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A Review of Methods for Assessment of the Rate of Gastric Emptying in the Dog and Cat: 1898–2002

C.A. Wyse, J. McLellan, A.M. Dickie, D.G.M. Sutton, T. Preston, and P.S. Yam

Gastric emptying is the process by which food is delivered to the small intestine at a rate and in a form that optimizes intestinal absorption of nutrients. The rate of gastric emptying is subject to alteration by physiological, pharmacological, and pathological conditions. Gastric emptying of solids is of greater clinical significance because disordered gastric emptying rarely is detectable in the liquid phase. Imaging techniques have the disadvantage of requiring restraint of the animal and access to expensive equipment. Radiographic methods require administration of test meals that are not similar to food. Scintigraphy is the gold standard method for assessment of gastric emptying but requires administration of a radioisotope. Magnetic resonance imaging has not yet been applied for assessment of gastric emptying in small animals. Ultrasonography is a potentially useful, but subjective, method for assessment of gastric emptying in dogs. Gastric tracer methods require insertion of gastric or intestinal cannulae and are rarely applied outside of the research laboratory. The paracetamol absorption test has been applied for assessment of liquid phase gastric emptying in the dog, but requires IV cannulation. The gastric emptying breath test is a noninvasive method for assessment of gastric emptying that has been applied in dogs and cats. This method can be carried out away from the veterinary hospital, but the effects of physiological and pathological abnormalities on the test are not known. Advances in technology will facilitate the development of reliable methods for assessment of gastric emptying in small animals.

Key words: Barium-impregnated polyethylene spheres; Breath test; Radiography; Scintigraphy; Ultrasonography.

The important role of the stomach in the digestion of food has been recognized for many centuries. The term "pylorus" dates from before the 5th century and is derived from the Greek, meaning "keeper of the gate," an indication that early physicians had some understanding of the physiological function of gastric emptying. The rate of gastric emptying was assessed noninvasively for the 1st time in 1898, when the Harvard physiologist, W.B. Cannon, used X-rays to trace the outline of a radiopaque meal passing through the stomach of a cat (Fig 1).[1] Over the next 6 years, Cannon used this method to characterize the functional significance of fundic and antral contractions and demonstrated the effect of emotion and food on the rate of gastric emptying.[1,2] Together, these studies formed the cornerstones of the study of gastric motility, and Cannon's findings continue to influence our understanding of gastric emptying to this day. Indeed, over 100 years later, the radiographic tracing of gastric emptying remains the most commonly applied method for assessment of gastric motility in veterinary medicine.[3]

More recently, the dog has been used as an animal model for the study of human gastric emptying in many physiological and pharmacological studies, and gastric emptying is now more clearly understood in the dog than in any other species. The neural regulation of gastric emptying has been studied in the cat,[4] but at present, few studies describe the clinical assessment of gastric emptying in this species.

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Gastric Emptying: Physiology

Gastric emptying is the process by which food is delivered to the small intestine at a rate and in a form that optimizes intestinal absorption of nutrients. The rate of gastric emptying is regulated by the tonic contraction of the proximal stomach (fundus), contraction of the distal stomach (antrum), and the inhibitory forces of pyloric and duodenal contraction (Fig 2). Solid phase gastric emptying is of greater interest to the veterinary clinician because there is some evidence that pathological disorders of gastric emptying are not always detectable in the liquid phase.[5] Proximal gastric tone is an important modulator of liquid emptying, and studies in dogs have demonstrated that recovery of fundic tone after ingestion of a liquid meal occurs concurrently with gastric emptying of the liquid phase.[6] However, the gastric emptying of liquids is not exclusively controlled by the proximal stomach, and outlet resistance from the antral and pyloric regions and the duodenum also are important.[7]

An important function of the process of solid phase gastric emptying is to act as a mill for the "trituration" of solid food. Trituration refers to the mechanical breakdown and mixing of food to a semiliquid chyme, and this effect is achieved by the repeated to-and-fro movement of ingesta in the antrum. Antral contraction is composed of circular rings of muscular contraction (peristalsis) that increase in amplitude and velocity as they travel distally toward the pylorus.[8] As the wave of contraction approaches the distal antrum, the pylorus and proximal antrum close and particles too large to pass through the pylorus (>2 mm) are propelled back into the body of the stomach. This action of contractile retropulsion reduces digestible food particles to a size suitable for gastric emptying (in the range of 0.1–

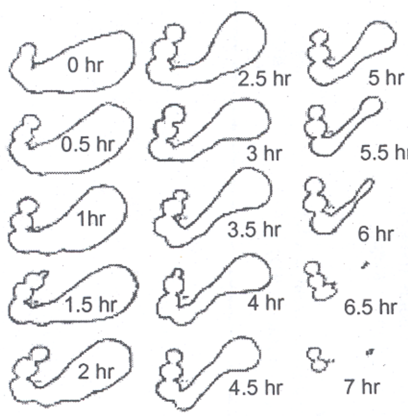

Fig 1. Tracing of the outline of a radiopaque fluid passing through the feline stomach.[1] The pictures were drawn by carefully tracing the outline of the stomach from X-rays taken at half-hourly intervals for 6 hours after ingestion of bismuth meal. These pictures document the 1st recording of the rate of gastric emptying, and were published in the inaugural issue of the *American Journal of Physiology* (reproduced with permission).[1]

0.63 mm in the dog).[9–11] Liquid phase emptying follows an exponential pattern in humans[12] and in the dog[10] and cat.[13] Solid meals empty in a slower, more linear pattern that often is preceded by a lag phase thought to be representative of the process of trituration.[10,14–17]

In the dog, small indigestible particles (diameter < 1.6 mm) empty promptly from the stomach, whereas large indigestible solids (diameter > 2 mm) that are resistant to trituration, are retained until the digestible solids have emptied and the interdigestive motor pattern is recovered.[9,16] However, in the horse and in humans, indigestible solids can empty with digestible food.[18,19] Interdigestive patterns of gastrointestinal motility vary greatly between species. The interdigestive state in humans and in the dog is associated with a cyclic recurring complex of motor activity, the migrating motor complex (MMC) that migrates periodically from the stomach to the distal small intestine.[20,21] The MMC is characterized by a band of intense contractile activity (Phase III) that is followed by a period of relative quiescence (Phase I) and then a period of irregular activity (Phase II).[22] The interdigestive MMC is interrupted by feeding in the dog and in humans and is replaced by a pattern of persistent phasic contractile activity that mixes and propels the gut contents.[23,24] The interdigestive motility pattern of the cat is unique and is associated with long, fused spike bursts (migrating spike complex) interspersed with short periods of irregular spiking activity.[25] The characteristic gastric physiology of each species has important implications for the interpretation of gastric emptying studies in veterinary practice. Detailed analyses of the gastric myoelectric activity of the cat and dog have been reported elsewhere.[20,21,25]

Gastric emptying is a highly regulated process that is subject to alteration by many physiological, pharmacological, and pathological conditions. The modulatory effect of physiological factors such as stress,[26,27] body size,[28] and meal composition[29,30] on the rate of gastric emptying in dogs and cats accounts for the wide variation in the rate of gastric emptying reported among and within subjects and

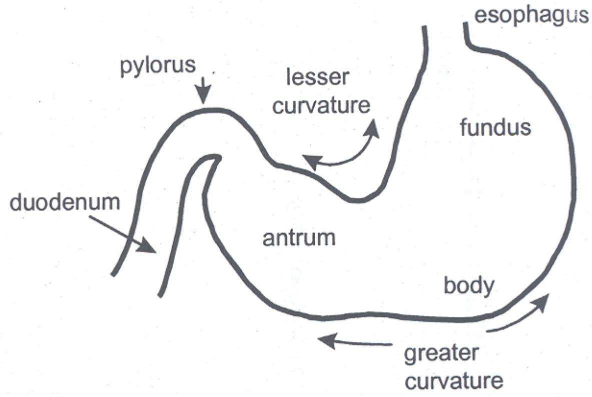

Fig 2. Anatomical regions of the canine stomach.

among different studies (Table 1).[31,32] This variation confounds the investigation of pathological or pharmacological modulation of gastric emptying, and only unequivocal results can be considered of clinical relevance. Reference ranges for solid phase gastric emptying in the dog and cat, measured by noninvasive techniques, are shown in Table 1. Animals with clinical signs of gastroparesis that have rates of gastric emptying outside of these ranges when the same protocol is applied might have delayed gastric emptying. However, many of these studies report gastric emptying rates in normal animals kept under experimental conditions; consequently, the reference ranges reported might not be representative of the gastric emptying rate of a normal animal presented to a veterinary clinic. Few studies have documented delayed gastric emptying associated with a pathological process in the dog and cat, possibly because of the technical difficulties in assessing the rate of solid phase gastric emptying in these species outside the laboratory. The limited information available on the rate of gastric emptying in the diseased animal combined with the wide variability of gastric emptying in the normal animal makes the definition of delayed gastric emptying difficult. Furthermore, the studies that are available are not comparable because different test meals and methods for assessment of gastric emptying were used. The definition of delayed gastric emptying in the dog and cat requires further work, and establishment of standard methods and reference ranges in large groups of healthy animals is necessary. Investigation of the sensitivity of each method in detecting disordered gastric emptying in diseased animals also is required.

