

Gastric emptying in infants and children

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Abbreviations

APT	applied potential tomography
CD	Crohn's disease
CF	cystic fibrosis
EBM	expressed breast milk
EGG	electrogastrography
GE	gastric emptying
GER	gastro-oesophageal reflux
hr	hour
IDDM	insulin-dependent diabetes mellitus
LCT	long chain triglycerides
MCT	medium chain triglycerides
mo	months
NICU	neonatal intensive care unit
t _{1/2}	gastric half-emptying time
wks	weeks
yrs	years

Introduction

Nutrients have to be taken in and assimilated by digestive and absorptive processes. The gastro-intestinal tract and gastro-intestinal motility are key in this process, which can be divided in different steps. One essential part is gastric emptying (GE). GE is influenced by multiple factors such as humoral control mechanisms, intrinsic and extrinsic neural regulation and composition of feedings.

Most of our understanding of GE is based on adult physiology. Little is known about GE in infants and children and more precisely about developmental differences that may predispose to problems such as gastro-oesophageal reflux (GER). Delayed GE can be part of a motility disorder and may cause a variety of symptoms in children including abdominal pain or bloating, nausea, vomiting or failure to thrive. GE studies in the pediatric age group are more difficult to perform and evaluate, especially in young infants.

Various techniques exist to measure GE but no single one describes all aspects (storage of foods, mixing and grinding, propulsion towards the pylorus,...). Studies are based on different techniques and therefore difficult to compare. Some techniques are also of questionable validity.

We here intent to review the current knowledge about GE in infants and children and to provide the state of the art of the available techniques to study GE in this young age group. As the reader will note, reports are few and often conflicting due to the variety of applied methods. We hope to provide a concise overview of published data in order to provide a 'base line' and to stimulate and facilitate further research with validated, non-invasive methods.

Mechanism of gastric emptying

A different mechanism for GE of liquids and solids has often been described (1,2). The stomach has two integrated but functionally distinct parts. The proximal stomach consisting of the fundus and the proximal third of the body, regulates the storage and emptying of liquids. Fluids are emptied at a rate that varies with the pressure gradient between the proximal stomach and the duodenum. The distal two thirds of the body, the antrum and pylorus act as a grinding/mixing organ for solids. Pressure waves or peristaltic contractions advance towards the pylorus, propelling gastric contents. These peristaltic contractions are controlled by the gastric pacemaker. As the wave reaches the pylorus, the antropyloric region restricts the emptying of particles larger than 1 mm in diameter. Larger particles are retained and fractionated into particles of less than 1 mm in size by antral contractile activity. Undigested particles remain in the stomach during the entire process. During fasting, the pylorus is open and after a high amplitude contraction, the remaining food particles are emptied through the pylorus into the duodenum.

Methods to measure gastric emptying

Since various methods have been used to study GE in infants and children, we will first briefly describe them.

The earliest used methods to study GE were invasive techniques requiring the aspiration of gastric contents. Presently, the aspiration of gastric contents to determine whether the next feeding can be given, is still often used in many neonatal intensive care units (NICU). Marker

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dilution tests and sampling techniques developed by George (3) using non-absorbable markers (phenol red, polyethyleneglycol) (4-6) have been widely used in infants and children (3,7-10). George's formula estimates the remaining gastric volume and has been adapted by Hurwitz (11). So far, most of our knowledge on GE in young infants is based on this technique but it is an invasive method that is difficult to perform and causes discomfort. The placement of a tube also influences motility (12). This method may be clinically useful but is obviously inaccurate. The reproducibility of this technique is very poor *in vitro* (unpublished data).

Imaging techniques are another group of methods to measure GE. Radiology is descriptive and can exclude mechanical obstruction and anatomical deformities. Radioscintigraphy is currently the gold standard for quantifying GE in adults (13-15). Radiation and transportation of the patient limits its application in small children. Magnetic resonance imaging generates images of the stomach and its contents. Disadvantages of this otherwise non-invasive technique are high costs of the equipment and the need for sedation to keep the infant immobile (16). Real-time ultrasound is a non-invasive, radiation free technique. A series of scans displays the volume of cross-sectional slices. Serial measurements of the 2 main axes of the antrum after a meal are related to GE. This elegant technique is however operator dependent and observation time is brief (17,18).

Epigastric impedance and applied potential tomography (APT) measure GE based on changes in electrical impedance in the upper abdomen. Epigastric impedance measures the impedance in the anterior-posterior plane by passing a current between two input electrodes, one anterior and one posterior to the stomach and recording the potential difference between two electrodes placed on opposite sides of the abdomen. APT uses 16 electrodes and generates tomographic images of changes in electrical resistivity. Computer assisted region-of-interest analysis of the serial images then yields a profile of gastric emptying. These techniques are attractive non-invasive methods that have recently been used in young infants (19,20).

Breath tests are non-invasive tests, using a substrate (acetate, octanoic acid) labelled with a stable isotope ^{13}C . After metabolization of the marker, $^{13}\text{CO}_2$ is expired in the air. The rate of appearance of $^{13}\text{CO}_2$ reflects GE (21-23). A breath test is easy to perform in children and is reproducible (24). Manometry and EGG are not directly able to evaluate gastric emptying but are useful to evaluate the quality of mechanical and myoelectrical phenomena underlying the emptying function. Antroduodenal manometry measures intraluminal pressures, generated by phasic contractions of the gut wall and enables to demonstrate motor dysfunctions (25). Electrogastrography detects gastric electrical activity through cutaneous electrodes attached to the epigastric skin. This is an attractive, non-invasive method that can be easily performed in infants and children and has no

risk of adverse effects but analysis can be hampered by artefacts (26).

Development of gastric emptying

The pre- and postnatal development of GE is presented schematically in figure 1. The gut tube is created by embryonic folding during the 6th gestational wk. The stomach appears as a fusiform dilatation by the foregut. By the end of the 7th wk the stomach has descended into the abdomen and acquires the anatomy characterizing its mature position (27). By about 7 mo gestation, the stomach muscles appear mature, both morphologically and histologically. In utero, GE of swallowed amniotic fluid has been noted as early as 26 wks gestation using a linear-array ultrasound scanner (28) and at 30 wks gestation using amniography (29). Nagata *et al.* also examined changes in gastric dimensions with real-time ultrasound (30). They found that measuring the fetal stomach is feasible after 10 - 12 wks of gestation and that longitudinal and anteroposterior gastric dimensions increase in a linear fashion with advancing gestation. The size of the stomach increases from 16 - 17 to 26 - 27 wks (possibly complementary to the growth of the fetus) but remains unchanged between 26 - 27 and 32 - 33 wks. This period probably corresponds to maturing gastrointestinal motility and propulsion of gastric contents through the pylorus into the intestine. The fetal gastric dimensions increase again from 32 - 33 to 36 - 37 wks of gestation.

