, whereas hypertonic beverages such as fruit juices and soft drinks require a greater period of time and, thereby, traverse a greater length of small intestine before the luminal contents regain isotonicity. Solutions with an osmolality of >290 mosmol/kg initially cause a net efflux of water from the body water pool into the intestinal lumen. The time required to achieve isotonicity reduces the rate of net water absorption as water efflux increases in proportion to the level of hyperosmolality of the luminal contents. Hypertonic solutions are eventually absorbed, but this occurs further down the small intestine, after the solution has been made isotonic. This delay coupled with the initial net movement of water from the circulation to dilute the luminal contents renders hypertonic solutions less effective in promoting rapid rehydration than beverages with a lower osmolality.

Absorption of solute from isotonic solutions can produce local osmotic gradients that are sufficient to promote net water absorption from the intestinal lumen. However, if the luminal contents have an osmolality of <270 mosmol/kg, water will follow the osmotic gradient and move from the lumen across the mucosa. Hypotonicity of the luminal contents can be an additive factor to that of solute absorption for promoting net water absorption. Many studies have demonstrated that faster rates of water absorption occur in the jejunum from hypotonic compared with isotonic CES. This would suggest that drinking water or mineral waters that are markedly hypotonic (i.e., with an osmolality generally between 5 and 15 mosmol/kg) would promote high rates of water absorption. However, water absorption is faster from isotonic CES than from plain water in the jejunum. Water absorption from plain water in the duodenum has been reported as being more rapid than that from CES but slower than from CES in the jejunum. This same group found that water absorption rates were faster from plain water with an osmolality of about 30 mosmol/kg than from a hypotonic 6% carbohydrate solution entering the duodenum with an osmolality of approximately 200 mosmol/kg, but the rates were similar to those from a 4% carbohydrate solution with an osmolality of 260 mosmol/kg.

In the absence of actively transported molecules (e.g., carbohydrates, amino acids), net sodium absorption from the duodenum and jejunum occurs only when the luminal concentration of this cation is about 127 mmol/L. This is thought to be the main reason for the relatively poor rate of water absorption from the infusion of plain water; the resulting efflux of electrolytes, mainly sodium, down concentration gradients will cause some body water to cross the mucosa into the jejunal lumen, thereby reducing the villous tip osmolality and, hence, the lumen-to-villous osmotic gradient. It has been proposed that it is the reabsorption of previously secreted endogenous...
bicarbonate from the luminal contents linked with sodium cotransport that creates osmotic gradients suitable for water absorption from plain water in the jejunum. As such, water absorption from plain water is considered to be relatively slower than from CES along the majority of the length of the proximal small intestine.

Most studies have shown that both glucose solutions and nutrient-free solutions with an osmolality of <200 mosmol/kg produce slower rates of water absorption in the jejunum than do similar solutions with an osmolality of between 200 and 260 mosmol/kg. Therefore, the most effective osmolality range for rehydration solutions appears to be relatively narrow because even small differences in osmolality have marked effects on water absorption. For example, in one study in which the total carbohydrate and sodium content of the perfusion solutions were similar, but osmolality differed, net water absorption was about twice as fast from a moderately hypotonic (229 mosmol/kg) solution than from an isotonic (277 mosmol/kg) solution, which was faster than from a moderately hypertonic (352 mosmol/kg) solution (Figure 3).

**Effect of electrolyte content on intestinal absorption**

In the human jejunum, sodium is actively cotransported with a variety of sugars, amino acids, peptides and pyrimidines, organic acids, and bile salts. Bicarbonate ions promote sodium absorption in the jejunum by a pH-independent, dual-coupled antiport system that involves chloride and hydrogen ions. Because of the essential role of sodium in active nutrient transport and water absorption, it has been thought necessary to have it included in oral rehydration solutions used to replace fecal losses in diarrheal disease. However, because sodium from the blood rapidly effluxes into the proximal small intestine, it has been argued that exogenous sodium is not required to activate nutrient transporters. Perfusion studies have shown that the exclusion of sodium from glucose solutions does not have a marked detrimental effect on water absorption. Nevertheless, substitution of mannitol or magnesium for sodium results in 23% and 45% reductions in glucose uptake, respectively. In addition, enhanced carbohydrate absorption from maltose and maltodextrin solutions has been associated with luminal sodium concentrations of >100 mmol/L.