Delayed gastric emptying has been reported in dogs with chronic hypertrophic pyloric gastropathy,[33–36] endotoxemia,[37] dysautonomia,[38] neoplasia,[39,40] gastric dilatation-volvulus,[41,42] and radiation-induced vomiting.[43] In the cat, delayed gastric emptying was reported in association with pylorospasm,[44] hypertrophic gastropathy,[45] and dysautonomia.[46] Delayed gastric emptying commonly is associated with human type I and type II diabetes[47,48] and has been demonstrated in experimentally induced diabetes in dogs.[49] The prevalence of delayed gastric emptying in diabetic dogs warrants investigation, particularly because erratic delivery of nutrients to the small intestine could contribute to poor glycemic control. The role of gastric emptying in the etiology of canine gastric dilatation-volvulus has been the focus of detailed research, and considerable evidence suggests

Table 1. Reference ranges for solid-phase gastric emptying in the dog and cat measured by noninvasive techniques.

Method	Species	Test Meal	n	Gastric Half-Emptying Time ($t^{1/2}$)[a]	Reference
Radioscintigraphy	Dog	Eggs, starch + glucose	27	66 min (median), 45–227 min (95% CI)	31
		Beef baby food + kibble	6	4.9 ± 1.96 hours (mean ± SD)	5
		Liver	4	About 2 hours	9
		Canned dog food + egg	6 (18 tests)	172 ± 17 min (mean ± SE)	32
		Canned dog food + egg	7 (14 tests)	285 ± 34 min (mean ± SD); 294 ± 39 min (mean ± SD)	74
		Canned dog food	6	77 min (mean)	15
	Cat	Dry cat food	10	2.47 ± 0.71 hours (mean ± SD)	17
		Liver + cream	6 (15 tests)	163 ± 11 min (mean ± SE)	77
		Canned cat food	20	2.69 ± 0.25 hours (mean ± SD)	29
		Dry cat food	20	3.86 ± 0.24 hours (mean ± SD)	29
		Eggs	10	330 min (median), 210–769 min (range)	89
Radiography	Dog	Dry dog food + radio-opaque solids	10	3.5 hours (median), 1–6 hours (range)	41
		Canned dog food + egg + BIPS	6 (18 tests)	Small BIPS 416 ± 81 min (mean ± SE)	32
		Canned dog food + BIPS	20	Small BIPS 6.05 ± 2.99 hours (mean ± SD) Large BIPS 7.11 ± 3.60 hours (mean ± SD)	28
		Kibble + BIPS	8	Small BIPS = 8.29 ± 1.62 hour (70% of dogs ± SE) Large BIPS = 29.21 ± 18.31 hours (70% of dogs ± SE)	50
	Cat	Kibble + liquid barium	9 (27 tests)	Total gastric emptying time = 7–15 hours (range)	56
		Kibble + liquid barium	4	Total gastric emptying time = 7.6 ± 1.98 hour (mean ± SE)	60
		Canned cat food + BIPS	10	Small BIPS 6.43 ± 2.59 hours (mean ± SD) Large BIPS 7.49 ± 4.09 hours (mean ± SD)	64
		Canned cat food + BIPS	6	Small BIPS—7.7 hours (median), 3.5–10.9 hours (range) Large BIPS—8.1 hours (median, 5–19.6 hours (range)	65
		Canned cat food + BIPS	10	Small BIPS—5.36 hours (median) Large BIPS—6.31 hours (median)	57
		Cat food + liquid barium	8	Gastric emptying time = 11.6 ± 0.9 hour (mean ± SD)	58
Gastric emptying breath test	Cat	Canned cat food	6	Peak ^{13}C excretion = 56.7 ± 9.8 min (mean ± SD)	120
	Dog	Bread, egg + margarine	6 (18 tests)	3.43 ± 0.50 hour (mean ± SD)	30

BIP, barium-impregnated polyethylene spheres.

[a] Gastric emptying rate is expressed as gastric half-emptying time unless otherwise stated.

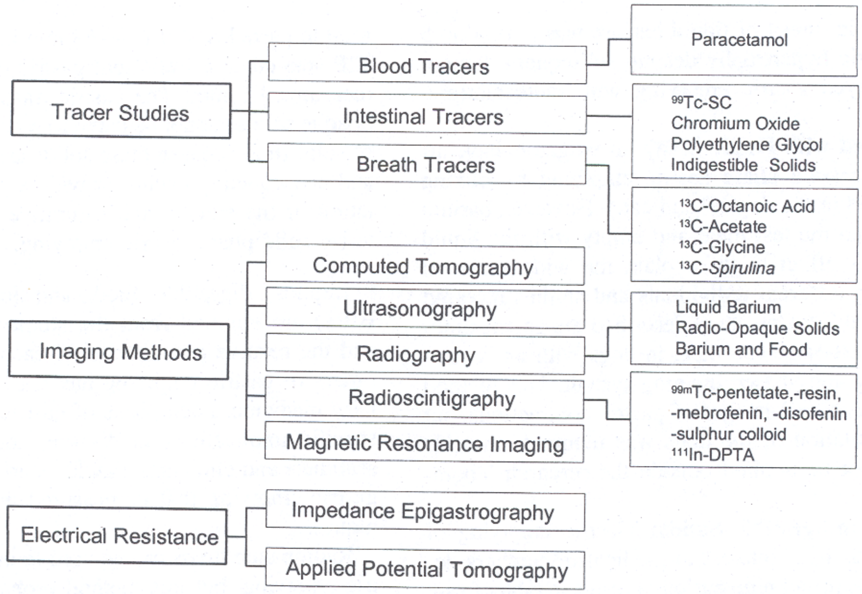

Fig 3. An outline of the methods described for assessment of solid and liquid phase gastric emptying. (DPTA, diethylene triamine pentacetic acid.)

that delayed gastric emptying might be a primary pathogenic mechanism in this disorder.[50] However, in comparison with human medicine, delayed gastric emptying has been described rarely in the veterinary literature. This observation almost certainly is due to the limited access to accurate methods for assessment of solid phase gastric emptying in animals. The development of simple and inexpensive methods for assessment of solid phase gastric emptying in veterinary medicine might show that clinical disorders of gastric emptying are more prevalent in dogs and cats than previously reported.

Methods for Assessment of Gastric Emptying

Gastroscopy can be used to exclude mechanical obstruction of the stomach,[51] but more subtle alterations in gastric emptying can be detected only by methods that can quantify the rate of gastric transit. The last decade has seen dramatic developments in the techniques available for assessment of gastric emptying in animals,[30,52,53] and several methods now available are realistic options for clinical application. This section reviews the methods that are available for assessment of gastric emptying and evaluates their application, or potential application, in veterinary medicine (Fig 3). Many of these tests currently are confined to the research laboratory, and these methods also will be reviewed in anticipation of technological developments that could facilitate their future clinical application in animals.

Diagnostic Imaging

Imaging methods frequently are used for assessment of gastric emptying in veterinary medicine, despite the frequent requirement for restraint or sedation of the animal during the procedure. Restraint can entail manual restraint,[5] sedation,[13,31] anesthesia,[13] or, in the case of the dog, restraint in a Pavlov sling.[15,54,55] All of these interventions potentially could affect the rate of gastric emptying. Imaging methods also can be difficult to apply in the clinical setting because of the necessity for sequential imaging over a long time period[5] and the requirement for special equipment and personnel.

Radiography. Radiography and fluoroscopy can be used to monitor the gastrointestinal transit of radiopaque solids and liquids, and these methods can provide qualitative and limited quantitative data on the rate and pattern of gastric emptying. The technique of radiographic assessment of gastric emptying involves sequential lateral and ventral images taken over a period of 4–12 hours after ingestion of a radiopaque meal. The movement of the meal through the stomach is assessed qualitatively, or by counting the radiopaque particles judged to be in the stomach.

Many radiopaque test meals have been used for radiographic assessment of gastric motility, including liquid barium, barium mixed with food, and radiopaque indigestible solids. The contrast media used in radiographic studies are not chemically or physically similar to food; consequently, the information provided might be of limited physiological importance. Furthermore, the palatability of radiopaque test meals has presented a difficulty in veterinary studies, often necessitating the use of chemical appetite stimulants, force feeding, or tube feeding.[56–58] Radiographic methods are useful tools for identification of gross abnormalities of gastric emptying and for detection of mucosal defects, gastric obstruction, neoplasia, and foreign bodies. These methods are less useful in detection of subtle modulations of the rate of gastric emptying because it is difficult to accurately quantify the rate of passage of radiopaque material from the stomach.