Developmental changes have also been studied in preterm and term infants. Manometric studies documented poorly developed antroduodenal motor activity prior to 30 wks gestation, cluster activity between 30 and 34 wks and a more mature pattern towards term (31). A study comparing preterm and term infants concluded that antroduodenal coordination increases with gestational age (32). A normal gastric electrical rhythm can be detected by surface electrodes in preterm infants of 29 - 34 wks gestational age and becomes dominant at around 35 wks (33). Gastric electrical activity using electrogastrography and gastric emptying using ultrasound have also been studied by Riezzo *et al.*, in preterm and term newborns. They demonstrated a progressive increase in normal slow wave percentage as gestation advanced (59% in preterms 28-32wks, 61% in preterms 32-36wks and 78% in full-term newborns). Gastric half emptying time was longer in the preterm newborns of 28-32 wks (83 min) than preterm newborns of 32-36 wks (70 min) and full term newborns (72 min) (34). Chen *et al.* also studied patterns of gastric myoelectrical activity in human subjects of different ages. They reported that the percentage of 2-4 cpm slow waves was 27% in preterms, 30% in full-term newborns, 70% in 2-6 mo old infants, 85% in 4-11 yrs children and 89% in adults (35).

A maturation process of gastric myoelectrical activity has also been described with advancing postnatal age.

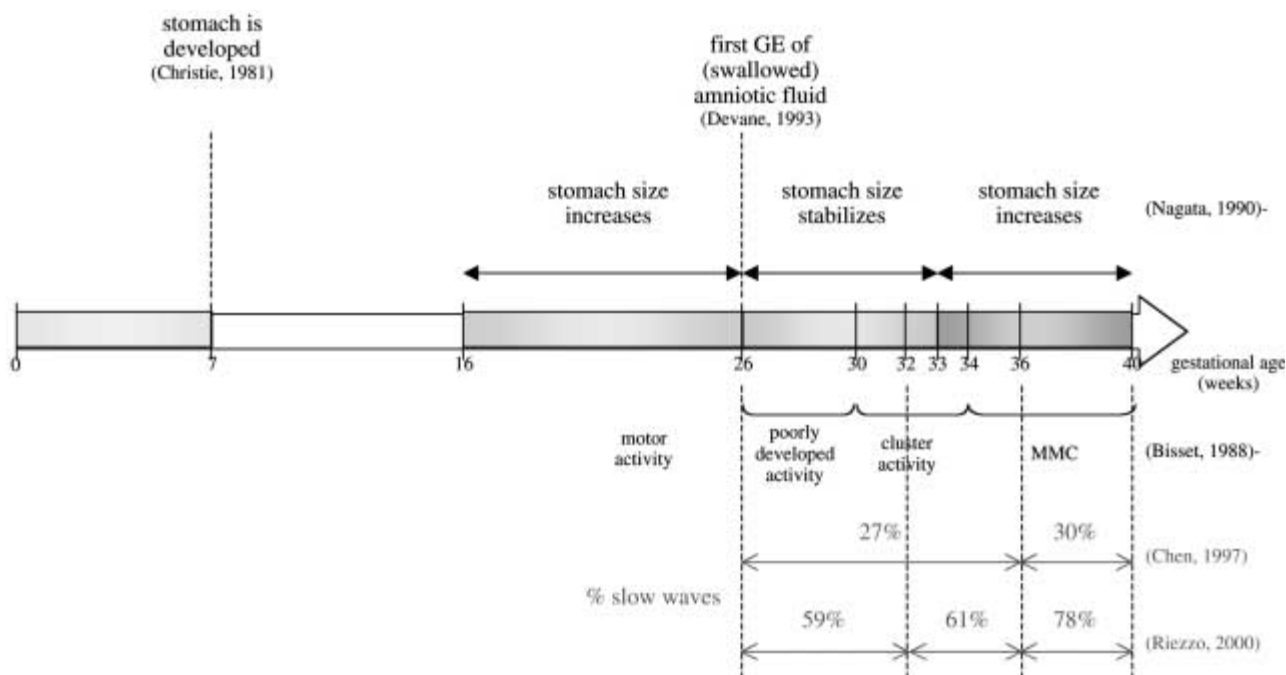


Fig. 1. — Development of gastric emptying

During the first days after birth, electrogastrography, showed a progressive increase in percentage normal slow waves : 36.7%, 37.8%, 47%, 52%, 55% and 65.8% at 1 and 2 wks and 1, 2, 4 and 6 mo respectively (36). A significant difference in percentage of regular slow waves between newborns and 2-6 mo old infants suggests a maturation process during these first months (35,36).

Clearly, all of these studies agree that GE commences during fetal life, improves towards term and becomes increasingly efficient during the first year of life.

Gastric emptying in healthy infants and children

Until now, only limited data for GE in healthy infants and children of different age groups have been published. Normal GE rates in children have been difficult to establish for ethical reasons because only invasive or radioactive methods were available. However, improved knowledge and understanding of normal physiology would allow clinicians to design more effective therapeutic modalities.

Table 1 provides an overview of GE studies performed in healthy preterm and term newborns. GE is expressed as $t_{1/2}$, the half-emptying time which is a valuable and meaningful parameter. The difference in techniques, the different gestational ages and postnatal ages and different testmeals (standard formula milk or expressed breast milk (EBM)) make comparisons difficult and meaningless. However, table 1 demonstrates faster emptying of clears than milk testmeal and faster emptying of human milk than formula. The mean half-

emptying time ($t_{1/2}$) in these studies (7,8,17,20,22-24,34,37) ranges from 25 to 36 min in breast fed preterm infants, from 45 to 83 min in formula fed preterm infants. In term infants, $t_{1/2}$ was a value of 48 min for human milk and ranges from 65 to 87 min for formula milk (20, 38-40). Non-caloric liquid (water) is emptied very quickly ($t_{1/2}$: 7min) (40).

Table 2 summarizes studies of liquid and solid emptying in healthy children (41-51). GE is expressed in $t_{1/2}$, in percentage emptied after 1 hr or in time necessary for complete emptying. A scintigraphically measured residual of milk of 36 to 68% at 1 hr in infants and 42 to 56% in older children was considered normal (42). Maxson reports as normal to have at least 32% emptied at 60 min (52) while Fonkalsrud *et al.* consider more than 40% emptied at 90 min as normal (53). However, it is impossible to establish reference values based on these data since different techniques, different outcomes and only a few studies with a small number of subjects are available. In addition, wide ranges were reported. Figure 2 lists GE values of normal infants and children reported in studies expressing results in $t_{1/2}$. It is clear from this table that solids empty slower than liquids and that milk empties slower than clear liquids. Reference values for GE, obtained with a consistent methodology in a large pediatric cohort are needed in order to discriminate normal from abnormal GE in infants and children.

