Effects of Glycerol-Containing Hyperhydration Solutions on Gastric Emptying and Intestinal Absorption in Humans and in Rats: What is Known and Unknown

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Running head: Glycerol hyperhydration and gastrointestinal functions
Abstract

Glycerol-induced hyperhydration (GIH) has been shown to improve fluid retention and endurance performance, compared with water-induced hyperhydration. The goal of this article is to report on what is known and unknown about how glycerol-containing hyperhydration solutions (GCHS) are processed at the stomach and intestine level, propose strategies to improve the efficacy of GIH and provide research questions for future studies. Through statistical analyses, it was demonstrated that the effectiveness of GCHS in increasing fluid retention is maximized when fluid ingestion is in the upper range of what is normally administered by studies (~26 ml · kg bodyweight\(^{-1}\)) and the duration of the protocol is no longer than the time it takes for the glycerol-fluid load to be totally or nearly completely integrated inside the body. The rate of gastric emptying and intestinal absorption of GCHS is unknown. However, based upon an analysis of indirect evidence obtained from human studies, it is proposed that most glycerol (~80 g) and fluid (~1700 ml) ingested during a typical GIH protocol can be integrated inside the body within 60 to 90 min. Whether the stress associated with competition could alter these figures is unknown. Research in rats indicates that combining glycerol with glucose at a 3:1 ratio accelerates the intestinal absorption of both glycerol and water, thereby potentially improving the efficacy of GIH. Human studies must be conducted to determine how GCHS are processed by the gastrointestinal system and if adding glucose to GCHS could improve the technique’s efficacy.

Keywords: overhydration, ergogenic aid, gastrointestinal function, stomach, intestine
**Introduction**

Although bodyweight (BW) change is not always a reliable measure of changes in hydration status (Maughan, Shirreffs, & Leiper, 2007), it is suggested that an exercise-induced loss in BW > 2% can impair endurance performance (Cheuvront, Carter, & Sawka, 2003; Sawka et al., 2007). Evidence indicates that endurance athletes lose more than 2% BW during prolonged exercise (Noakes, 1993). The use of pre-exercise hyperhydration, by delaying or preventing the 2% BW loss threshold, could therefore be advantageous in situations where it is anticipated that a BW loss > 2% could occur if the exercise is started in a euhydrated state only.

In a recent meta-analysis, glycerol-induced hyperhydration (GIH) has been demonstrated to significantly enhance fluid retention and power output during prolonged exercise by respectively 50% and 2.6%, compared with water-induced hyperhydration (WIH) (Goulet, Plante, Aubertin-Leheudre, & Dionne, 2007). Moreover, it has recently been shown that, compared with pre-exercise euhydration, GIH improved peak power output by 5% during an incremental test to exhaustion following 2 h of cycling during which fluid consumption replaced only 33% of sweat losses (Goulet, Rousseau, Lamboley, Plante, & Dionne, 2008).

Some individual studies showed no effect of GIH on endurance performance, compared with WIH (Goulet, Robergs, Labrecque, Royer, & Dionne, 2006; Marino, Kay, & Daniels, 2003; Nishijima et al., 2007; Wingo et al., 2004). Moreover, the effects of GIH on cardiovascular and thermoregulatory functions during prolonged exercise are equivocal (Nelson & Robergs, 2007). The discrepancy between findings could be due to the different GIH and exercise protocols used by studies.

Isotonic sodium-containing hyperhydration solutions have been shown to improve endurance performance, compared with hypotonic solutions (Coles & Luetkemeier, 2005; Sims, Rehrer, Bell, & Cotter, 2007). However, the use of GIH may prove more advantageous than sodium-induced
hyperhydration, because it has been shown to improve fluid retention significantly more (Griffin et al., 1999).