The other major electrolytes of the body (e.g., potassium, magnesium, calcium) are absorbed down electrochemical gradients or by carrier-mediated processes. The inclusion of electrolytes in rehydration solutions increases the osmolality of the solution and, with the exception of sodium, the presence of electrolytes does not enhance water absorption. Most studies that have investigated the effect of sodium on water absorption have used chloride as the accompanying anion. Nevertheless, other anions such as acetate or citrate can enhance water absorption from glucose–sodium solutions. In all of these studies, however, the major anion in the intestinal lumen was chloride. For reasons of palatability, chloride is probably the anion of choice in beverages that contain sodium.

**Effect of beverage temperature on intestinal absorption**

The stomach rapidly equilibrates the temperature of ingested beverages to approximate internal body temperature. Consequently, it is unlikely that significant amounts of markedly hot or cold fluid are emptied into the duodenum.

**Effect of beverage pH on intestinal absorption**

Several studies in animals have examined the effect of alterations in acid–base balance on water and solute absorption in the small intestine; changes in intestinal luminal pH are known to affect mucosal ion transport. Little work has been carried out in humans, in one study, perfusing the jejunum with a CES containing 23 mmol/L bicarbonate produced a mean luminal pH of 6.6, which was higher than that produced when tartrate was used. Water and glucose absorption was faster from the bicarbonate solution than from the tartrate. However, it is unclear from this study whether the improved absorption rates were due directly to...
bicarbonate uptake that enhanced intestinal transport or to a buffering effect that increased active absorption of glucose.

Most commercial beverages are acidic, in part, to extend their shelf life and to improve their palatability.6 However, these beverages have little buffering capacity, and the pH of the intestinal luminal contents is probably little affected by the levels of acidity present in most beverages.

**Effect of exercise on intestinal absorption**

Few studies have investigated the effect of exercise on intestinal absorption. This is largely due to the practical difficulties associated with perfusing the small intestine in individuals who are exercising. In an early study, treadmill exercise at 70% of VO\textsubscript{2max} was shown to have no discernible effect on intestinal absorption of water or solute.116 Another investigation found no difference in absorption rates between rest and moderate cycle exercise (30–70% VO\textsubscript{2max}) from either water or a CES.81

In a series of studies using a triple lumen perfusion model sited in the duodeno–jejunum, with gastric emptying controlled at a steady rate, the effects of beverage osmolality, sodium concentration, and carbohydrate content on fluid absorption during constant load cycle exercise at or below 70% VO\textsubscript{2max} was investigated. These studies indicated that net water absorption was fastest in the duodenum from plain water than from any of the three 6% CES tested. However, over the entire 50 cm of perfused intestinal segment, no differences in water uptake could be detected among plain water and hypotonic, isotonic, or hypertonic CES.104 Increasing the sodium concentration over the range 0–50 mmol/L in 6% carbohydrate beverages failed to improve water uptake, but luminal sodium concentration increased markedly along the length of perfused segment.115 In exercising individuals who were previously hypohydrated by 2.7%, net water uptake was fastest from plain water and an isotonic 6% carbohydrate solution compared with a hypertonic 8% carbohydrate solution, which was greater than from a hypertonic 9% carbohydrate solution.117 While the gastric emptying rate of all solutions was fixed, which is not what would have been expected to happen if the beverages had been normally ingested, the same group of investigators showed that individuals can repeatedly ingest carbohydrate beverages in quantities that maintain gastric emptying rates at a relatively fixed rate similar to that used in perfusion studies.92

![Plasma deuterium accumulation at rest and during exercise at 42%, 61%, or 80% VO\textsubscript{2max} after ingestion of the same carbohydrate–electrolyte solution containing deuterium oxide.](https://academic.oup.com/nutritionreviews/article-abstract/73/suppl_2/57/1930269/2571930269)

Using a water tracer technique, the accumulation rate of the isotopic label in the circulation decreased in proportion to exercise intensity (40%–80% VO\textsubscript{2max}), and the time to peak tracer concentration in the blood was longer with increasing exercise intensities118 (Figure 4). These results suggest a decreased availability of ingested fluids during exercise; however, whether this was due to changes in intestinal absorption or

---

**Figure 4** Plasma deuterium accumulation at rest and during exercise at 42%, 61%, or 80% VO\textsubscript{2max} after ingestion of the same carbohydrate–electrolyte solution containing deuterium oxide. Reproduced from Lambert et al.130 with permission.
perfusion of the splanchnic vascular bed could not be ascertained.\textsuperscript{118} It is likely that intermittent high-intensity sprinting will reduce absorption to at least the same extent as it affects gastric emptying.\textsuperscript{68,69,70}

**INTEGRATION OF MEASURES OF GASTRIC EMPTYING AND INTESTINAL ABSORPTION**

Several studies have directly measured both gastric emptying and intestinal absorption rates separately and have derived estimates of the relative importance of each in determining the incorporation of beverage constituents in the body water pools.\textsuperscript{92,116} These studies are rather artificial as the conditions of the model are never likely to occur naturally in the gastrointestinal tract, yet they have produced important basic information regarding factors that affect intestinal absorption of ingested solutions.