Variables affecting gastric emptying

GE rates are influenced by chemical, nutritional and physicochemical properties of ingested food, probably due to neural and hormonal influences on gastric muscle

Table 1. — Gastric emptying in healthy preterm and term infants according to various methods

Method	Population	Gest age	Postnatal age	Testmeal	Result	(min-max) / $\pm$ SD	Reference
radioscintigraphy	25 term infants		1-10 wks	formula milk	T1/2 : 87 min	$\pm$ 29	Signer, 75
marker dilution technique	11 preterms	33-38 wks	1-9 wks	human milk formula milk	T1/2 : 25 min T1/2 : 51 min	$\pm$ 11.5 $\pm$ 9.8	Cavell, 79 Cavell, 82
marker dilution technique	17 term infants	NA	NA	human milk formula milk	T1/2 : 48 min T1/2 : 78 min	$\pm$ 15 $\pm$ 14	Cavell, 81
ultrasound	17 preterm infants	25-36 wks	1-8 wks	human milk formula milk	T1/2 : 35 min T1/2 : 45 min	(20-63) (20-63)	Newell, 93
ultrasound	14 preterm infants	30-35 wks	4-26 d	human milk formula milk	T1/2 : 36 min T1/2 : 72 min	(10-70) (40-120)	Ewer, 94
ultrasound	6 term infants	NA	14-49 d	formula milk	T1/2 : 75 min	$\pm$ 13	Lambrecht, 88
ultrasound	12 preterms 11 preterms 10 term infants	28-32 wks 32-36 wks > 37 wks	NA NA NA	formula milk formula milk formula milk	T1/2 : 83.4 min T1/2 : 70 min T1/2 : 71.8 min	(76-108) (57-89) (55-81)	Riezzo, 2000
APT	53 preterm infants	25-36 wks	19-30 d	formula milk / EBM electrolyte solution	T1/2 : 44.5 min T1/2 : 21.5 min	$\pm$ 3.1 $\pm$ 2.3	Nour, 95
APT	29 term infants	NA	5-7 wks	formula mik / EBM electrolyte solution	T1/2 : 41.3 min T1/2 : 22.0 min	$\pm$ 3.1 $\pm$ 1.8	
epigastric impedance	26 term infants	36-42 wks	NA	water	T1/2 : 7 min	(2.8-12.5)	Lange, 97
¹³ C octanoie acid BT	11 preterm infants	27-35 wks	NA	formula milk	T1/2 : 57 min	(17-100)	Veereman- Wauters, 96
¹³ C octanoie acid BT	28 preterm infants	25-36 wks	5-64 d	formula milk/EBM	T1/2 : 42 min	$\pm$ 48	Barnett, 90
¹³ C octanoie acid BT	29 preterms/term inf	27-41 wks	7-74 d	human milk formula milk	T1/2 : 47 min T1/2 : 65 min	(16-86) (27-98)	Van Den Driessche, 99

NA : not available.

Table 2. — Gastric emptying of liquids and solids in healthy infants and children

Method	Population	Age	Testmeal age	Result	(min-max) / $\pm$ SD	Reference
LIQUIDS						
marker dilution technique	20 infants/children	2-24 mo	water	53% after 15 min	$\pm$ 22.3	Euler, 80
radioscintigraphy	41 infants 8 children	1-23 mo 2-14 yrs	milk milk	48% emptied after 1 hr 51% emptied after 1 hr	$\pm$ 16 $\pm$ 7	Seibert, 82
epigastric impedance	45 children	7 mo-17 yrs	orange squash (liq)	T1/2 : 13.5 min	$\pm$ 7.2	Smith, 93
APT	6 children	3 mo-17 yrs	cow's milk 5% glucose	T1/2 : 61.5 min T1/2 : 10.7 min	$\pm$ 8.6 $\pm$ 2.3	Ravelli, 92
ultrasound	12 infants	3-13 mo	formula milk	complete GE after 79 min	$\pm$ 19.3	Carroccio, 92
¹³ C octanoic acid breath test	15 children	4-15 yrs	full cream milk	T1/2 : 86 min	(20-240)	Maes, 95
¹³ C acetate breath test	30 children	4.4 $\pm$ 3.5 yrs	milk	T1/2 : 74 min	$\pm$ 12	Gatti, 2000
SOLIDS						
radioscintigraphy	17 children	NA	pancake	T1/2 : 72.2 min	(61-83)	Collins, 97
radioscintigraphy	11 children	5-11 yrs	pancake	T1/2 : 78 min	$\pm$ 18	Montgomery, 98
radioscintigraphy	8 children	6-12 yrs	omelet sandwich	58% retention after 1 hr	$\pm$ 7	Okan, 97
radioscintigraphy	8 children	3-12 yrs	scrambled egg	55% retention after 1 hr	$\pm$ 11	Staiano, 96
¹³ C octanoic acid breath test	15 children	4-15 yrs	pancake 150 kcal	T1/2 : 58 min	(40-125)	Maes, 95
¹³ C octanoic acid breath test			pancake 250 kcal	T1/2 : 91 min	(35-240)	

NA : data not available.

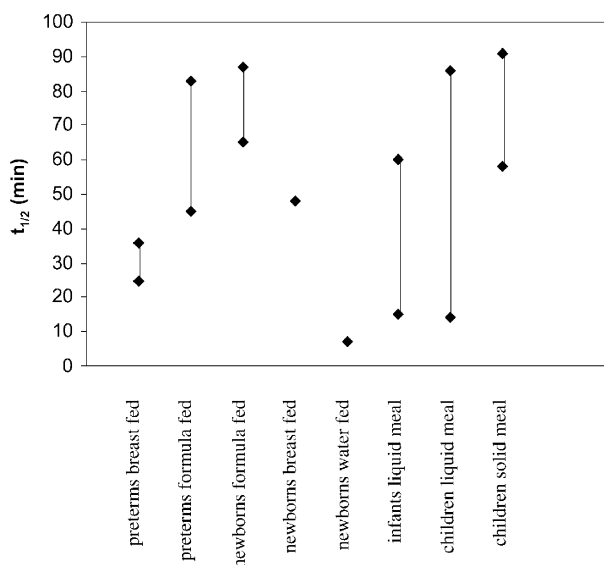


Fig. 2. — Ranges of $t_{1/2}$ in various pediatric age groups

contractility. Again, the application of different techniques may yield conflicting results.

In infants the importance of *osmolarity* was demonstrated: a high osmolar load delays GE (54). Collares *et al.* described after aspiration of gastric contents that gastric retention 10 min following ingestion of a 422 mOsm/kg, a 312 mOsm/kg and a 224 mOsm/kg solution was 50, 30 and 15% respectively (55). Based on those results, 200-300 mOsm/kg formula's were recommended in clinical practice. However, Siegel *et al.* reported using the marker dilution technique that a relatively higher osmolar load (448 mOsm/kg vs 279 mOsm/kg) does not inhibit GE (9). Similar GE times were noted for both formulas with approximately half of the initial gastric contents remaining at 30 min. This illustrates the importance of using a reliable technique. Based on clinical experience it seems probable that osmolarity influences GE.

The effect of *caloric density* on GE in preterm infants has been studied by Siegel and Husband (56,57). Using the dilution technique, they now demonstrated a significant inhibition of GE related to increasing caloric density. According to Hancock *et al.*, gastric contractions decreased when a 24 kcal/oz (0.80 kcal/ml) formula was ingested in comparison with a 20 kcal/oz (0.66 kcal/ml) formula with similar osmolarity (58).