Three review papers are found in the literature which provide important insights into the physiology of GIH (Latzka & Sawka, 2000; Nelson & Robergs, 2007; Robergs & Griffin, 1998). Taken together, those papers cover most of the topics on GIH, including a review of the biochemistry and pharmacokinetics of glycerol and how GIH affects thermoregulatory and cardiovascular functions as well as fluid retention and plasma volume regulation before, during and after exercise. However, no review exists which reports on how glycerol-containing hyperhydration solutions (GCHS) are processed at the stomach and intestine level. This is an issue that merits particular attention, since the stomach and gut represent the two barriers that need to be crossed before any of the water and glycerol ingested during GIH can be integrated into the body fluid pools to produce their respective physiological effects. Therefore, understanding how GCHS interact with the stomach and intestine should help optimize the use and by extension the efficacy of GIH. The goal of this paper is to report on what is known and unknown about how the glycerol and water ingested during GIH are handled by the gastrointestinal system, propose strategies and hypotheses with the hope of improving the efficacy of this hydration strategy and provide research questions for future studies.

The rates of gastric emptying and intestinal absorption of the glycerol and water ingested during GIH will be discussed. It is important to be aware of those rates, because as it will be demonstrated, the efficacy of GCHS in increasing fluid retention is maximized when fluid ingestion is in the upper range of what is normally administered by studies and the duration of the protocol is no longer than the time it takes for the fluid-glycerol load to be totally or nearly completely integrated inside the body. Because of the absence of human studies, an attempt will be made at predicting those rates based upon an analysis of indirect data obtained from relevant human studies.
Research in rats that looked at the gastric absorption of glycerol, the intestinal absorption rate of glycerol and the intestinal absorption rate of the water ingested with glycerol will be reviewed. Furthermore, the mechanisms involved in the absorption of glycerol at the brush border of the intestine and how this facilitates water absorption will also be discussed.

**Glycerol and Glycerol-Induced Hyperhydration**

**What is glycerol?**

Glycerol is also commonly known under the names of glycerin, trihydroxypropane or 1,2,3-propanetriol. It is a naturally occurring 3-carbon alcohol metabolite (C₃H₈O₃) that constitutes the structural core of the triglyceride molecules in human (Frank, Nahata, & Hilty, 1981). Glycerol is an extremely sweet-tasting substance, which is colorless, odorless and viscous. It is a potent osmotic agent, which has a molecular weight of 92.10 and a specific gravity of 1.26. Glycerol is usually available in pharmacies and its use is considered safe (Robergs & Griffin, 1998).

**Glycerol-induced hyperhydration**

*Volume of fluid*

Studies administered between 20-29 ml of fluid · kg BW⁻¹ (1400–2200 ml), with an average corresponding to 24 ml · kg BW⁻¹ or 1700 ml (Anderson, Cotter, Garnham, Casley, & Febbraio, 2001; Coutts, Reauburn, Mummery, & Holmes, 2002; Freund et al., 1995; Goulet et al., 2006, 2007, 2008; Griffin et al., 1999; Hitchins et al., 1999; Latzka et al., 1997, 1998; Lyons, Riedesel, Meuli, & Chick, 1990; Magal et al., 2003; Marino et al., 2003; Montner et al., 1996, 1999; Nishijima et al., 2007; O’Brien, Freund, Young, & Sawka, 2005; Riedesel, Allen, Peake, & Al-Qattan, 1987; Wingo et al., 2004). As shown in Fig 1., there is a significant positive correlation between the quantity of fluid administered and the ability of GCHS in increasing fluid retention. Hence, the efficacy of GIH is maximized when the volume of fluid administered is in the upper range of the quantities normally
provided. Goulet et al. (2007) indicated that a fluid dose of 26 ml · kg BW<sup>-1</sup> should maximize fluid retention.