Liquid Barium: The administration of liquid barium is a commonly used method for radiographic or fluoroscopic assessment of gastric emptying of liquids, but investigation of liquid phase emptying is an insensitive method for detection of abnormalities of gastric emptying.[59] For example, in 1 study, gastric transit of liquid barium was normal in 5 dogs with pyloric hypertrophy despite subsequent demonstration of delayed gastric emptying with radioscintigraphy.[5]

Barium Mixed with Food: Many investigators have attempted to trace solid phase gastric emptying by mixing barium with food in the dog[56,60] and cat.[58] However, barium can separate from the test meal and empty with the liquid phase,[60] and this effect might explain the wide variation observed among different individuals and studies reported using this method.[56,60] One study described the gastric emptying of a contrast-enhanced meal in dogs with an X-ray–computed tomography-based imaging system. This method produced 3-dimensional images of gastric contractions, but mechanical ventilation of the dogs was required, and this method could not be applied outside the research laboratory.[61]

Radiopaque Indigestible Solids: Gastric emptying of indigestible solids is of interest to medical researchers developing methods for administration of drugs in tablet form; consequently, many reports detail the mechanisms of gastric retention and emptying of indigestible solids in dogs.[16,62,63] Radiopaque markers have been administered enclosed in gelatin shells to assess the gastric emptying of indigestible solids in the dog,[62] or mixed with food to assess solid phase gastric emptying in the dog[28,32,50,53] and cat.[64–66] The types of marker used in these studies were sections of radiopaque tubing,[41] polyamide and polypropylene spheres,[62,67] and barium-impregnated polyethylene spheres (BIPS™).[53,65] BIPS are radiopaque markers that are promoted by the manufacturers as markers for assessment of solid phase gastric emptying in dogs and cats. A 1.5-mm sphere is designed to mimic gastric emptying of digestible food, and a 5-mm sphere is designed to accumulate orad to an obstructing lesion.[53,68]

Gastric emptying of indigestible solids in the dog is dependent on particle size and density, and meal viscosity[16,63]: Larger markers (>2 mm) are retropelled into the proximal stomach and empty during the interdigestive motor pattern,[67] whereas smaller sized markers can empty in the liquid or solid phase.[16] In the horse[18] and in humans,[19] gastric emptying of larger indigestible markers can occur unrelated to patterns of interdigestive motility.

Large BIPS (>2 mm diameter) are resistant to further reduction of particle size; consequently, they are retropelled into the proximal stomach, where they might then be expected to empty from the stomach during the interdigestive motility pattern. Smaller sized BIPS might be expected to either empty immediately from the stomach or be retropelled into the antrum for trituration. Intermediate-sized markers (1.5–2 mm diameter) can empty with solid food, but this occurs subject to extensive variation among and within individual animals.[16,32,65] This variation could explain why the gastric emptying of BIPS did not correlate with the emptying of a radiolabeled solid meal in cats[66] or dogs.[32] Conversely, 1 study indicated that gastric emptying of both large (5 mm) and small (1.5 mm) BIPS was significantly correlated with the gastric emptying of concurrently ingested food.[53]

Studies have shown that the triturative functions of the canine stomach reduce the particle size of most digestible food to particles of 0.10–0.63 mm in diameter,[10,16,69] but the BIP size taken to represent gastric emptying of solid food measures 1.5 mm. The gastric transit of indigestible radiopaque solids cannot be taken to represent the gastric transit of solid food because these solids are resistant to trituration and consequently cannot provide a physiological representation of the sieving and triturative functions that characterize solid phase gastric emptying.

Liquids, digestible food, and indigestible solids (eg, BIPS) are emptied from the stomach in separate phases, and the relative contribution of each phase to clinical disorders of gastric emptying has not been studied in veterinary medicine. Each phase of gastric emptying might have specific implications in disease, and for this reason, researchers and clinicians should clearly identify the phase of gastric emptying that is measured with radiographic techniques.

Radiopaque fluids can be used to assess liquid phase gastric emptying, but this method probably is not sufficiently sensitive for detection of all abnormalities in the rate of gastric emptying. Radiopaque solids can be used to detect abnormalities of gastric emptying of indigestible particles, but the clinical relevance of this process in the dog has not yet been studied. An accurate radiopaque marker for quantitative assessment of the rate of gastric emptying of digestible food has yet to be described. Whereas radiopaque solids such as BIPS probably are sufficiently sensitive markers for detection of grossly delayed gastric emptying in clinical practice, more subtle alterations in solid phase gastric emptying might not be detected by these methods. However, the primary advantage of radiographic methods for assessment of gastric emptying in small animals is the widespread availability of radiographic equipment and expertise, and for this reason, these methods will continue to be useful tools for investigation of clinical abnormalities of gastric emptying.

Radioscintigraphy. The evaluation of gastrointestinal motility by scintigraphic imaging after ingestion of a radionuclide-labeled meal was 1st described in 1966,[70] and radioscintigraphy now is considered to be the standard method against which all new methods must be correlated.[59] The Society of Nuclear Medicine recently defined a standard protocol for radioscintigraphic evaluation of gastric emptying in human medicine,[71] and reference ranges based on large study groups and multicenter trials are now available.[72,73] Radioscintigraphy has been applied for assessment of gastric emptying in animals, in a variety of species including dogs,[5,15,31,32,74–76] cats,[13,17,41,77–79] horses,[80,81] rats,[82] monkeys,[83] and pigs.[84]

The radioisotopes usually employed in scintigraphic studies of gastric emptying are ^{99m}Technetium (^{99m}Tc, bound to pentetate, sulfur, tin or albumin colloid, disofenin, mebrofenin, or resin beads) and ^{111}Indium (bound to diethylene triamine pentacetic acid [DPTA]). These radionuclides have short half lives of 6 hours and 2.2 days, respectively, and because they emit gamma radiation at different energies, they can be combined to preferentially label the solid and liquid phases of gastric emptying. Specific analysis of the gastric emptying of solids and liquids with 1 radiolabeled meal is called the "dual isotope" method and allows the mechanisms and rates of each emptying phase to be monitored simultaneously.[59] The radiopharmaceutical used to assess the gastric emptying of solids must be shown to remain bound to the solid phase, and must not be absorbed or adsorbed in the gastrointestinal tract. ^{99m}Tc-disofenin and ^{99m}Tc-mebrofenin are recommended for use in the cat and dog respectively, on the basis of vitro and in vivo studies of labeling efficiency.[85,86] Solid phase labels generally are baked in liver or egg and mixed with canned animal food or meat. Although it has been demonstrated that radiolabeled steak and liver are emptied in parallel from the canine stomach,[16] it is possible that radiolabeled food might not empty concurrently with the ingested meal. Although the gastric emptying of radiolabeled egg or liver would still represent the process of solid phase gastric emptying, the dispersion of radiolabeled food among the ingested test meal requires further study.

In most veterinary scintigraphic studies, the animal is fasted for 12–24 hours to ensure an empty stomach, after which a test meal incorporating a radioisotope is ingested. Left and right lateral, and ventral images are acquired with a gamma-camera and integrated nuclear medicine computer system. The gastric region of interest is defined by hand[29] or computer,[13] and the radioactive counts in this region are recorded, usually at regular intervals for 6–9 hours.

Correction factors are necessary to allow for radioactive decay of the isotope over the duration of the test. Movement of the marker in the stomach could cause attenuation of the activity of the radionuclide, and the lag phase of gastric emptying might be overestimated because the marker has moved to lie closer to the camera.[87] The calculation of the geometric mean (square root of the product) of the right and left lateral images attempts to correct for some attenuation of the isotope.[88] Spreading of food in the stomach might cause some of the readings early in the test to be greater than the initial count, and overlap of activity in the small intestine or colon over the area of interest in the stomach also might be a problem.[78] Data are converted to fractional retention of radiation after decay correction. Mathematical curve fitting is used to model the data and to calculate coefficients to describe the rate of gastric emptying. Alternatively, the percent isotope remaining in the stomach at 2 and 4 hours can be calculated. This calculation reduces the number of scans necessary and has been shown to have a high predictive value in detecting alterations in gastric emptying.[51]

The application of scintigraphy in animals is limited by the requirement for a nuclear medicine facility and the radiation hazard involved. Scintigraphic facilities are now available at most veterinary academic institutions, and reference ranges based on small study groups are available. Scintigraphy protocols have been described for assessment of gastric emptying in the dog[74] and cat.[89] The test meal used in scintigraphic studies is similar to the food the animal might normally ingest; in small-animal studies, proprietary pet food or radiolabeled liver often are used.[32] Scintigraphy provides a useful standard against which new methods for assessment of gastric emptying can be compared, but the widespread clinical application of scintigraphy in dogs and cats always will be limited by the radiation hazard and the expense of this method.

Ultrasonography. Technological advances in medical ultrasonography have facilitated the application of this method for the assessment of gastric emptying. A close correlation between the rate of both liquid and solid phase gastric emptying measured by ultrasonography and by scintigraphy has been demonstrated in humans.[90,91] Ultrasonography is used to quantitatively assess gastric emptying by measuring the flow volume through a defined area of interest and allows visualization of antral contraction. However, the rate of gastric emptying measured by ultrasonography is based on the estimated change in antral volume, and this measurement might not accurately represent gastric emptying, especially if antral contents are retropelled into the fundus.[92]

The main disadvantage of ultrasonography for assessment of gastric emptying is that it requires a skilled operator and is subjective in nature; however, studies have shown that variance among operators is not unduly large.[93] Ultrasonography cannot be used to discriminate between liquid and solid emptying, and measurements are affected by gastric secretion. The presence of gas in the stomach could complicate the assessment of gastric emptying by this method,[94] and the technique might be difficult to apply in obese subjects. The principal advantage of ultrasonography is that it allows gastric emptying and antral contraction to be assessed in real time and with minimal restraint of the animal.