Feeding composition significantly affects GE in infants. Human milk empties faster than formula milk, as shown by various methods, with a difference in $t_{1/2}$ of 48 and 78 min (marker dilution technique) (8); 36 and 72 min (ultrasound) (37) and 47 and 65 min (breath test) respectively (23). The nature of the milk also influences the interdigestive motility pattern. As demonstrated by Tomomasa, the MMC appeared in 75% of breast fed infants but only in 17% of formula fed infants (59). Since human milk and infant formulas used in these

studies have equal osmolarities and almost similar caloric densities, the reason for their different emptying may be their protein and/or fat composition.

Addition of a *breast milk fortifier* impairs GE according to Ewer but not to Mc Clure (60,61). Ewer found, using an ultrasonic technique, a $t_{1/2}$ of 21 min for unfortified breast milk and 48 min for fortified breast milk. $T_{1/2}$ according to Mc Clure, who also used ultrasonography, was 46 min for unfortified breast milk and 47.2 min for breast milk with added fortifier. The different caloric content of both breast milk fortifiers (18 vs 10 kcal/100ml) probably explains this discrepancy. It is the higher caloric content that affects GE.

Traditional nutrients may also have a variable influence on gastric emptying. The use of formulas with *medium chain triglycerides* (MCT) as fat content resulted in faster GE than *long chain triglycerides* (LCT) using the double sampling method (62). However, Sidebottom *et al.* and Pascale *et al.* reported that the fatty acid chain length of the triglycerides do not influence GE (54,63). The rapid emptying of *starch* in comparison to glucose in young infants with a known pancreatic amylase deficiency could suggest that emptying is rapid when digestion is impaired (57). *Protein composition* is another essential factor contributing to differences in GE. Infants fed casein-predominant formulas have significantly slower GE rates than infants fed whey-predominant formulas, as shown by scintigraphy (64,65). Promptly emptied milks (human milk, hydrolysed proteins, acidified cow's milk and whey predominant formulas) could be distinguished from slowly emptied milks (follow-up formulas, cow's milk and casein based formulas) by scintigraphy (66). Soy formula was shown to empty faster than casein but slower than whey using scintigraphy (64). On the other hand, Thorkelsson *et al.* concluded, again based on scintigraphy, that GE of preterm infants fed casein predominant formulas is similar to those fed whey formulas (67). A probable explanation for the slower emptying of casein is the flocculation occurring at the low pH, thus forming curds in the stomach while whey remains liquid (68). Moreover, casein releases opioid peptides during digestion, which inhibit gastro-intestinal motility by direct interaction with gut opiate receptors (69).

Claims about the effect of non-nutritive factors, including *temperature*, *phototherapy*, *position* and *non-nutritive sucking* on GE times are variable. Changes in body position may affect GE. More rapid emptying has been reported in the prone and right lateral positions, delayed GE in the left lateral and supine positions (70,71). However, Blumenthal *et al.* indicated no significant postural differences in the pattern of stomach emptying (72). Jaundice was shown to decrease GE, with resolution after phototherapy when jaundice resolved (10). This is a contradiction with an earlier report showing that phototherapy had no effect on GE (73). It has been speculated that sucking may improve gastro-intestinal motor function: gastric retention decreased

when infants were using a pacifier (74). Szabo *et al.* however, failed to demonstrate that non-nutritive or nutritive sucking would improve GE in healthy preterm infants (75). Temperature differences of formula milk (6°C, 24°C, 37°C) do not seem to have any effect on GE (76). However, Gonzales *et al.* and Collares *et al.* found larger gastric retentions for low temperature solutions (4-10°C versus 27-37°C) (77,78).

Therapeutic agents that increase GE in children and adults are effective candidates for treating gastric retention in premature infants. Metoclopramide increases GE rate in preterm and term infants (79,80). Cisapride and low-dose erythromycin increase emptying rates in preterm infants (81-83). On the other hand, a recent study demonstrated that cisapride delays GE in preterm infants (84). Moreover, in children with chronic intestinal pseudoobstruction, cisapride increased postprandial duodenal motility but also failed to improve GE (85).

In summary, important factors influencing GE are caloric density, osmolality and protein composition. A higher caloric content, a higher osmolality and a caseine predominant formula probably slow GE. Minor factors are the non-nutritive factors. However, we lack information on many other potentially therapeutic interventions such as continuous versus intermittent tube feeding and specific formula's since compositions vary in many aspects. It is clear that the effect of prokinetics is so far very poorly documented in infants and children. Studies, using validated methods, would serve an evidence based approach of pediatric motility problems.

Gastric emptying in infants in disease state

An important question is the effect of various pediatric diseases on GE. In *cystic fibrosis* (CF) GE appears to be faster: Cavell showed (using the marker dilution technique) that liquids empty faster (8) and Collins that solids empty significantly faster in CF subjects compared with normal, healthy controls (53 vs 72 min) (48). Maldigestion, influencing the variables discussed previously, may play an important role. However, Cucchiara *et al.* demonstrated a prolonged GE rate in 26 of 29 patients with CF using ultrasonography (240 vs 140 min) (86). Also, in a study of De Boeck *et al.*, 4 of 11 patients with CF had a delayed gastric emptying (using the ¹³C octanoic acid breath test) (87).

In *Crohn's disease* (CD), solid emptying was significantly delayed in 5 of 7 children (9-18 yrs) who were also malnourished (88). Gryboski also showed that 15 of 45 children with CD had delayed solid and 1 had delayed liquid emptying. Studies repeated 6-15 mo later, after establishment of weight gain showed significant improvement in GE. Our own data demonstrate normal GE (using the ¹³C octanoic acid breath test) in 16/20 children with inactive CD (89).

The relationship between GER and GE remains unclear. During infancy, GER is commonly seen in

otherwise healthy babies. Multiple mechanisms have been suggested to account for GER in this patient group, including inappropriate relaxation of the LES, delayed esophageal acid clearance and delayed GE.

Hillemeier studied infants less than 2 yrs and indicated that infants with severe GER were likely to have significantly delayed GE (90). GE was prospectively evaluated in 99 infants and children with symptomatic GER. Twenty eight percent of patients with GER had delayed GE (91). Livoti applied ultrasonography to evaluate GE in infants under 6 mo with GER. The authors described 3 types of GE rates and curves: normal, abnormal and intermediate (92). Di Lorenzo investigated 477 infants and children (93). A significant delay in GE was found only in GER patients over 6 yrs. Gastric motility was investigated by simultaneous measurement of GE by ultrasonography and gastric electrical activity with electrogastrography (94). Abnormal gastric electrical activity was commonly detected in GER patients in association with delayed GE. Delayed GE has often been demonstrated in neurologically impaired children with GER (95-97). Damage to the developing central nervous system may result in significant dysfunction in the gastro-intestinal tract and is reflected in GER. However, some authors found no relationship between GE and GER. Ewer and Rosen found no association between GE and GER in preterm infants and pediatric patients using ultrasonography and scintigraphy respectively (0-16 yrs) (98,99). Jolley studied 109 children referred for an evaluation of GER and concluded that GE of clear liquids was not decreased in most children with GER, regardless of symptoms (100). Moreover, the GE rate of water in 30 children without and 15 with GER was similar at all time intervals (101). Thus, findings are controversial but we would comment that again the methods and test meals are of utmost importance. For example, water evacuates very rapidly from the stomach and may not be a sufficient challenge to demonstrate differences in GE. Also, in patients with more complex GI motility disturbances, such as cerebral palsy, it seems obvious that GER and gastroparesis both occur.