**Quantity of glycerol**

Studies administered between 0.9-1.5 g glycerol · kg BW<sup>-1</sup> (69-110 g), with an average corresponding to 1.1 g · kg BW<sup>-1</sup> or 80 g (Anderson et al., 2001; Coutts et al., 2002; Freund et al., 1995; Goulet et al., 2006, 2007, 2008; Griffin et al., 1999; Hitchins et al., 1999; Latzka et al., 1997, 1998; Lyons et al., 1990; Magal et al., 2003; Marino et al., 2003; Montner et al., 1996, 1999; Nishijima et al., 2007; O’Brien et al., 2005; Riedesel et al., 1987; Wingo et al., 2004). There is no significant relationship between the amount of glycerol administered and the efficacy of GCHS in increasing fluid retention. This may be due to the lack of variation in the amount of glycerol administered by studies. Nevertheless, Goulet et al. (2007) indicated that the ideal quantity of glycerol that should be ingested to maximize fluid retention is between 1-1.2 g · kg BW<sup>-1</sup>.

Some studies administered the glycerol as a bolus at the start of the ingestion protocol (Freund et al., 1995; Latzka et al., 1997, 1998; Lyons et al., 1990; Magal et al., 2003; Montner et al., 1996, 1999; Nishijima et al., 2007; O’Brien et al., 2005; Riedesel et al., 1987), whereas others mixed it with the total fluid load to be ingested throughout the protocol (Anderson et al., 2001; Coutts et al., 2002; Goulet et al., 2006, 2008; Griffin et al., 1999; Hitchins et al., 1999; Marino et al., 2003; Nishijima et al., 2007; Wingo et al., 2004). A statistical analysis (independent t-test) reveals that the fluid retention provided by both types of protocols does not differ significantly (Fig. 2). Because of the sweetness of glycerol, it must be noted that the ingestion of glycerol as a bolus may produce side-effects such as nausea and vomiting (Latzka et al., 1997).
Length of protocol

Studies that looked at the effect of GIH prior to exercise used protocols ranging in length from 60 to 180 min (Anderson et al., 2001; Coutts et al., 2002; Goulet et al., 2006, 2008; Hitchins et al., 1999; Latzka et al., 1997, 1998; Lyons et al., 1990; Magal et al., 2003; Marino et al., 2003; Montner et al., 1996, 1999; Nishijima et al., 2007; Wingo et al., 2004). Four studies with no period of exercise examined the effect of GIH on total body water during time-periods ranging from 210 to 300 min (Freund et al., 1995; Griffin et al., 1999; O’Brien et al., 2005; Riedesel et al., 1987). The average length of a typical GIH protocol is 136 min (Goulet et al., 2007). There is a trend towards an inverse relationship between the effectiveness of GCHS in increasing fluid retention and protocol length ($r = -0.38$, $P = 0.09$, $n = 22$ studies).

Elapsed time between end of ingestion of GCHS and start of exercise

The interval of time between the end of ingestion of GCHS and the start of exercise may significantly impact GCHS’ ability in increasing fluid retention. It varies a lot between studies with values ranging from 0 to 120 min. As shown in Fig. 3, there is a significant negative relationship between the fluid retention provided by GCHS and the elapsed time between the end of ingestion of the fluid-glycerol load and the start of exercise. This suggests that the effectiveness of a GIH protocol in increasing fluid retention should be maximized when its duration equals to the minimal time it takes for the fluid-glycerol load to be totally or nearly completely integrated inside the body. In fact, if the ingestion period and/or the waiting time after ingestion are inappropriately long, a substantial part of the circulating fluid-glycerol load will be excreted through the kidneys before exercise. This will reduce fluid retention and diminish the physiological effect of the strategy during exercise. However, based on results of Fig. 3, one should note that for any elapsed time between the end of ingestion of the fluid-glycerol load and the start of exercise there could be some variations in fluid retention between individuals.
**Predictor (s) of the ability of GCHS in increasing fluid retention**