In dogs, gastric contractions can be visualized with ultrasonography, and delayed gastric emptying might be indicated by prolonged retention of fluid.[68,95] Recent studies have indicated that ultrasonography could be a potentially useful method for quantification of solid phase[96] and liquid phase[94] gastric emptying in the dog. Ultrasonographic equipment is widely available in veterinary practice, and ultrasonography might be a useful noninvasive method for quantitative assessment of gastric emptying in small animals. Further research is necessary to validate this method against radioscintigraphy in the dog and to describe reference ranges in healthy and diseased animals. Clinical application of this method then will be feasible and could allow simple and inexpensive assessment of gastric emptying in practice.

Magnetic Resonance Imaging. Magnetic resonance imaging (MRI) can be used to provide a 3-dimensional image of the stomach and allows gastric emptying and gastric motility to be assessed simultaneously and noninvasively.[97] MRI originally was reported as a method to assess liquid phase gastric emptying,[97] but a solid phase marker that should facilitate further application of this method recently has been described.[98] The use of MRI for assessment of gastric emptying in animals has not yet been described. Although MRI might have useful applications in veterinary research, the use of MRI for clinical assessment of gastric emptying in animals is limited by the expense and necessity for access to specialized equipment.

Electrical Resistance

The rate of gastric emptying can be assessed with the techniques of impedance epigastrography and applied potential tomography (APT) to monitor the fluctuation in an alternating current applied across the epigastric region after

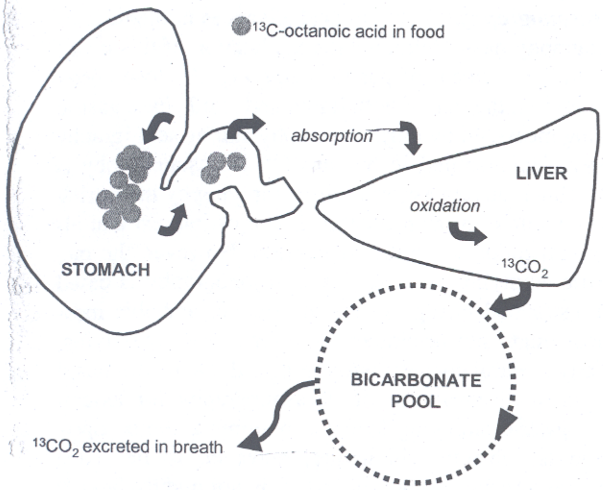

Fig 4. The rationale of the gastric emptying breath test.

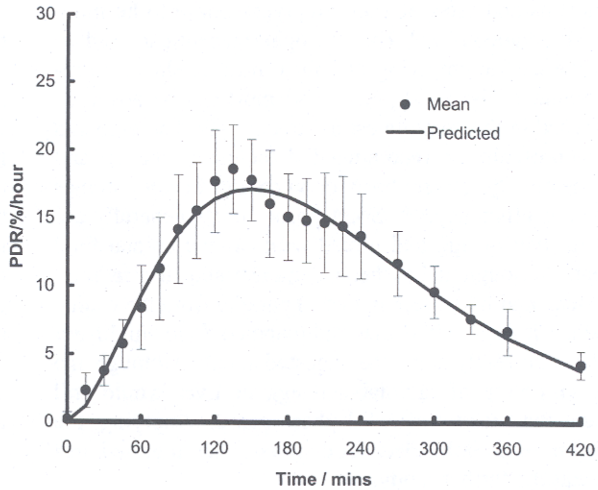

Fig 5. Application of the ^{13}C-OBT in 4 dogs illustrating pattern of solid phase gastric emptying and intersubject variability. The solid line shows the predicted gastric emptying curve, and the points and error bars are the standard deviation and mean values when the test was repeated in each animal on 3 separate occasions. PDR, percentage of administered ^{13}C dose recovered per hour. (Data from reference 30.)

ingestion of a test meal. An alternating current is applied with standard ECG electrodes, and similar electrodes are used to monitor the change in potential difference.[99] The ingestion of a meal causes increased electrical resistance across the stomach followed by an exponential decrease in impedance, and these changes are an indirect representative of gastric emptying.[100] APT involves the use of a multi-electrode array to enclose the upper abdomen, whereas impedance epigastrography uses just 2 pairs of electrodes. Both techniques are very sensitive to artifacts induced by even slight body movement during the test.[99] Nevertheless, impedance epigastrography has correlated well with liquid phase gastric emptying rates measured by scintigraphy in humans,[101] but a solid phase marker for use with this method has not yet been described. The use of either technique in small animals has not been reported, but impedance epigastrography was successfully used to monitor gastric emptying in small foals.[52] Because of the sensitivity of these methods to body movement, however, their future application in dogs and cats probably is confined to the assessment of gastric emptying in the research laboratory.

Tracer Studies

Gastric Tracers. Tracer studies involve the serial aspiration of samples of gastric contents after administration in food or by gastric intubation of a known concentration of nonabsorbable marker substance. The change in concentration of the marker is used to calculate the rate of gastric emptying. Samples of gastrointestinal contents are obtained through an oro- or nasogastric tube or a fistula or catheter inserted in the gastric or small intestinal wall. This method has been widely applied for assessment of gastrointestinal transit in dog,[26,62,69,102,103] cat,[104–106] pig,[107] and horse.[108] Some intestinal tracer studies required euthanizing the animals at defined time periods after ingestion of a meal in order to determine the rate of gastric transit of the tracer.[53,109]

Nonabsorbable substrates used as intestinal tracers of solid phase gastric emptying include indigestible solids,[16,62,63] radiolabeled food,[10] freeze-dried food,[110] and chromium oxide.[111] Liquid phase tracers include polyethylene glycol[112] and phenol red.[12] Studies with these agents assume that a homogeneous suspension is formed with the gut secretion. Intestinal tracer studies have provided valuable information on the physiology of gastric emptying, but the invasive nature of these studies confines their use to the research laboratory.

Plasma Tracers. The paracetamol (acetaminophen) absorption test has been described for assessment of the rate of liquid phase,[113] and more recently, solid phase gastric emptying.[114] Plasma drug concentrations are measured in serial blood samples after ingestion of paracetamol in solution, and the rate of gastric emptying is related to the appearance of paracetamol in the blood.[115] Paracetamol is poorly absorbed in the stomach and rapidly absorbed from the duodenum[115] and does not affect the rate of gastric emptying.[116] The paracetamol absorption test has been correlated with scintigraphic measurement of gastric emptying in humans[115] but not yet in the dog. Paracetamol can be measured easily in serum by chromatography,[117] and the absorption test protocol is relatively simple. The paracetamol absorption test has been applied for assessment of the effect of prokinetic drugs and different test meals on the rate of gastric emptying in the dog.[49,114,118] A disadvantage of the paracetamol absorption test is that intravenous catheterization is required, and the method has not been validated for assessment of solid phase gastric emptying. Paracetamol might be subject to limited absorption in the stomach, which could result in substantial variation in the results.[113] As with all methods for assessment of gastric emptying that rely on the metabolism of a tracer, the paracetamol absorption test might be affected by disordered small intestinal or liver function. Further validation of this method in diseased animals is necessary before clinical application is possible.

Breath Tracers. The assessment of gastric emptying by stable isotope breath tests involves ingestion of a ^{13}C-labeled substrate that is rapidly absorbed and metabolized to $^{13}CO_2$ after gastric emptying to produce a detectable increase in $^{13}CO_2$ in the exhaled breath. (Fig 4). If gastric

Table 2. Advantages and disadvantages of gastric emptying assessment methods.

Method	Advantages	Disadvantages
Breath test ^{13}C-octanoate ^{13}C-acetate ^{13}C-glycine	Noninvasive and nonradioactive No specialist equipment necessary Can be performed away from the analytical center Test meal resembles food; minimal restraint necessary	Expensive and not yet widely available Effects of disease on the test are poorly understood Indirect method, measurements are not real-time Assumes normal absorption and metabolism of substrate
Radiography Liquid barium Barium and food Indigestible solids	Noninvasive Equipment and expertise is widely available Real-time measurements	Requires exposure of personnel to X-rays Restraint necessary; semiquantitative data provided Nonphysiological test meal (plastic solids or barium) Barium may dissociate from solid test meal
Ultrasonography	Noninvasive and nonradioactive Real-time measurements Allows visualization of antral contractions	Interpretation is semiquantitative; restraint necessary Requires specialized equipment and personnel Imaging is affected by gastric secretion
Blood tracers Paracetamol	Simple, no specialist equipment necessary Paracetamol easily measured by HPLC Nonsubjective measurements	Requires IV catheterization Not yet validated for solid phase emptying Indirect method, assumes normal substrate metabolism
Radioscintigraphy	Noninvasive, standard method, real-time measurements Test meal resembles food Preferential monitoring of solids and liquids possible	Requires administration of a radioisotope Specialist equipment and personnel necessary Restraint is necessary
Magnetic resonance imaging	Noninvasive and nonradioactive Motility and flow can be assessed simultaneously Real-time results	Requires specialist equipment and personnel Expensive and not widely available Restraint necessary
Electrical resistance Impedance epigastrography Applied potential Tomography	Noninvasive Nonradioactive Real-time results	Complex protocol and confined to liquid phase Even slight body movement produces artefacts Restraint necessary and positioning of electrodes difficult
Intestinal tracers	Well-established method and simple protocol Wide variety of tracers available	Requires euthanasia or gastric cannulation