The influence of feeding on the association of delayed GE and GER was also studied. Heacock *et al.* showed significant differences in newborns fed human or formula milk (102). Human milk resulted in faster GE and less GER, while formula induced a longer GE process as well as more GER. The difference in GE of 3 formulas (casein, soy and whey) was studied in infants with GER. Casein based milk emptied slower than soy and whey based formula. Therefore, replacement of casein by soy or whey based formula may reduce GER.

Sutphen studied the effect of various carbohydrate solutions with different osmolality, the effect of different feeding volumes and the addition of MCT's (103-105). High osmolality feedings and large feeding volumes were related to more GER and corresponded with slower GE. Adding MCT's produced no improvement in GER rates. These data support the association between GER

and GE and offer therapeutic options by modulating nutritional factors.

Delayed GE was occasionally described in various other diseases : in girls with *Turner syndrome* (51), in infants with *congenital heart disease* (106), in children with *acute rotaviral gastroenteritis* (107), in *esophageal atresia* (49), in *chronic renal failure* (108) and in a case of *Sandifer syndrome* (109). Again delayed GE or gastroparesis may be part of more generalized GI dysmotility, as is the case in *insulin-dependent diabetes mellitus* (IDDM). GE studied by ultrasonography was delayed in 65% of IDDM children (mean age 9 yrs) (110).

GE was also studied by real-time ultrasonography in children with *non-ulcer dyspepsia* by Cucchiara (26). Mean GE time was significantly prolonged in dyspeptic patients compared with controls (182 vs 102 min). Abnormal gastric myoelectrical activity may play a role in the pathogenesis of pediatric functional dyspepsia (111).

GE was investigated by Nour *et al.* using APT in a group of 49 vomiting infants with infantile *hypertrophic pyloric stenosis* (112). The results confirmed little or absent GE of a Dioralyte feed before the operation and a gradual return to normal emptying by the 7th postoperative day. GE was evaluated by ultrasonography in 41 healthy children (2 to 18 yrs) and 30 patients (1-19 yrs) who had undergone pyloromyotomy. GE post pyloromyotomy was similar to healthy controls (113).

Conclusion

Gastric emptying has been first detected at 26 wks of gestation and matures progressively towards term. After birth, changes in gastric motor activity suggest further maturation during the first months of life. Various methods exist to measure GE. The introduction of a number of non-invasive techniques facilitate clinical research so that insight in normal physiology rapidly progresses. GE is clearly influenced by dietary and non-dietary factors and is affected in a number of pediatric diseases and may explain some functional conditions. Abnormal GE has been documented in a wide variety of clinical conditions. Patients usually present with non-specific symptoms such as intermittent or constant nausea, vomiting, bloating or post-prandial abdominal pain. Initial work-up usually includes X-rays and/or upper GI endoscopy. These studies are necessary to rule out mechanical obstruction. When these examinations fail to explain the patient's symptoms, functional problems, various non-invasive methods are available to study GE or gastric electrical activity. More data are needed on their effect. But in order to evaluate their action, we also need reference data. Further research on GE will allow a better understanding of normal and abnormal physiology and evaluation of therapeutic modalities.

References

1. SIEGEL M., LEBENTHAL E. Development of gastrointestinal motility and gastric emptying during the fetal and newborn periods. In : *Gastroenterology and Nutrition in Infancy*. New York : Raven Press, 1981, p. 121-138.
2. DUMONT R., RUDOLPH C. Development of gastrointestinal motility in the infant and child. *Pediatr. Gastroenterology*, 1994, **23** : 655-671.
3. GEORGE J. New clinical method for measuring the rate of gastric emptying : the double sampling test meal. *Gut*, 1968, **9** : 237-242.
4. IVEY K., HP S. Gastric nonabsorbable indicators for studies in man. *Gastroenterology*, 1970, **59** : 234-239.
5. BOULTER J., MC MICHAEL H. Modification of polyethylene glycol estimation suitable for use with small mammals. *Gut*, 1970, **11** : 268-270.
6. SPERBER I., HYDEN S., EKMAN J. The use of polyethylene glycol as a reference substance in the study of ruminant digestion. *Ann. Agr. Coll. (Sweden)*, 1953, **20** : 337-344.
7. CAVELL B. Gastric emptying in preterm infants. *Acta Paediatr. Scand.*, 1979, **68** : 725-730.
8. CAVELL B. Gastric emptying in infants fed human milk or infant formula. *Acta Paediatr. Scand.*, 1981, **70** : 639-941.
9. SIEGEL M., LEBENTHAL E., TOPPER W. Gastric emptying in pretermatures of isocaloric feedings with different osmolarities. *Pediatr. Res.*, 1986, **16** : 141-147.
10. COSTALOS C., RUSSELL G., BISTARAKIS L., PANGALI A., PHILIPIDOU A. Effects of jaundice and phototherapy on gastric emptying in the newborn. *Biol. Neonate*, 1984, **46** : 57-60.
11. HURWITZ A. Measuring gastric volumes by dye dilution. *Gut*, 1981, **22** : 85-93.
12. NOVISKI N., BEN YEHUDA Y., SEROUR F., GORENSTEIN A., MANDELBERG A. Does the size of nasogastric tubes affect gastroesophageal reflux in children ? *J. Pediatr. Gastroenterol. Nutr.*, 1999, **29** : 448-451.
13. SCARPIGNATO C. Gastric emptying measurement in man. In : SCARPIGNATO C., BIANCHI P. (eds.). *Clinical Investigation of Gastric Function*. Basel : Karger, 1990, p. 198-246.
14. JONDERKO K. Short- and long-term reproducibility of radioisotopic examination of gastric emptying. *Nucl. Med. Biol.*, 1990, **17** : 297-301.
15. HEYMAN S. Gastric emptying in children. *J. Nucl. Med.*, 1998, **39** : 865-869.
16. SCHWIZER W., FRIED M., SIEBOLD K. Magnetic resonance imaging (MRI) : a new tool to measure gastric emptying in man. *Gastroenterology*, 1990, **98** : A389.
17. NEWELL S., CHAPMAN S., BOOTH I. Ultrasonic assessment of gastric emptying in the preterm infant. *Arch. Dis. Child.*, 1993, **69** : 32-36.
18. CUCCHIARA S., MINELLA R., IORIO R., EMILIANO M., AZZEQUEH N., VALLONE G. *et al.* Real-time ultrasound reveals gastric motor abnormalities in children investigated for dyspeptic symptoms. *J. Pediatr. Gastroenterol. Nutr.*, 1995, **21** : 446-453.
19. MC CLELLAND G., SUTTON J. Epigastric impedance : a non-invasive method for the assessment of gastric emptying and motility. *Gut*, 1985, **26** : 607-614.
20. NOUR S., MANGNALL Y., DICKSON J., JOHNSON A., PEARSE R. Applied potential tomography in the measurement of gastric emptying in infants. *J. Pediatr. Gastroenterol. Nutr.*, 1995, **20** : 65-72.
21. MAES B., GHOOS Y., GEYPENS B., MYS G., HIELE M., RUTLEGERS P. *et al.* Combined carbon ¹³glycine/carbon ¹³octanoic acid breath test to monitor gastric emptying rates of liquids and solids. *J. Nucl. Med.*, 1994, **35** : 824-831.
22. VEEREMAN-WAUTERS G., GHOOS Y., VAN DER SCHOOR S., MAES B., HEBBALKAR N., DEVLIEGER H. *et al.* The ¹³C-octanoic acid breath test : a noninvasive technique to assess gastric emptying in preterm infants. *J. Pediatr. Gastroenterol. Nutr.*, 1996, **23** : 111-117.
23. VAN DEN DRIESSCHE M., PEETERS K., MARIEN P., GHOOS Y., DEVLIEGER H., VEEREMAN-WAUTERS G. Gastric emptying in formula-fed and breast-fed infants measured with the ¹³C octanoic acid breath test. *J. Pediatr. Gastroenterol. Nutr.*, 1999, **29** : 46-51.
24. BARNETT C., SNEL A., OMARI T., DAVIDSON G., HASLAM R., BUTLER R. Reproducibility of the ¹³C octanoic acid breath test for assessment of gastric emptying in healthy preterm infants. *J. Pediatr. Gastroenterol. Nutr.*, 1999, **29** : 26-30.
25. BERSETH C., NORDYKE C. Manometry can predict feeding readiness in preterm infants. *Gastroenterology*, 1992, **103** : 1523-1528.
26. CUCCHIARA S., RIEZZO G., MINELLA R., PEZZOLLA F., GIORGIO I., AURICCHIO S. Electrogastrography in non-ulcer dyspepsia. *Arch. Dis. Child.*, 1992, **67** : 613-617.