To determine the best predictor (s) of the efficacy of GCHS in increasing fluid retention, five key influential variables (glycerol and fluid dose, length of protocol, glycerol administered as a bolus or not and the time span between the end of ingestion and start of exercise) were entered in a stepwise regression analysis. Only the time span between the end of ingestion and start of exercise was retained into the model, explaining 25% of the variation in fluid retention results. Using a hierarchical regression analysis with all five aforementioned variables entered separately, the quantity of fluid administered along with the time span between the end of ingestion and start of exercise contributed in explaining 50% of the variation in fluid retention results, with the other variables not contributing in significantly improving the model. Taken together, the previous findings emphasize the importance of trying to define with as much precision as possible the rate of gastric emptying and intestinal absorption of the glycerol and water ingested during GIH in order to be capable of better defining the optimal length of a GIH protocol.

**Handling of Glycerol by the Stomach and Intestine**

**Gastric emptying and intestinal absorption rates of glycerol in humans**

No study has yet evaluated the rates of gastric emptying and intestinal absorption of glycerol in humans and whether they are dose-dependent or not. Therefore, research is needed on these topics. Despite the absence of human studies, indirect evidence indicates that glycerol is rapidly emptied from the stomach, absorbed by the intestine, integrated into the body and distributed among the body fluid pools. For example, Freund et al. (1995) administered in a single bolus 0.9 g glycerol · kg BW⁻¹ followed by the ingestion of 22 ml of fluid · kg BW⁻¹ within a 30 min period and then observed the changes in plasma glycerol concentration over the next 150 min. A peak plasma glycerol concentration of 1250 mg · L⁻¹ was reached 60 min after glycerol ingestion followed by a steady and linear decrease
over time due to glycerol turnover and urinary excretion. Using an identical GIH protocol, O’Brien et al. (2005) obtained a peak plasma glycerol value comparable to that observed by Freund et al. (1995) 90 min following glycerol ingestion. Hitchins et al. (1999) had subjects ingest 1 g glycerol · kg BW\(^{-1}\) with 22 ml of fluid · kg BW\(^{-1}\) within a 30 min period and observed a peak plasma glycerol concentration of 920 mg · L\(^{-1}\) 60 min following the end of ingestion. As glycerol elimination through urine and metabolism is a relatively slow process, e.g., three hours after ingestion, Freund et al. (1995) estimated that 62% of the ingested glycerol was still inside the body, the above results taken together indicate that the bulk of the ingested glycerol can be integrated inside the body 60 to 90 min after ingestion. This assumption is reasonable, because if important quantities of glycerol would still have been absorbed by the intestine after 60 to 90 min, then plasma glycerol values should have remained at a peak much longer or even continue to increase over time, which was not the case.

**Gastric emptying and intestinal absorption of glycerol in the rat**

*Gastric absorption and emptying rates*

I am aware of no study that determined in rats the rate at which glycerol is emptied from the stomach. However, it has been demonstrated that small quantities of glycerol can be absorbed by the rats’ stomach wall (Embree, Harris, & Herting, 1956). The authors argued that the likely mechanism was via passive diffusion, although this hypothesis was not directly tested. Whether glycerol can be absorbed (and at what rate) from the human stomach is not known and remains to be studied. However, because the time spent by glycerol in the stomach during GIH is likely short (based on the observations reported above), very little glycerol is likely to be absorbed.

*Rate of intestinal absorption*

Yuasa et al. (2003) observed that the rate of glycerol absorption in the rat’s small intestine is rapid. In fact, when they introduced into 5-cm closed loops of rats small intestines in situ 0.5 ml of glycerol
solutions concentrated at 0.002, 1.0 and 40.0 mM, the fraction of the doses absorbed after 30 min reached 92, 90 and 73%, respectively.