HPLC, high-performance liquid chromatography.

emptying is the rate-limiting step in the metabolism of the substrate to CO_2, then the pattern of isotope recovery in breath is a reflection of the rate and pattern of gastric emptying. Early studies used the radionuclide ^{14}C; however, the evolution of quick and accurate methods for detection of stable isotopes has permitted the use of the nonradioactive isotope of carbon, ^{13}C.[119]

The breath test protocol is simple and does not require any special equipment or expertise. Breath samples can be collected from animals with a face mask,[30,81,120] with a nasal prong,[121,122] or by placing the animal in a breath collection chamber.[123] The breath sampling procedure can be completed rapidly and with minimal restraint in horses, dogs, and cats.[30,81,120] ^{13}C has a natural abundance of 1.1% of the total carbon so that all ^{13}C breath tests are carried out against a background level of the naturally occurring isotope.[124] For this reason, it is necessary to ensure that basal levels of $^{13}CO_2$ excretion are stable before commencing a breath test. Foods derived from tropical grasses such as cane sugar and maize should be avoided because these have photosynthetic mechanisms that cause natural enrichment of ^{13}C. However, studies in dogs have demonstrated that under conditions of routine animal husbandry in the United Kingdom and abstinence from ^{13}C-rich foods, variation in ^{13}C excretion in dogs is negligible.[30] The animal must remain at rest during the test to ensure that the rate of CO_2 production remains constant. Breath samples can be stored in sealed tubes for up to 60 days,[124] and samples can be posted to the laboratory for analysis. The ^{13}C : ^{12}C ratio is determined by isotope-ratio mass spectrometry, and the results are plotted against time. Mathematical curve fitting can be used to derive coefficients to describe the rate of gastric emptying.

Liquid Phase Markers: The 1st breath tests to be described for measuring gastric emptying in humans were the ^{13}C-acetate breath test[125] and the ^{13}C-bicarbonate breath test.[126] Despite promising initial results, the ^{13}C-bicarbonate gastric emptying breath test could not be correlated with a simultaneous scintigraphic study; hence, it does not appear to be a suitable substrate for use in assessment of gastric emptying.[127] The ^{13}C-acetate liquid phase gastric emptying breath test has been correlated with scintigraphic[127] and dye dilution methods[125] and has been applied for assessment of liquid phase gastric emptying in pharmacology and exercise physiology studies in man.[128–130] A ^{13}C-glycine breath test can also be used for assessment of liquid phase gastric emptying, and this test showed good correlation with the rate

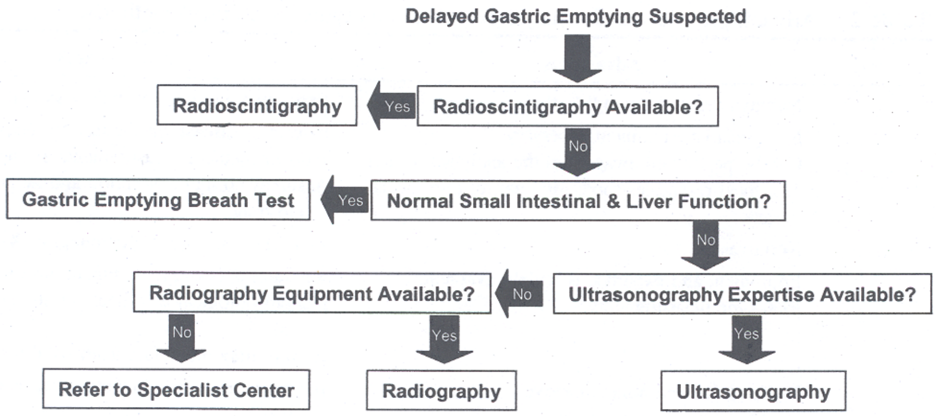

Fig 6. Flowchart for selection of suitable method for assessment of solid phase gastric emptying in the dog and cat.

of gastric emptying measured by ultrasonography, despite wide intersubject variation.[131]

Solid Phase Markers: The ^{13}C-octanoic breath test (^{13}C-OBT) was described for assessment of solid phase gastric emptying in humans in 1993,[132] and the test has now been applied in the horse,[81,122] dog,[30] cat,[120] and mouse.[123] The ^{13}C-OBT has been compared to scintigraphy in humans[132–134] and in the horse[81] and against ultrasonography in humans[135] and in the dog.[96]

Octanoic acid is a medium chain fatty acid that is rapidly absorbed in the duodenum and oxidized in the liver to produce carbon dioxide, which enters the bicarbonate pool before being excreted in breath[136] (Fig 4). Entry of the carbon label into the bicarbonate pool imposes an inevitable delay before recovery of isotope in the breath. Studies in humans,[132] horses,[81] and dogs[137] have proposed suitable correction factors to compensate for this delay.

Inter- and intrasubject variability by the ^{13}C-OBT in the dog was relatively low[30] (Fig 5) and comparable to previous studies with radioscintigraphy.[74] The test was shown to be sensitive to alterations in gastric emptying induced with different meal composition in humans,[138] dogs,[30] and horses[122] and to pharmacological modulation of gastric emptying in humans.[128] Recent innovations in the use of the ^{13}C gastric emptying breath test in human medicine include the validation of a novel substrate, ^{13}C-*Spirulina*.[139] *Spirulina* is an edible alga that is cultured in $^{13}CO_2$ to produce a 99% ^{13}C-enriched substrate that is thought to be more representative of the food matrix than octanoic acid.[140] The implied consequence is that adequate digestive enzyme activities must be present. This requirement could preclude the use of this test in subjects where, for instance, pancreatic enzyme insufficiency is suspected. In the ^{13}C-OBT, gastric emptying is likely to remain the rate-limiting step, controlling appearance of $^{13}CO_2$ in breath in these subjects. The incorporation of ^{13}C substrate into prepackaged meals and the simplification of the test protocol have now established the ^{13}C gastric emptying breath test as an investigative method that can be applied at the "point of care" in human medicine.[139–142] However, routine clinical application of this test currently is limited by poor understanding of the effects of physiological and pathological abnormalities (eg, hepatic and intestinal disease) on the performance of the test. Nevertheless, the ^{13}C-OBT has been applied for investigation of gastric emptying in many clinical disorders in human medicine, including cystic fibrosis,[143] diabetes,[133] and motor neuron disease,[144] and in critical care patients.[145]

The principal advantage of the gastric emptying breath test is that it is completely noninvasive and can be carried out away from the veterinary hospital. Analysis of breath test data can be completely automated and provides data describing the rate and pattern of gastric emptying that is nonsubjective and quantitative. The test meal in the gastric emptying breath test is similar to food normally ingested by the animal, and neither the octanoic acid substrate nor the ^{13}C label pose any risk to health.

The gastric emptying breath test is an indirect method for assessment of gastric emptying and its accuracy is dependent on rapid and reproducible absorption and metabolism of octanoic acid after entry into the duodenum. Further studies are necessary to validate this assumption in different physiological and pathological states. Application of the gastric emptying breath test currently is also limited by the requirement for expensive and technically complex methods of measurement of the carbon isotope ratio. The introduction of continuous-flow isotope ratio mass spectrometry[119,145] was a key development in the application of $^{13}CO_2$ breath tests in medicine and was followed closely by commercial instrumentation on the basis of this principle.[146] Future technological developments, likely based on spectroscopic techniques, will generate the next generation of $^{13}CO_2$ breath analyzers and facilitate wider application of the ^{13}C gastric emptying breath test. The gastric emptying breath test has considerable potential for development as a "point of care" method for assessment of gastric emptying in small animals.

Whereas the gastric emptying breath tests have been validated for application in healthy subjects, relatively few studies have investigated the effect of disease on the kinetics of tracer absorption and excretion. These tests might prove to be simple and noninvasive methods for assessment of gastric emptying in animals, but further research is necessary to determine the metabolic fate of the tracers and to validate the tests for use in all subjects.

Conclusion

Several methods now are available for assessment of gastric emptying (Table 2), both for research purposes and for clinical investigation. When available, radioscintigraphy is the method of choice, and the gastric emptying breath test could be a useful alternative in animals with normal hepatic and small intestinal function. Ultrasonography is a potentially useful method for assessment of gastric emptying in the dog, and the description of reference ranges and protocols will facilitate future application of this method. The widespread availability of radiographic equipment will ensure the continued application of radiopaque markers for detection of disordered gastric emptying of indigestible solids and liquids. The method chosen for assessment of gastric emptying in veterinary clinical practice depends on the facilities, funding, and expertise available and on the sensitivity required (Fig 6). Meanwhile, research is continuing in human and veterinary medicine to develop a noninvasive, inexpensive, and sensitive method for assessment of solid phase gastric emptying. Development of such a method would lead to a greater understanding of the clinical relevance of disordered gastric emptying in veterinary practice.

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References

1. Cannon WB. The movements of the stomach studied by means of the Roentgen rays. Am J Physiol 1898;1:359–382.

2. Cannon WB. The passage of different foodstuffs from the stomach and through the small intestine. Am J Physiol 1904;12:387–418.