27. CHRISTIE D. Development of gastric function during the first month of life. In: Textbook of Gastroenterology and Nutrition in Infancy. NY: Raven Press, 1981, p. 109-120.
28. DEVANE S., SOOTHILL P., CANDY D. Temporal changes in gastric volume in the human fetus in late pregnancy. *Early Human Developm.*, 1993, **33**: 109-116.
29. MC LAIN C. Amniography studies of the gastrointestinal motility of the human fetus. *Am. J. Obst. Gynec.*, 1963, **86**: 1079-1087.
30. NAGATA S., KOYANAGI T., HORIMOTO N., SATOH S., NAKANO H. Chronological development of the fetal stomach assessed using real-time ultrasound. *Early Human Developm.*, 1990, **22**: 15-22.
31. BISSET W., WATT J., RIVERS R., MILLA P. Measurement of small intestinal motor activity in the preterm infant. *J. Biomed. Eng.*, 1988, **10**: 155-158.
32. ITTMAN P., AMARNATH R., BERSETH C. Maturation of antroduodenal motor activity in preterm and term infants. *Dig. Dis. Sc.*, 1992, **37**: 14-19.
33. CUCCHIARA S., SALVIA G., SCARCELLA A., RAPAGIOLO S., BORRELLI O., BOCCIA G. *et al.* Gestational maturation of electrical activity of the stomach. *Dig. Dis. Sci.*, 1999, **44**: 2008-2013.
34. RIEZZO G., INDRIO F., MONTAGNA O., TRIPALDI C., LA-FORGIA N., CHILOIRO M. *et al.* Gastric electrical activity and gastric emptying in term and preterm infants. *Neurogastroenterol. Motil.*, 2000, **12**: 223-229.
35. CHEN J., LIANG J., PAN J., SUTPHEN J., TORRES-PINEDO R., ORR W. Patterns of gastric myoelectrical activity in human subjects of different ages. *Gastrointest. Liver Physiol.*, 1997, **35**: G1022-G1027.
36. LIANG J., CO E., ZHANG M., PINEDA J., CHEN J. Development of gastric slow waves in preterm infants measured by electrogastronomy. *Am. J. Physiol.*, 1998, **274**: G503-G508.
37. EWER A., DURBIN G., MORGAN M., BOOTH I. Gastric emptying in preterm infants. *Arch. Dis. Child.*, 1994, **71**: F24-F27.
38. SIGNER E., FRIDRICH R. Gastric emptying in newborn and young infants. *Acta Paediatr. Scand.*, 1975, **64**: 525-530.
39. LAMBRECHT L., ROBBERECHT E., DESCHYNKEL K., AFSCHRIFT M. Ultrasonic evaluation of gastric clearing in young infants. *Pediatr. Radiol.*, 1988, **18**: 314-318.
40. LANGE A., FUNCH-JENSEN P., THOMMENSEN P., SCHIOTZ P. Gastric emptying patterns of a liquid meal in newborn infants measured by epigastric impedance. *Neurogastroenterol. Mot.*, 1997, **9**: 55-62.
41. EULER A., BYRNE W. The gastric emptying rate of water in normal human children. *Pediatr. Res.*, 1980, **14**: 498.
42. SEIBERT J., BYRNE W., EULER A. Gastric emptying in children: unusual patterns detected by scintigraphy. *AJR*, 1983, **141**: 49-51.
43. GATTI C., DI-ABRIOLA F., DALL'OGGIO L., VILLA M., FRANCHINI F., AMARRI S. Is the ¹³C-acetate breath test a valid procedure to analyse gastric emptying in children? *J. Pediatr. Surg.*, 2000, **35**: 62-65.
44. SMITH H., HOLLINS G., BOOTH I. Epigastric impedance recording for measuring gastric emptying in children: how useful is it? *J. Pediatr. Gastroenterol. Nutr.*, 1993, **17**: 201-206.
45. RAVELLI A., SPITZ L., MILLA P. Gastric emptying in children with gastric transposition. *J. Pediatr. Gastroenterol. Nutr.*, 1994, **19**: 403-409.
46. CARROCCIO A., IACONO G., LIVOTI G., MONTALTO G., CAVATAIO F., TULONE V. *et al.* Gastric emptying in infants with gastroesophageal reflux. *Scand. J. Gastroenterol.*, 1992, **27**: 799-804.
47. MAES B., GHOOS Y., GEYSENS B., HIELE M., RUTGEERTS P. Relation between gastric emptying rate and energy intake in children compared with adults. *Gut*, 1995, **36**: 183-188.
48. COLLINS C., FRANCIS J., THOMAS P., HENRY R., O'LOUGHLIN E. Gastric emptying time is faster in cystic fibrosis. *J. Pediatr. Gastroenterol. Nutr.*, 1997, **25**: 492-498.
49. MONTGOMERY M., ESCOBAR-BILLING R., HELLSTRÖM P., KARLSSON K., FRENCKNER B. Impaired gastric emptying in children with repaired esophageal atresia: a controlled study. *J. Pediatr. Surg.*, 1998, **33**: 476-480.
50. OKAN M., ALPER E., CIL E., ERALP O., AGIR H. Gastric emptying time in children with progressive muscular dystrophy. *Turk. J. Pediatr.*, 1997, **39**: 69-74.
51. STAIANO A., SALERNO M., DI MAIO S., MARSULLO G., MARINO A., CONCOLINO D. *et al.* Delayed gastric emptying: a novel gastrointestinal finding in Turner's syndrome. *Arch. Dis. Child.*, 1996, **75**: 440-443.
52. MAXSON R., HARP S., JACKSON R. Delayed gastric emptying in neurologically impaired children with gastroesophageal reflux: the role of pyloroplasty. *J. Pediatr. Surg.*, 1994, **29**: 726-729.
53. FONKALSRUD E., AMENT M., VARGAS J. Gastric antroplasty for the treatment of delayed gastric emptying and gastroesophageal reflux in children. *Am. J. Surg.*, 1992, **164**: 327-331.