Allen, Wingertzhan, Teichberg, & Wapnir (1999) perfused (10-12 ml · h⁻¹) 20- to 30-cm long segments of rats jejunum with a low osmolality (228 mOsmol · kg H₂O⁻¹) solution containing 2.6 g NaCl · L⁻¹ and 7 g · L⁻¹ glycerol over a 3 h period and observed a rate of glycerol absorption of 104 nmol · min⁻¹ · cm⁻¹. Interestingly, they also showed that the presence of glucose improves the rate of intestinal glycerol absorption. In fact, when they perfused a low osmolality (225 mOsmol · kg H₂O⁻¹) solution containing 2.6 g NaCl · L⁻¹, 6 g of glycerol · L⁻¹ and 1.8 g of glucose · L⁻¹, the rate of glycerol absorption increased threefold. Other glycerol:glucose ratios were tested, but none produced absorption rates as high as the one just reported. Thus, in rats a ratio of 3 g glycerol for 1 g glucose maximizes the entry of glycerol inside the body.

This finding could have important practical implications for the formulation of GCHS. In fact, it suggests that adding some glucose to a fluid-glycerol load could potentially speed up glycerol absorption into the body and, in turn, lead to a more rapid creation of the optimal osmotic gradient needed at the kidney level to maximize fluid retention (Nelson & Robergs, 2007). Definitely, human studies must be conducted on this topic.

Kato, Hayashi, Inoue, & Yuasa (2004) showed that some glycerol can be absorbed by the colon, but at a rate that is about 10 times lower than that of the small intestine. As a result of the important absorption of glycerol taking place in the small intestine and colon, all orally-ingested glycerol is made available to the body (Sommer, Nau, Wieland, & Prange, 1993). The fact that studies on GIH did not report diarrhea supports this idea.
**Mechanisms of glycerol absorption**

Because glycerol is a small hydrophilic solute (Kato et al., 2004), it was assumed until recently that its absorption by the small intestine was occurring strictly by passive diffusion via the paracellular route (Yuasa et al., 2003). However, using the *in vitro* everted sac method involving the rat small intestine, Kato et al. (2004) showed that the transport of glycerol through the epithelial cells is saturable and primarily mediated by Na\(^{+}\)-dependent and secondary active carrier and, to a lesser extent, by passive diffusion. In the colon, the uptake of glycerol is also saturable and also likely governed by a Na\(^{+}\)-dependent carrier-mediated transport system (Kato et al., 2004). It is known that a group of aquaglyceroporins found in the rats’ and humans’ intestine act as channels for small neutral solutes such as urea and glycerol (Kato et al., 2004). However, it was argued by Kato et al. (2004) that it is unlikely that these aquaglyceroporins are involved in the carrier-mediated transport of glycerol, because permeation through channels is expected to be a linear process (unsaturable), therefore kinetically different from the saturable transport found for glycerol.

Glucose is actively transported along with sodium from the lumen of the small intestine into the cytoplasm of the enterocytes (Leiper, 1998). The reason behind the capacity of glucose in increasing glycerol transport across the mucosa of the small intestine is likely because its presence allows for the recruitment of more sodium-dependent active carriers which are also needed for the absorption of glycerol (Allen et al., 1999). Another mechanism may explain the facilitating effect of glucose upon glycerol absorption. Paracellular transport is coupled with sodium-dependent transcellular transport because the latter mechanism provides the osmotic force for solvent drag between the enterocytes and increases the permeability of absorptive cells (Leiper, 1998; Schedl, Maughan, & Gisolfi, 1994). Hence, the presence of glucose may enhance glycerol absorption through increased paracellular transport of glycerol.
Processing of the Water Ingested Along with Glycerol by the Stomach and Intestine

Gastric emptying and intestinal absorption rates of the fluid ingested during GIH in humans

No study has yet determined in humans the rate at which the water ingested with glycerol is emptied from the stomach and absorbed by the gut. It will thus be important to shed some light on these issues in future studies. There is also no study that examined the rate at which the fluid ingested with glycerol is emptied from the stomach of rats or any other animals.