Isotopic tracers were used in perfusion studies in the early 1960s to differentiate the effects of the bidirectional fluxes of water and sodium on the specific rates of the net absorption of each.\textsuperscript{119} Although the isotopic water tracer technique does not determine net rates of gastric emptying and/or intestinal fluid absorption, comparison of the unidirectional flux of the tracer appears to give a measure of the relative rates of absorption from different beverages.\textsuperscript{8} In addition, this technique has demonstrated differences among beverages that reflect the known combined gastric emptying and intestinal absorption patterns of those beverages.\textsuperscript{8,55,120,121} While some investigations have cast doubt on the usefulness of the isotopic technique for comparing water uptake from beverages,\textsuperscript{122,123} the disparities in the studies’ findings have been explained by technical difficulties in the respective experimental protocols.\textsuperscript{24}

**USE OF ISOTOPIC TRACERS TO ASSESS UPTAKE OF WATER FROM THE GASTROINTESTINAL TRACT INTO THE BODY WATER POOLS**

The stable isotope deuterium oxide (2H\textsubscript{2}O) and the radioactive isotope tritium oxide appear to be appropriate tracers for water\textsuperscript{124,125} and have been used in studies that investigated the total body water content, body water turnover, water exchange between tissues,\textsuperscript{124,125} and water availability from ingested beverages.\textsuperscript{8,120,121,126–128} Tritium oxide is radioactive, and its use raises health issues. However, it can be utilized in small doses, and it has a biological half-life of 7–14 days in the human body.\textsuperscript{125} The stable isotope oxygen-18 has also been used to determine total body water in humans\textsuperscript{129}; it could be used to assess water uptake from the gastrointestinal tract, and it has the advantage that it can be detected in breath samples.\textsuperscript{129}

These tracers are easily incorporated into beverages, are tasteless and odorless, and are distributed into the body water pools from ingested beverages at a rate that is comparable to water. The volume of test beverage consumed in investigations can be similar to that usually ingested by euhydration individuals.\textsuperscript{55,130}

**LIMITATIONS OF WATER TRACER METHODOLOGY**

Measurement of 2H\textsubscript{2}O by mass spectrometry has a sensitivity of approximately 0.2 ppm\textsuperscript{131} and a cv of <2%.\textsuperscript{132} Determination by infrared spectrometry can reliably detect differences of ≥10 ppm and a cv of 4.8%.\textsuperscript{17} Between-subject variance in deuterium (\textsuperscript{2}H) accumulation rates in the circulation from an ingested CES was 38% measured by mass spectrometry,\textsuperscript{132} and 40% by infrared spectrometry.\textsuperscript{130} Power analysis indicates that for a sample size of 10 individuals, there is an 80% chance of identifying a real difference in water absorption rates only when the fluid absorption characteristics of the beverages differ by ≥35%. Quantification of the tritium tracer can be made using liquid scintillation counters, with assay sensitivity similar to that of mass spectrometry. The radioactive dose received by individuals can be maintained within normal background radiation levels.\textsuperscript{125}