54. PASCALE J., MIMS L., GREENBERG M., ALEXANDER J. Gastric response in low birth weight infants fed various formulas. *Biol. Neonate*, 1978, **34**: 150-154.
55. COLLARES E., DE SOUZA N. Esvaziamento gastrico em criancas. Influencia da osmolaridade da solucao hidratante de uso oral. *Arq. Gastroent.*, 1982, **19**: 83-86.
56. SIEGEL M., LEBENTHAL E., KRANTZ B. Effect of caloric density on gastric emptying in premature infants. *J. Pediatr.*, 1984, **104**: 118-122.
57. HUSBAND J., HUSBAND P., MALLINSON C. Gastric emptying of starch meals in the newborn. *Lancet*, 1970, **2**: 290-292.
58. HANCOCK P., BANCALARI E. Gastric motility in premature infants fed two different formulas. *J. Pediatr. Gastroenterol. Nutr.*, 1984, **3**: 696-699.
59. TOMOMASA T., HYMAN P., ITOH Z., KOIZUMI T., KUROUME T. Gastrointestinal motility in neonates: response of human milk compared with cow's milk formula. *Pediatrics*, 1987, **80**: 434-438.
60. EWER A., YU V. Gastric emptying in preterm infants: the effect of breast milk fortifier. *Acta Paediatr.*, 1996, **85**: 1112-1115.
61. MC CLURE R., NEWELL S. Effect of fortifying breast milk on gastric emptying. *Arch. Dis. Child.*, 1996, **74**: F60-F62.
62. SIEGEL M., KRANTZ B., LEBENTHAL E. Effect of fat and carbohydrate composition on the gastric emptying of isocaloric feedings in premature infants. *Gastroenterology*, 1985, **89**: 785-790.
63. SIDEBOTTOM R., CURRAN J., WILLIAMS P., KANAREK K., BRAMSON R. Effect of long-chain vs medium-chain triglycerides on gastric emptying time in premature infants. *J. Pediatr.*, 1983, **102** (3): 448-450.
64. TOLIA V., LIN C., KUHN L. Gastric emptying using three different formulas in infants with gastroesophageal reflux. *J. Pediatr. Gastroenterol. Nutr.*, 1992, **15**: 297-301.
65. FRIED M., KHOSOO V., SECKER D., GILADY D., ASH J., PENCHARZ P. Decrease in gastric emptying time and episodes of regurgitation in children with spastic quadriplegia fed a whey-based formula. *J. Pediatr.*, 1992, **120**: 569-572.
66. BILLEAUD C., GUILLET J., SANDLER B. Gastric emptying in infants with or without gastroesophageal reflux according to the type of milk. *Eur. J. Clin. Nutr.*, 1990, **44**: 577-583.
67. THORKESSON T., MIMOUNI F., NAMGUNG R., FERNANDEZ-ULLOA M., KRUG-WISPÉ S., TSANG R. Similar gastric emptying rates for casein- and whey predominant formulas in preterm infants. *Pediatr. Res.*, 1994, **36**: 329-333.
68. NAKAI S., LICHAN E. Effect of clotting in stomachs of infants on protein digestibility of milk. *Food Microstructure*, 1987, **6**: 161-170.
69. DANIEL H., VOHWINKEL M., REHNER G. Effect of casein and beta-casomorphins on gastrointestinal motility in rats. *J. Nutr.*, 1990, **120**: 252-257.
70. YU V. Effect of body position on gastric emptying in the neonate. *Arch. Dis. Child.*, 1975, **50**: 500-504.
71. SILVA P.D., COLLARES E. Esvaziamento gastrico em criancas. Influencia da posicao do corpo, utilizando como refeicao de prova uma solucao hidratante de uso oral. *Arq. Gastroenterol.*, 1988, **25**: 104-109.
72. BLUMENTHAL I., EBEL A., PLIDES R. Effect of posture on the pattern of stomach emptying in the newborn. *Pediatrics*, 1979, **63**: 532-536.
73. BLUMENTHAL I., LEALMAN G., SHOESMITH D. Effect of feed temperature and phototherapy on gastric emptying in the neonate. *Arch. Dis. Child.*, 1980, **55**: 562-564.
74. WIDSTRÖM A., MARCHINI G., MATTHIESEN A., WERNER S., WINBERG J., UVNÄS-MOBERG K. Nonnutritive sucking in tube-fed preterm infants: effects on gastric motility and gastric contents of somatostatin. *J. Pediatr. Gastroenterol. Nutr.*, 1988, **7**: 517-523.
75. SZABO S.J., HILLEMEIER A.C., OH W. Effect of non-nutritive and nutritive suck on gastric emptying in premature infants. *J. Pediatr. Gastroenterol. Nutr.*, 1985, **4**: 348-351.
76. ANDERSON C., BERSETH C. Neither motor responses nor gastric emptying vary in response to formula temperature in preterm infants. *Biol. Neonate*, 1996, **70**: 265-270.
77. GONZALES I., DURYEA E., VASQUEZ E., GERAGHTY N. Effect of enteral feeding temperature on feeding tolerance in preterm infants. *Neonatal Network*, 1995, **14**: 39-43.
78. COLLARES E., BRASIL M. Esvaziamento gastrico em criancas. Influencia da temperatura de uma solucao hidratante de uso oral. *Arq. Gastroent.*, 1981, **18**: 123-126.
79. HYMAN P., ABRAMS C., DUBOIS A. Gastric emptying in infants: Response to metoclopramide depends on the underlying condition. *J. Pediatr. Gastroenterol. Nutr.*, 1988, **1988**: 181-184.
80. SANKARAN K., YEBOAH E., BRINGHAM W. Use of metoclopramide in preterm infants. *Dev. Pharmacol. Ther.*, 1982, **5**: 114-119.
81. MELIS K., JANSSENS G. Long-term use of cisapride (Prepulsid) in premature neonates. *Acta Gastroenterol. Belg.*, 1990, **53**: 372-375.