Studies that evaluated the effect of carbohydrate-electrolyte solutions on the rate of gastric emptying and intestinal absorption in humans could provide some insights into the speed at which GIH could be integrated inside the body. The first barrier to the availability of ingested fluids is the rate of gastric emptying, which is a reflection of the rate at which fluid is delivered to the absorptive surface of the small intestine (Leiper, 1998). The primary determinants of the rate of gastric emptying are gastric volume and the energy density of the ingested fluid (Noakes, Rehrer, & Maughan, 1991).

Typical GCHS composed of 80 g of glycerol and 1700 ml of fluid have an energy density of 5%. According to Noakes et al. (1991), who estimated the effect of drinking pattern (volume) and energy density (via carbohydrate) on gastric emptying rate, 60 min should be long enough for complete or nearly complete emptying of the water contained in a typical glycerol solution if an initial intake of 600 ml would be followed by the ingestion of 300 ml every 10 min for 40 min. Although the ingestion of such a fluid load within this short amount of time may seem physiologically unreasonable, it must be noted that Coutts et al. (2002) as well as Lyons et al. (1990) administered fluid-glycerol loads of 2 L within 60 min and observed no side-effect other than minor gastrointestinal bloating that disappeared shortly after the end of ingestion. Hitchins et al. (1999) and Anderson et al. (2001) administered a fluid-glycerol load of ~1.5 L within 30 min and 15 min respectively and reported no
symptoms of discomfort or gastrointestinal distress. On the other hand, up to, but not more than 90 min should be required to empty such a fluid-glycerol load if a slightly more ‘‘manageable and conservative’’ drinking pattern would be employed (initial bolus of 600 ml, followed by 400 ml every 20 min for 60 min). Such a GIH protocol has been shown to be very well-tolerated by athletes and to produce no side-effect (Goulet et al., 2008). The absence of side-effect in the above-reported protocols suggests that GIH likely produces very high rates of gastric emptying. The decision to use a 60 or 90 min long protocol depends on individual tolerance of high gastric volume.

It is not easy from human studies to provide an approximation of the rate of intestinal absorption of typical GCHS. The principal determinant of the rate of intestinal water absorption is the osmolality of the ingested solution (Leiper, 1998). Typical GCHS possess an osmolality of ~500 mOsmol · kg H2O⁻¹. Using the triple lumen tube technique with humans, Duchman et al. (1997) perfused a 40-cm duodenojejunum test segment with a glucose-electrolyte solution (energy density of 6% and osmolality of 400 mOsmol · kg H2O⁻¹, both factors comparable to typical GCHS) at rates equivalent to the purported rates of gastric emptying of a typical fluid-glycerol load when ingested in the ways reported above, i.e., 18 or 28 ml · min⁻¹, and obtained on average a rate of fluid absorption of 13 ml · cm⁻¹ · h⁻¹. Shi et al. (1994) perfused the duodenojejunum (40-cm test segment) of six male volunteers with a 6%, 400 mOsmol · kg H2O⁻¹ glucose/fructose electrolyte solution at a rate of 15 ml · min⁻¹ and observed a rate of fluid absorption of 16 ml · cm⁻¹ · h⁻¹. Taken together, these results indicate a possible fluid absorption rate of GCHS of ~600 ml · h⁻¹ or 900 ml · 90 min⁻¹ over the distal duodenum and proximal jejunum. As the duodenojejunum length is ~275 cm, obviously fluid absorption will occur throughout this segment but at a rate that will be reduced compared with its proximal section due to the reduction in fluid flow rate and total solute absorption (Lambert, Chang, Xia, Summers, & Gisolfi, 1997). After the first 75 cm of the duodenojejunum, fluid absorption rate between a carbohydrate-electrolyte
solution and a water solution has been shown to be similar because at this stage both solutions have reached isotonicity and therefore the osmotic gradient for fluid absorption is comparable between solutions (Lambert et al., 1997). Santangelo & Krejs (1985) perfused human stomachs with water (22 ml · min⁻¹) and examined water absorption at 140-cm into a jejunum test segment. Their results indicated a rate of fluid absorption of the order of 2 ml · cm⁻¹ · h⁻¹. Soergel, Whalen, & Harris (1968) perfused human ileums (30-cm test segment) with an isotonic solution at a rate of 9-9.5 ml · min⁻¹ and observed a rate of fluid absorption of 1 ml · cm⁻¹ · h⁻¹. Given the length of the duodenojejunum and ileum (300-cm), and if it is assumed that fluid absorption from the first 50 cm of the duodenojejunum is 600 ml · h⁻¹, 500 ml · h⁻¹ for the remainder of the duodenojejunum and 300 ml · h⁻¹ for the ileum, then the maximal absorptive capacity of the small intestine for GCHS could be ~1400 ml · h⁻¹.