3. Hall JA, Washabau RJ. Diagnosis and treatment of gastric motility disorders. Vet Clin North Am Small Anim Pract 1999;29:377–395.

4. Abrahamsson H, Glise H. Sympathetic nervous control of gastric motility and interaction with vagal activity. Scand J Gastroenterol 1984;89(Suppl):83–87.

5. Hornof WJ, Koblik PD, Strombeck DR, et al. Scintigraphic evaluation of solid-phase gastric emptying in the dog. Vet Radiol 1989; 30:242–248.

6. Azpiroz F, Malagelada J-R. Pressure activity patterns in the canine proximal stomach: Response to distension. Am J Physiol 1994; 247:G265–G272.

7. Weisbrodt NW, Wiley JN, Overholt BF, et al. A relation between gastroduodenal muscle contractions and gastric emptying. Gut 1969; 10:543–548.

8. Minami H, McCallum RW. The physiology and pathophysiology of gastric emptying in humans. Gastroenterology 1984;86:1592–1610.

9. Hinder RA, Kelly KA. Canine gastric emptying of solids and liquids. Am J Physiol 1977;233:E335–E340.

10. Meyer JH, Thomson JB, Cohen MB, et al. Sieving of solid food by the canine stomach and sieving after gastric surgery. Gastroenterology 1979;76:804–813.

11. Hinder RA, van Garde S. Individual and combined roles of the pylorus and the antrum in the canine gastric emptying of a liquid and a digestible solid. Gastroenterology 1983;84:281–286.

12. Hunt JN, Spurrell WR. The pattern of gastric emptying of the human stomach. J Physiol 1951;113:157–168.

13. Willson CA, Bushnell D, Keshavarzian A. The effect of acute and chronic ethanol administration on gastric emptying in cats. Dig Dis Sci 1990;35:444–448.

14. Houghton LA, Read NW, Heddle R, et al. Relationship of the motor activity of the antrum, pylorus and duodenum to gastric emptying of a solid-liquid mixed meal. Gastroenterology 1988;94:1285–1291.

15. Theodorakis MC. External scintigraphy in measuring rate of gastric emptying in beagles. Am J Physiol 1980;239:G39–G43.

16. Meyer JH, Dressman J, Fink A, et al. Effect of size and density on canine gastric emptying of nondigestible solids. Gastroenterology 1985;89:805–813.

17. Steyn PF, Twedt DT, Toombs W. The scintigraphic evaluation of solid phase gastric emptying in normal cats. Vet Radiol Ultrasound 1995;36:327–331.

18. Baker SJ, Gerring EL. Gastric emptying of solid, non-digestible, radiopaque markers in ponies. Res Vet Sci 1994;56:386–388.

19. Stotzer PO, Abrahamsson H. Human postprandial gastric emptying of indigestible solids can occur unrelated to antral phase III. Neurogastroenterol Motil 2000;12:415–419.

20. Code CF, Marlett JA. The interdigestive myo-electric comlex of the stomach and small bowel of dogs. J Physiol 1975;246:289–309.

21. Sarna SK. Cyclic motor activity; migrating motor complex: 1985. Gastroenterology 1985;89:894–913.

22. Szurszewski JH. A migrating electric complex of canine small intestine. Am J Physiol 1969;217:1757–1763.

23. Bueno L, Rayner V, Ruckebusch Y. Initiation of the migrating myoelectric complex in dogs. J Physiol 1981;316:309–318.

24. Kunze WA, Furness JB. The enteric nervous system and regulation of intestinal motility. Annu Rev Physiol 1999;61:117–142.

25. Roche M, Bueno L, Vagne M, et al. Patterns of electrical activity in the digestive tract of the conscious cat. Br J Nutr 1982;48: 129–135.

26. Gue M, Honde C, Pascaud X, et al. CNS blockade of acoustic stress-induced gastric motor inhibition by kappa-opiate agonists in dogs. Am J Physiol 1988;254:G802–G807.

27. Gue M, Peeters T, Depoortere G, et al. Stress-induced changes in gastric emptying, postprandial motility and plasma gut hormone levels in dogs. Gastroenterology 1989;97:1101–1107.

28. Allan FJ, Guilford GW, Robertson ID, et al. Gastric emptying of solid radiopaque markers in healthy dogs. Vet Radiol Ultrasound 1996;37:336–344.

29. Goggin JM, Hoskinson JJ, Butine MD, et al. Scintigraphic assessment of gastric emptying of canned and dry diets in healthy cats. Am J Vet Res 1998;59:388–392.

30. Wyse CA, Preston T, Morrison DJ, et al. The ^{13}C-octanoic acid breath test for assessment of solid phase gastric emptying in dogs. Am J Vet Res 2001;62:1939–1944.

31. van den Brom WE, Happé RP. Gastric emptying of a radionuclide-labelled test meal in healthy dogs: A new mathematical analysis and reference values. Am J Vet Res 1985;47:2170–2174.

32. Lester NV, Roberts GD, Newell SM, et al. Assessment of barium impregnated polyethylene spheres (BIPS) as a measure of solid-phase gastric emptying in normal dogs—Comparison to scintigraphy. Vet Radiol Ultrasound 1999;40:465–471.

33. Bellenger CR, Maddison JE, MacPherson GC, et al. Chronic hypertrophic pyloric gastropathy in 14 dogs. Aust Vet J 1990;67:317–320.

34. Walter MC, Goldschmidt MH, Stone EA, et al. Chronic hypertrophic pyloric gastropathy as a cause of pyloric obstruction in the dog. J Am Vet Med Assoc 1985;186:157–161.

35. Mathiesen DT, Walter MC. Surgical treatment of chronic hypertrophic pyloric gastropathy in 45 dogs. J Am Anim Hosp Assoc 1986;22:241–247.

36. Sikes RI, Birchard S, Patnaik A, et al. Chronic hypertrophic pyloric gastropathy: A review of 16 cases. J Am Anim Hosp Assoc 1986;22:99–104.

37. Cullen JJ, Titler S, Ephgrave KS, et al. Gastric emptying of

liquids and postprandial pancreatobiliary secretion are temporarily impaired during endotoxemia. Dig Dis Sci 1999;44:2172–2177.

38. Wise LA, Lappin MR. A syndrome resembling feline dysautonomia (Key-Gaskell syndrome) in a dog. J Am Vet Med Assoc 1991; 198:2103–2106.

39. Sautter JH, Hanlon GF. Gastric neoplasms in the dog: A report of 20 cases. J Am Vet Med Assoc 1975;166:691–696.

40. Fonda D, Gualtieri M, Scanziani E. Gastric carcinoma in the dog: A clinicopathological study of 11 cases. J Small Anim Pract 1989;30:353–360.

41. Hall JA, Willer RL, Seim HB, et al. Gastric emptying of nondigestible radiopaque markers after circumcostal gastropexy in clinically normal dogs and dogs with gastric dilatation-volvulus. Am J Vet Res 1992;53:1961–1965.

42. Funkquist B, Garner L. Pathogenic and therapeutic aspects of torsion of the canine stomach. J Small Anim Pract 1967;8:523–532.

43. Dubois A, Jacobus JP, Grissom MP, et al. Altered gastric emptying and prevention of radiation-induced vomiting in dogs. Gastroenterology 1984;86:444–448.

44. Pearson H, Gaskell CJ, Gibbs C, et al. Pyloric and oesophageal dysfunction in the cat. J Small Anim Pract 1974;15:487–501.

45. Dennis R, Herrtage ME, Jefferies AR, et al. A case of hyperplastic gastropathy in a cat. J Small Anim Pract 1987;28:491–504.

46. Canton DD, Sharp NJ, Aguirre GD. Dysautonomia in a cat. J Am Vet Med Assoc 1988;192:1293–1296.

47. Lyrenas EB, Olsson EHK, Arvidsson UC, et al. Prevalence and determinants of solid and liquid gastric emptying in unstable type I diabetes: Relationship to post-prandial glucose concentrations. Diabetes Care 1997;20:413–418.

48. Merio R, Festa A, Bergmann H, et al. Slow gastric emptying in type I diabetes: Relation to autonomic and peripheral neuropathy, blood glucose and glycemic control. Diabetes Care 1997;20:419–423.

49. Takeda M, Mizutani Y, Yamano M, et al. Gastric emptying in diabetic gastroparetic dogs: Effects of SK-951,a novel prokinetic agent. Pharmacology 2001;62:23–28.

50. Nelson OL, Jergens AE, Miles KG, et al. Gastric emptying as assessed by barium-impregnated polyethylene spheres in healthy dogs consuming a commercial kibble ration. J Am Anim Hosp Assoc 2001; 37:444–452.

51. Camilleri M, Hasler WL, Parkman HP, et al. Measurement of gastrointestinal motility in the GI laboratory. Gastroenterology 1998; 115:747–762.

52. Baker SJ, Gerring EL. Measurement of gastric emptying of water in foals by impedance epigastrography. Res Vet Sci 1994;56:256–258.

53. Guilford WG, Lawoko D, Allan FJ. Accuracy of localizing radiopaque markers by abdominal radiography and correlation between their gastric emptying rate and that of a canned food in dogs. Am J Vet Res 1997;58:1359–1363.