82. JANSSENS G., MELIS K., VAERENBERG M. Long-term use of cisapride (propulsid) in premature neonates of < 34 w gestational age. *J. Pediatr. Gastroenterol. Nutr.*, 1990, **11** : 420-425.
83. TOMOMASA T., MIYAZAKI M., KOIZUMI T. Erythromycin increases gastric antral motility in human premature infants. *Biol. Neonate*, 1993, **63** : 349-352.
84. MC CLURE R., KRISTENSEN J., GRAUAUG A. Randomised controlled trial of cisapride in preterm infants. *Arch. Dis. Child. Fetal Neonatal Ed.*, 1999, **80** : F174-F177.
85. DI LORENZO C., REDDY N., VILLANUEVA-MEYER J., MENA I., MARTIN S., HYMAN P. Cisapride in children with chronic intestinal pseudoobstruction. *Gastroenterology*, 1991, **101** : 1564-1570.
86. CUCCHIARA S., RAIA V., MINELLA R., FREZZA T., DE VIZIA B., DE RITIS G. Ultrasound measurement of gastric emptying time in patients with cystic fibrosis and effect of ranitidine on delayed gastric emptying. *J. Pediatr.*, 1996, **128** : 485-488.
87. DE BOECK K., DELBEKE I., EGGERMONT E., VEEREMAN-WAUTERS G., GHOOS Y. Lipid digestion in cystic fibrosis : comparison of conventional and high lipase enzyme therapy using the mixed triglyceride breath test. *J. Pediatr. Gastroenterol. Nutr.*, 1998, **26** : 408-411.
88. GRILL B., LANGE R., MARKOWITZ R., HILLEMEIER A., MC CALLUM R., GRYBOSKI J. Delayed gastric emptying in children with Crohn's disease. *J. Clin. Gastroenterol.*, 1985, **7** : 216-226.
89. VAN DEN DRIESSCHE M. Study of gastro-intestinal motility in infants and children using ¹³C breath tests [PhD]. Leuven : Catholic University, 2001.
90. HILLEMEIER A., R L, R M, J S, GRYBOSKI J. Delayed gastric emptying in infants with gastroesophageal reflux. *J. Pediatr.*, 1981, **92** : 190-193.
91. PAPAILA J., WILMOT D., GROSFELD J., RESCORLA F., WEST K., VANE D. Increased incidence of delayed gastric emptying in children with gastroesophageal reflux. *Arch. Surg.*, 1989, **124** : 933-936.
92. LIVOTI G., TULONE V., BRUNO R., CATALIOTTI F., IACONO G., CAVATAIO F. *et al.* Ultrasonography and gastric emptying : evaluation in infants with gastroesophageal reflux. *J. Pediatr. Gastroenterol. Nutr.*, 1992, **14** : 397-399.
93. DI LORENZO C., PIEPSZ A., HAM H., CADRANEL S. Gastric emptying with gastroesophageal reflux. *Arch. Dis. Child.*, 1987, **62** : 449-453.
94. CUCCHIARA S., SALVIA G., BORRELLI O., CICCIMARRA E., AZ-ZEQUEH N., RAPAGIOLO S. *et al.* Gastric electrical dysrhythmias and delayed gastric emptying in gastroesophageal reflux disease. *Am. J. Gastroenterol.*, 1997, **92** : 1103-1108.
95. SULLIVAN P. Gastrointestinal problems in the neurologically impaired child. *Baillière's Clin. Gastroenterol.*, 1997, **11** : 529-547.
96. RAVELLI A., MILLA P. Vomiting and gastroesophageal motor activity in children with disorders of the central nervous system. *J. Pediatr. Gastroenterol. Nutr.*, 1998, **26** : 56-63.
97. ALEXANDER F., WYLLIE R., JIROUSEK K., SECIC M., PORVASNIK S. Delayed gastric emptying affects outcome of Nissen fundoplication in neurologically impaired children. *Surgery*, 1997, **122** : 690-698.
98. EWER A., DURBIN G., MORGAN M., BOOTH I. Gastric emptying and gastro-oesophageal reflux in preterm infants. *Arch. Dis. Child.*, 1996, **75** : F117-F121.
99. ROSEN P., TREVES S. The relationship of gastroesophageal reflux and gastric emptying in infants and children : concise communication. *J. Nucl. Med.*, 1984, **25** : 571-574.
100. JOLLEY S., LEONARD J., TUNELL W. Gastric emptying in children with gastroesophageal reflux. An estimate of effective gastric emptying. *J. Ped. Surg.*, 1987, **22** : 923-926.
101. EULER A., BYRNE W. Gastric emptying times of water in infants and children : comparison of those with and without gastroesophageal reflux. *J. Pediatr. Gastroenterol. Nutr.*, 1983, **2** : 595-598.
102. HEACOCK H., JEFFERY H., BAKER J., PAGE M. Influence of breast versus formula milk on physiological gastroesophageal reflux in healthy, newborn infants. *J. Pediatr. Gastroenterol. Nutr.*, 1992, **14** : 41-46.
103. SUTPHEN J., DILLARD V. Effect of feeding volume on early postcibal gastroesophageal reflux in infants. *J. Pediatr. Gastroenterol. Nutr.*, 1988, **7** : 185-188.
104. SUTPHEN J., DILLARD V. Dietary caloric density and osmolality influence gastroesophageal reflux in infants. *Gastroenterology*, 1989, **97** : 601-604.
105. SUTPHEN J., DILLARD V. Medium chain triglyceride in the therapy of gastroesophageal reflux. *J. Pediatr. Gastroenterol. Nutr.*, 1992, **14** : 38-40.
106. CAVELL B. Gastric emptying in infants with congenital heart disease. *Acta Paediatr. Scand.*, 1981, **70** : 517-520.
107. BARDHAN P., SALAM M., MOLLA A. Gastric emptying of liquid in children suffering from acute rotaviral gastroenteritis. *Gut*, 1992, **33** : 26-29.
108. RAVELLI A., LEDERMANN S., BISSET W., TROMPETER R., BARRATT T., MILLA P. ForeGut motor function in chronic renal failure. *Arch. Dis. Child.*, 1992, **67** : 1343-1347.
109. CARDI E., CORRADO G., CAVALIERE M., CAPOCACCIA P., MATRUNOLA M., REA P. *et al.* Delayed gastric emptying in an infant with Sandifer syndrome. *Ital. J. Gastroenterol.*, 1996, **28** : 518-519.
110. CUCCHIARA S., FRANZESE A., SALVIA G., ALFONSI L., IULA V., MONTISCIA. *et al.* Gastric emptying delay and gastric electrical derangement in IDDM. *Diab. Care*, 1998, **21** : 438-443.
111. CHEN J., LIN X., ZHANG M., TORRES-PINEDO R., ORR W. Gastric myoelectrical activity in healthy children and children with functional dyspepsia. *Dig. Dis. Sci.*, 1998, **43** : 2384-2391.
112. NOUR S., MANGNALL Y., DICKSON J., PEARSE R., JOHNSON A. Measurement of gastric emptying in infants with pyloric stenosis using applied potential tomography. *Arch. Dis. Child.*, 1993, **68** : 484-486.
113. ASAI A., TAKEHARA H., HARADA M., TASHIRO S. Ultrasonographic evaluation of gastric emptying in normal children and children after pyloromyotomy. *Pediatr. Surg. Int.*, 1997, **12** : 344-347.