The change in plasma volume reflects the net effect of fluid absorption (Shi et al., 1994). Gisolfi, Summers, Lambert, & Xia (1998) showed that a hypertonic carbohydrate-electrolyte solution is absorbed as rapidly as water in the distal duodenum and proximal jejunum and that both solutions have a similar effect on plasma volume regulation during exercise. Over a 3 h period, Freund et al. (1995) demonstrated that GCHS do not alter plasma volume compared with water, indirectly suggesting that they are absorbed as fast as water or a carbohydrate-electrolyte solution.

Although the composition of GCHS differs from that of a carbohydrate-electrolyte solution, based on the results reported above, it is reasonable to suggest that the water found in standard GCHS is likely to be totally or nearly totally integrated inside the body within a period of 60 min, if an aggressive drinking pattern is used, and within 90 minutes when a more ‘‘relaxed’’ drinking pattern is used. This assumption obviously needs to be tested in futures studies.

It is important to indicate that the effect of GIH on endurance performance has been tested only under controlled laboratory conditions and not under real-world stressful situations such as before key
competitions. This is an important factor that ultimately prevents us from knowing or advocating an optimal timing ingestion before competition. For example, nervousness before competition might alter gastrointestinal kinetics. On the other hand, nobody has demonstrated that fluid retention and the ergogenic benefit of GCHS could not be maximized for some competitions (e.g., cycle road race or ultra-distance triathlon) when drinking is accelerated or completed at exercise onset. This would allow fluid conservation responses to be initiated before the volume load takes full effect and thus might attenuate diuresis. Research is needed to delineate the effect of stress on gastrointestinal symptoms during GIH.

**Intestinal absorption of water ingested with glycerol in rats**

*Rate of absorption*

Using procedures that have been reported above, Allen et al. (1999) determined the rate of intestinal absorption of water ingested with glycerol in the rats’ jejunum. In this segment of the intestine, they observed a mean rate of water absorption of 0.96 µl · min⁻¹ · cm⁻¹ when a low osmolality (228 mOsmol · kg H₂O⁻¹) solution composed of 2.6 g NaCl · L⁻¹ and 7 g · L⁻¹ glycerol was perfused over a 3-h period. On the other hand, the perfusion of a glucose solution (2.6 g NaCl · L⁻¹ with 13.5 g glucose · L⁻¹ (243 mOsmol · kg H₂O⁻¹)) allowed a rate of water absorption of 1.6 µl · min⁻¹ · cm⁻¹. However, when solutions (all containing 2.6 g NaCl · L⁻¹) with the same osmolar load but composed of glycerol and glucose at a ratio of 25:50, 37.5:37.5, 50:25 and 65:10 (mmol · L⁻¹) were perfused, the rate of water absorption increased to 1.9, 2.1, 2.8 and 2.6 µl · min⁻¹ · cm⁻¹, respectively. These latter rates of intestinal absorption are interesting in that they were significantly greater than those allowed by the perfusion of either the glycerol or glucose solution alone. Wapnir, Sia, & Fisher (1996) also arrived at similar conclusions and showed that the presence of glycerol in a rehydration formula comprising
carbohydrate, sodium citrate and potassium enhances the rate of water absorption into the body compared with a rehydration formula devoid of glycerol.