54. Gullikson GW, Loeffler RF, Virina MA. Relationship of serotonin-3 receptor antagonist activity to gastric emptying and motor-stimulating actions of prokinetic drugs in dogs. J Pharmacol Exp Ther 1991;258:103–110.

55. Lawaetz O, Olesen HP, Andreasen R. Evaluation of gastric emptying by a simple isotope technique. A methodological study in the dog. Scand J Gastroenterol 1981;16:737–748.

56. Burns J, Fox SM. The use of a barium meal to evaluate total gastric emptying time in the dog. Vet Radiol 1986;27:169–172.

57. Chandler ML, Guilford WG, Lawoko CR, et al. Gastric emptying and intestinal transit times of radiopaque markers in cats fed a high-fiber diet with and without low-dose intravenous diazepam. Vet Radiol Ultrasound 1999;40:3–8.

58. Steyn PF, Tweldt DC. Gastric emptying in the normal cat. J Am Anim Hosp Assoc 1994;30:78–80.

59. Parkman HP, Harris AD, Krevsky B, et al. Gastroduodenal motility and dysmotility: An update on techniques available for evaluation. Am J Gastroenterol 1995;90:869–892.

60. Miyabayashi T, Morgan JP. Gastric emptying in the normal dog. Vet Radiol 1984;25:187–191.

61. Seide K, Ritman EL. Three-dimensional dynamic X-ray–computed tomography imaging of stomach motility. Am J Physiol 1984; 247:G574–G581.

62. Gruber P, Rubinstein A, Hon Kin Li V, et al. Gastric emptying of nondigestible solids in the fasted dog. J Pharm Sci 1987;76:117–121.

63. Sirois PJ, Amidon GL, Meyer JH, et al. Gastric emptying of nondigestible solids in dogs: A hydrodynamic correlation. Am J Physiol 1990;258:G65–G72.

64. Chandler ML, Guilford G, Lawoko CR. Radiopaque markers to evaluate gastric emptying and small intestinal transit time in healthy cats. J Vet Intern Med 1997;11:361–364.

65. Sparkes AH, Papasouliotis K, Barr FJ, et al. Reference ranges for gastrointestinal transit of barium-impregnated polyethylene spheres in healthy cats. J Small Anim Pract 1997;38:340–343.

66. Goggin JM, Hoskinson JJ, Kirk CA, et al. Comparison of gastric emptying times in healthy cats simultaneously evaluated with radiopaque markers and nuclear scintigraphy. Vet Radiol Ultrasound 1999;40:89–95.

67. Wilbur BG, Kelly KA. Effect of proximal gastric complete gastric and truncal vagotomy on canine gastric electric activity, motility and emptying. Annal Surg 1973;178:295–303.

68. Lamb CR. Recent developments in diagnostic imaging of the gastrointestinal tract of the dog and cat. Vet Clin North Am Small Anim Pract 1999;29:307–342.

69. Becker JM, Kelly KA. Antral control of canine gastric emptying of solids. Am J Physiol 1983;245:G334—G338.

70. Griffith GH, Owen GM, Kirkman S, et al. Measurement of rate of gastric emptying using chromium-51. Lancet 1966;1:1244–1245.

71. Donohoe KJ, Maurer AH, Ziessman HA, et al. Procedure guideline for gastric emptying and motility. Society of Nuclear Medicine. J Nucl Med 1999;40:1236–1239.

72. Tougas G, Chen Y, Coates G, et al. Standardization of a simplified scintigraphic methodology for the assessment of gastric emptying in a multicenter setting. Am J Gastroenterol 2000;95:78–86.

73. Gryback P, Hermansson G, Lyrenas E, et al. Nationwide standardisation and evaluation of scintigraphic gastric emptying: Reference values and comparisons between sub-groups in a multicentre trial. Eur J Nucl Med 2000;27:647–655.

74. Iwanaga Y, Wen J, Thollander MS, et al. Scintigraphic measurement of regional gastrointestinal transit in the dog. Am J Physiol 1998;275:G904—G910.

75. Malagelada JR, Carter SE, Brown ML, et al. Radiolabeled fiber: A physiologic marker for gastric emptying and intestinal transit of solids. Dig Dis Sci 1980;25:81–87.

76. Burrows CF, Bright RM, Spencer CP. Influence of dietary composition on gastric emptying and motility in dogs: Potential involvement in acute gastric dilatation. Am J Vet Res 1985;46:2609–2612.

77. Gould RJ, Fioravanti C, Cook PG, et al. A model of gastric emptying in cats shows solid emptying is promoted by MK-329: A CCK antagonist. J Nucl Med 1990;31:1494–1499.

78. Steyn PF, Twedt D, Toombs W. The effect of intravenous diazepam on solid phase gastric emptying in normal cats. Vet Radiol Ultrasound 1997;38:469–473.

79. Smith SA, Ludlow CL, Hoskinson JJ, et al. Effect of percutaneous endoscopic gastrostomy on gastric emptying in clinically normal cats. Am J Vet Res 1998;59:1414–1416.

80. Ringger NC, Lester GD, Neuwirth L, et al. Effect of bethanechol or erythromycin on gastric emptying in horses. Am J Vet Res 1996;57:1771–1775.

81. Sutton DGM, Bahr A, Preston T, et al. Equine gastric motility: Validation of the ^{13}C-octanoic acid breath test for measurement of gastric emptying rate of solids using radioscintigraphy. Equine Vet J 2001. In press.

82. Duval-Araujo I, De Magal-Aes Queiroz DM, Magnago AG, et

al. Increased gastric emptying induced by *Helicobacter heilmannii* type 1 infection in rats. J Med Microbiol 2000;49:627–634.

83. Bruley des Varannes S, Mizrahi M, Dubois A. Relation between postprandial gastric emptying and cutaneous electrogastrogram in primates. Am J Physiol 1991;261:G248–G255.

84. Blat S, Guerin S, Chauvin A, et al. Role of vagal innervation on intragastric distribution and emptying of liquid and semisolid meals in conscious pigs. Neurogastroenterol Motil 2001;13:73–80.

85. Hoskinson JJ, Goggin JM, Butine MD. Evaluation of solid-phase labels for gastric emptying studies in cats. J Nucl Med 1997; 38:495–499.

86. Kunze CP, Hoskinson JJ, Butine MD, et al., Evaluation of solid phase radiolabels of dog food for gastric emptying. Vet Radiol Ultrasound 1999;40:169–173.

87. Christian PE, Datz FL, Sorenson JA, et al. Technical factors in gastric emptying studies. J Nucl Med 1983;24:264–268.

88. Tothill P, McLoughlin GP, Heading RC. Techniques and errors in scintigraphic measurements of gastric emptying. J Nucl Med 1978; 19:256–261.

89. Costello M, Papasouliotis K, Barr FJ, et al. Determination of solid- and liquid-phase gastric emptying half times in cats by use of nuclear scintigraphy. Am J Vet Res 1999;60:1222–1226.

90. Bolondi L, Bortolotti M, Santi V, et al. Measurement of gastric emptying time by real-time ultrasonography. Gastroenterology 1985; 89:752–759.

91. Benini L, Sembenini C, Heading RC, et al. Simultaneous measurement of gastric emptying of a solid meal by ultrasound and by scintigraphy. Am J Gastroenterol 1999;94:2861–2865.

92. Ahluwalia NK, Thompson DG. Ultrasonography. In: Kumar D, Wingate D, eds. An Illustrated Guide to Gastrointestinal Motility. Edinburgh: Churchill-Livingston; 1993:242–255.

93. Irvine EJ, Tougas G, Lappalainen R, et al. Reliability and interobserver variability of ultrasonographic measurement of gastric emptying rate. Dig Dis Sci 1993;38:803–810.

94. Choi M, Seo M, Jung J, et al. Evaluation of canine gastric motility with ultrasonography. J Vet Med Sci 2002;64:17–21.

95. Costello M. Assessing GI motility. Proceedings of the Annual Congress of the British Small Animal Veterinary Associatiion, Birmingham, United Kingdom, April 2001;129–130.

96. McLellan J, Dickie A, Preston T, Yam PS. Comparison of real time ultrasound and ^{13}C-octanoic acid breath test for assessment of gastric emptying in dogs. Proceedings of the Annual Congress of the British Small Animal Veterinary Association, Birmingham, April 2002;654.

97. Schwizer W, Fraser R, Borovicka J, et al. Measurement of gastric emptying and gastric motility by magnetic resonance imaging (MRI). Dig Dis Sci 1994;39:101S–103S.

98. Feinle C, Kunz P, Boesiger P, et al. Scintigraphic validation of a magnetic resonance imaging method to study gastric emptying of a solid meal in humans. Gut 1999;44:106–111.

99. Spyrou NM, Castillo FD. Electrical impedence measurement. In: Kumar D, Wingate D, eds. An Illustrated Guide to Gastrointestinal Motility. Edinburgh: Churchill-Livingston; 1993:276–278.

100. Sutton JA, Thompson S, Sobnack R. Measurement of gastric emptying rates by radioactive isotope scanning and epigastric impedance. Lancet 1985;1:898–900.

101. Magnall YF, Barnish C, Brown BH, et al. Comparison of applied potential tomography and impedance epigastrography as methods of measuring gastric emptying. Clin Phys Physiol Meas 1988;9:249–254.