Several methods have been used to model the absorption of water tracers from ingested solutions. In many studies investigating unidirectional \textsuperscript{2}H fluxes, the temporal appearance of the tracer in the circulation over the whole of the sampling period has been incorporated into the circulation.\textsuperscript{120,123,126–128} Davis et al.\textsuperscript{120,127,128} used blood \textsuperscript{2}H enrichment area-under-the-curve (AUC) profiles produced by their different test beverages sampled over 180 min post-ingestion. While they found that the \textsuperscript{2}H AUC was less for beverages containing 40% and 15% glucose than from hypotonic saline or a 6% glucose solution, they could not identify differences between the 2 beverages with the highest levels of carbohydrate nor between the saline and the 6% glucose solution. Currell et al.\textsuperscript{126} demonstrated a smaller AUC following ingestion of a 6% glucose beverage compared with that from water or a 6% glucose–fructose solution. This group also showed that the \textsuperscript{2}H AUC was greater from a 3% glucose solution than from water, which was greater than from a 6% or a 9% glucose solution.\textsuperscript{133} The addition of sodium (range 0–60 mmol/L) to a 6% glucose solution did not noticeably affect the enrichment curve.\textsuperscript{133} In another study, no differences in \textsuperscript{2}H AUC profiles were found between water and 4 different CESs containing various carbohydrates ranging in concentration from 6% to 8%.\textsuperscript{127}
The use of the AUC measure, which can include a disproportionately large section of the dissipation and equilibration phases of the tracer contained in the ingested beverages, is likely to decrease the sensitivity of comparisons of absorption rates between solutions (Figure 5). A more rational comparison for evaluating water absorption rates from ingested beverages would appear to be the accumulation slope to peak concentration of the tracer in the circulation. A more rational comparison for evaluating water absorption rates from ingested beverages would appear to be the accumulation slope to peak concentration of the tracer in the circulation.

The slope of the $^2$H accumulation rate in the circulation to time to peak enrichment ($T_{\text{max}}$), calculated by linear regression from samples collected before and after ingestion of the test beverages, was found to be faster following consumption of a 3.6% CES than from water. However, no differences were detected in AUC enrichment post-ingestion or in peak concentration between the 2 solutions. Using the same measure, $^2$H enrichment in the circulation was faster from dilute glucose solutions than from fructose solutions with the same carbohydrate concentration, and from a 2% glucose solution compared with a 10% glucose solution. The use of the parameters $T_{\text{max}}$, $P_{\text{max}}$, and rate of deuterium accumulation to $T_{\text{max}}$, appear to adequately model the known gastric emptying and intestinal absorption rates of most of the carbohydrate solutions tested to date.

**CONCLUSION**

The volume of fluid ingested for rehydration is essential in determining the restoration of euhydration. However, the formulation of beverages is also important as it affects the rate at which the beverage’s water content enters the body water pool and, hence, its effect on the hydration status of an individual. Because there is no net absorption of water in the stomach, the gastric emptying and small intestinal absorption rates of consumed beverages critically affect the speed at which the aqueous portion of a beverage is assimilated into the body. Both a high volume and a low energy content of a beverage improve the rate of gastric emptying. Low osmolality also speeds emptying from the stomach; nevertheless, it is energy density that has the greater effect. Water is rapidly emptied, but 2%–4% glucose solutions appear to leave the stomach just as quickly. Net water uptake from the proximal intestinal lumen occurs along osmotic gradients that are promoted by the absorption of solute. The active cotransport of glucose and amino acids is facilitated by the presence of sodium in the intestinal lumen.

---

**Figure 5** Typical plasma deuterium enrichment curve following ingestion of a dilute carbohydrate–electrolyte solution labelled with the tracer. Influx is the net movement of deuterium from the small intestine into the circulation. Efflux is the movement of deuterium from the circulation into the extravascular water pools.
acids with sodium enhances water absorption. Moderate hypotonicity of the luminal contents enhances water absorption.

Measurement of gastric emptying rates of solutions indicates between-subject variability to be about 30%, while within-subject variability is <10%. Intestinal perfusion techniques that bypass the stomach have between-subject variability levels of approximately 22% and within-subject variability of ≤12%. Whether it is learned responses based on the dietary habits of the individual or the individual’s genetic makeup that determines the specific gastric emptying and intestinal absorption rates is, at present, unknown. The mechanisms that establish the relatively small within-subject variance compared with that of between-subject variance requires further research. Studies have been carried out using a combination of gastric emptying and intestinal perfusion to try to determine overall rates of water assimilation from beverages. Although each of these techniques is rather artificial, they have produced important basic information regarding factors that affect absorption of ingested solutions. The unidirectional accumulation rate of isotopic water tracers into body fluids broadly follows the pattern of the integrated effects of gastric emptying and intestinal absorption of these labeled beverages.

Further research is needed to identify the interaction of neurotransmitters and hormone responses following consumption of beverages and their relative influence on the control of net absorption of water and solute from ingested solutions.

Acknowledgments

The author thanks the staff of the European Hydration Institute for their hard work in setting up and running the Workshop on Human Hydration, Health and Performance.

Funding. J.B.L. was contracted and funded by the European Hydration Institute. He received financial reimbursement for travel and accommodation expenses and an honorarium from the European Hydration Institute for his participation in the conference and for writing this manuscript.

Declaration of interest. The author has no relevant interests to declare.

REFERENCES