Taken together, the foregoing results suggest that the addition of glucose to GCHS could increase the rate of water absorption and, thus, potentially accelerate the hyperhydration process. On the other hand, adding glucose to GCHS will further increase its energy density, which may slow gastric emptying and nullify the facilitating effect of glucose upon fluid absorption. Studies must be conducted to determine how the combination glucose-glycerol influences fluid absorption in human.

**Mechanism of glycerol-induced water absorption**

Water movement into the absorptive cells is a passive process. The transport of solutes moves water into the enterocytes down the osmotic gradient produced by solute movements. As reported above, the absorption of glycerol is mediated via Na\(^+\)-dependent and secondary active transport and, to a lesser extent, by passive diffusion. As glycerol is transported along with sodium, the excess water ingested during hyperhydration will follow those two solutes as the transport process creates a favorable osmotic gradient. Obviously, the fact that glycerol is a small size molecule with hydrophilic property offers a clear advantage for water transport across the mucosal brush borders (Wapnir et al., 1996).

The combination glucose-glycerol has been shown to improve fluid absorption in rats. The concomitant ingestion of glucose and glycerol likely potentiates water absorption by activating more and diverse active sodium-nutrient cotransporters as well as allowing a greater efflux of water between enterocytes.

**Conclusions**

There are presently no studies that determined in humans the rate of gastric emptying and intestinal absorption of GCHS. It is important to pursue studies on these issues in the future. It was demonstrated in this review that the best predictor of the efficacy of GCHS in increasing fluid retention was the
elapsed time between the end of ingestion of GCHS and the onset of exercise: the shorter it is, the higher will be the retention of fluid. This suggests that the efficacy of GIH is maximized when the duration of the protocol is no longer than the time it takes for the fluid-glycerol load to be totally or nearly completely integrated inside the body. The amount of fluid ingested during GIH also has an important impact on the efficacy of GIH: the higher is the amount of fluid ingested, the higher is the retention of fluid. However, this factor has less impact on the efficacy of GIH than the elapsed time between the end of ingestion of the fluid-glycerol load and the onset of exercise, at least within the fluid doses that have been administered by studies. These findings combined together emphasize the importance of being aware of the rate of gastric emptying and intestinal absorption of GCHS. Based upon indirect evidence provided by human studies, it is proposed that a GIH protocol lasting from 60 to 90 min should be sufficient for the integration of all or nearly all water and glycerol inside the body. Whether or not this assumption makes sense needs to be tested in future studies. Research in rats suggests that combining glycerol with glucose at a 3:1 ratio can accelerate the rate of glycerol and fluid absorption in the intestine, thereby potentially speeding up the hyperhydration process and further improving the efficacy of GIH. Whether similar results could be obtained in humans must be tested. The stress associated with competition may slow gastrointestinal function. Whether this could prolong the time required for the fluid-glycerol load to be integrated inside the body requires further investigation.
References


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Figure legends

**Figure 1.**
Correlation between the relative volume of fluid administered during GIH and the relative fluid retention provided by GIH. n = 22 studies.

**Figure 2.**
Difference in fluid retention between GIH protocols using glycerol boluses or not. Results are means ± SEM. n = 22 studies.

**Figure 3.**
Correlation between the elapsed time between end of ingestion of the fluid-glycerol load and the onset of exercise and the relative retention of fluid provided by GIH. n = 17 studies.
Figure 1.

\[ y = 0.7294x - 3.835 \]

\[ r = 0.43, P = 0.045 \]
Figure 2.
Figure 3.

\[ y = -0.0642x + 16.927 \]

\[ r = -0.56, P = 0.021 \]