102. Muller-Lissner SA, Sonnenberg A, Schattenmann G, et al. Gastric emptying and postprandial duodenogastric reflux in pylorectomized dogs. Am J Physiol 1982;242:G9–G14.

103. Haba T, Sarna SK. Regulation of gastroduodenal emptying of solids by gastropyloroduodenal contractions. Am J Physiol 199361–G271.

104. Hillemeier C, McCallum R, Oertel R, et al. Effect of bethanechol and metoclopramide on upper gastrointestinal motility in the kitten. J Ped Gastroentrol Nutr 1986;5:134–137.

105. Stemper TJ, Cooke AR. Effect of a fixed pyloric opening on gastric emptying in the cat and dog. Am J Physiol 1976;230:813–817.

106. Chikh-Issa AR, Scarpignato C, Collinet M, et al. Dual effect of bombesin and gastrin releasing peptide on gastric emptying in conscious cats. Peptides 1989;10:281–287.

107. Johansen HN, Knudsen KE, Sandstrom B, et al. Effects of varying content of soluble dietary fibre from wheat flour and oat milling fractions on gastric emptying in pigs. Br J Nutr 1996;75:339–351.

108. Baker SJ, Gerring EL. Gastric emptying of four liquid meals in pony foals. Res Vet Sci 1994;56:164–169.

109. Argenzio RA, Lowe JE, Pickard DW, et al. Digesta passage and water exchange in the equine large intestine. Am J Physiol 1974; 226:1035–1042.

110. Tanaka T, Mizumoto A, Haga N, et al. A new method to measure gastric emptying in conscious dogs: A validity study and effects of EM523 and L-NNA. Am J Physiol 1997;272:G909–G915.

111. Cowles VE, Nellans HN, Seifert TR, et al. Effect of novel motilide ABT-229 versus erythromycin and cisapride on gastric emptying in dogs. J Pharmacol Exp Ther 2000;293:1106–1111.

112. Orihata M, Sarna SK. Contractile mechanisms of action of gastroprokinetic agents: Cisapride, metoclopramide, and domperidone. Am J Physiol 1994;266:G665–G676.

113. Heading RC, Nimmo J, Prescott LF, et al. The dependence of paracetamol absorption on the rate of gastric emptying. Br J Pharmacol 1973;47:415–421.

114. Sato F, Marui S, Inatomi N, et al. EM574, an erythromycin derivative, improves delayed gastric emptying of semi-solid meals in conscious dogs. Eur J Pharmacol 2000;395:165–172.

115. Clements JA, Heading RC, Nimmo WS, et al. Kinetics of acetaminophen absorption and gastric emptying in man. Clin Pharmacol Ther 1978;24:420–431.

116. Maurer AH, Krevsky B, Knight LC, et al. Opioid and opioid-like drug effects on whole-gut transit measured by scintigraphy. J Nucl Med 1996;37:818–822.

117. al-Obaidy SS, Li Wan Po A, McKiernan PJ, et al. Assay of paracetamol and its metabolites in urine, plasma and saliva of children with chronic liver disease. J Pharm Biomed Anal 1995;13:1033–1039.

118. Mizuta H, Kawazoe Y, Haga K, et al. Effects of meals on gastric-emptying and small intestinal transit times of a suspension in the beagle dog assessed using acetaminophen and salicylazosulfapyridine as markers. Chem Pharm Bull 1990;38:2224–2227.

119. Preston T, McMillan DC. Rapid sample throughput for biomedical stable isotope tracer studies. Biomed Environ Mass Spectrom 1988;16:229–235.

120. Peachey SE, Dawson JM, Harper EJ. Gastrointestinal transit times in young and old cats. Comp Biochem Physiol A Mol Integr Physiol 2000;126:85–90.

121. Murphy D, Reid SW, Love S. Breath hydrogen measurement in ponies: A preliminary study. Res Vet Sci 1998;65:47–51.

122. Wyse CA, Murphy DM, Preston T, et al. Assessment of the rate of solid-phase gastric emptying in ponies by means of the ^{13}C-octanoic acid breath test: A preliminary study. Equine Vet J 2001;33: 197–203.

123. Symonds EL, Butler RN, Omari TI. Assessment of gastric emptying in the mouse using the [^{13}C]-octanoic acid breath test. Clin Exp Pharmacol Physiol 2000;27:671–675.

124. Mossi S, Meyer-Wyss B, Beglinger C, et al. Gastric emptying of liquid meals measured noninvasively in humans with [13C]acetate breath test. Dig Dis Sci 1994;39:107S–109S.

125. Bjorkman DJ, Moore JG, Klein PD, et al. ^{13}C-bicarbonate breath test as a measure of gastric emptying. Am J Gastroenterol 1991; 86:821–823.

126. Braden B, Adams S, Duan LP, et al. The [^{13}C]acetate breath test accurately reflects gastric emptying of liquids in both liquid and semisolid test meals. Gastroenterology 1995;108:1048–1055.

127. Duan L-P, Braden B, Caspary WF, et al. Influence of cisapride on gastric emptying of solids and liquids monitored by ^{13}C breath tests. Dig Dis Sci 1995;40:2200–2206.

128. Leese GP, Bowtell J, Mudambo S, et al. Post-exercise gastric emptying of carbohydrate solutions determined using the ^{13}C acetate breath test. Eur J Appl Physiol Occup Physiol 1995;71:306–310.

129. Mudambo KS, Leese GP, Rennie MJ. Gastric emptying in soldiers during and after field exercise in the heat measured with the [13C]acetate breath test method. Eur J Appl Physiol Occup Physiol 1997;75:109–114.

130. Ghoos YF, Maes BD, Geypens BJ, et al. Measurement of gastric emptying rate of solids by means of a carbon-labelled octanoic acid breath test. Gastroenterology 1993;104:1640–1647.

131. Benamouzig R, Mahe S, Tsakiris L, et al. Effect of carbonated water on gastric emptying of liquids monitored by ultrasonography and [^{13}C]-glycine breath test. Annual Meeting of the American Gastroenterological Association, Florida, 1999;957.

132. Ziegler D, Schadewaldt P, Pour Mirza A, et al. [^{13}C] octanoic acid breath test for non-invasive assessment of gastric emptying in diabetic patients: Validation and relationship of gastric symptoms and cardiovascular autonomic function Diabetologia 1996;39:823–830.

133. Delbende B, Perri F, Couturier O, et al. ^{13}C-octanoic acid breath test for gastric emptying measurement. Eur J Gastroenterol Hepatol 2000;12:85–91.

134. Cappello G, Malatesta MG, Ferri A, et al. Gastric emptying of a solid-liquid meal measured with ^{13}C-octanoic acid breath test and real-time ultrasonography: A comparative study. Am J Gastroenterol 2000;59:3097–3100.

135. Schwabe AD, Bennett LR, Bowman LP. Octanoic acid absorption and oxidation in humans. J Appl Physiol 1964;19:335–337.

136. Peracchi M, Gebbia C, Ogliari C, et al. Influence of caloric intake on gastric emptying of solids assessed by ^{13}C-octanoic acid breath test. Scand J Gastroenterol 2000;35:814–818.

137. Wyse CA, Preston T, Slater C, Yam PS. A comparison of the ^{13}C-octanoate breath test and the ^{2}H-octanoate saliva test for assessment of solid phase gastric emptying in the dog. Proceedings of the Annual Meeting of the European Society of Veterinary Internal Medicine, Dublin, September 2001.

138. Lee JS, Camilleri M, Zinsmeister AR, et al. A valid accurate office based non-radioactive test for gastric emptying of solids. Gut 2000;46:768–773.

139. Lee JS, Camilleri M, Zinsmeister AR, et al. Toward office-based measurement of gastric emptying in symptomatic diabetics using [^{13}C]octanoic acid breath test. Am J Gastroenterol 2000;95:2751–2761.

140. Bromer MQ, Parkman HP. Office-based testing for gastric emptying: A breath away? J Clin Gastroenterol 2001;32:374–376.

141. Chey WD, Shapiro B, Zawadski A, et al. Gastric emptying characteristics of a novel (13)C-octanoate–labeled muffin meal. J Clin Gastroenterol 2001;32:394–399.

142. Taylor CJ, Hillel PG, Ghosal S, et al. Gastric emptying and intestinal transit of pancreatic enzyme supplements in cystic fibrosis. Arch Dis Child 1999;80:149–152.

143. Toepfer M, Folwaczny C, Lochmuller H, et al. Noninvasive (13)C-octanoic acid breath test shows delayed gastric emptying in patients with amyotrophic lateral sclerosis. Digestion 1999;60:567–571.

144. Ritz MA, Fraser R, Edwards N, et al. Delayed gastric emptying in ventilated critically ill patients: Measurement by ^{13}C-octanoic acid breath test. Crit Care Med 2001;29:1744–1749.

145. Prosser SJ, Brookes ST, Linton A, et al. Rapid automatic analysis of ^{13}C and ^{18}O of CO_2 in gas samples by continuous flow isotope ratio mass spectrometry. Biomed Envir Mass Spectrom 1991;20:724–730.

146. Klein PD, Helge H. Methodology for the study of metabolism: Breath testing. In: Colvett RM, ed. Principles of Perinatal-Neonatal Metabolism, 2nd ed. New York: Springer-Verlag; 1998:17–23.