The published peer-reviewed literature on OBT in functional and organic disease has been searched on PubMed using the key words 13C breath test, octanoic acid and gastric emptying. The more significant referenced articles from recent published manuscripts and abstracts from national and international meetings have been included in this review, apart from pharmacological studies which have been instead excluded.

### Functional Disease

Although gastric dysmotility and dyspeptic symptoms are often associated, their relationship remains unclear. The aim of many studies has been to evaluate the relationship between GE and clinical features in functional dyspepsia (FD). In 1996, by means of the scintigraphic method, Stanghellini et al. have demonstrated that female sex, relevant and severe postprandial fullness, and severe vomiting are independently associated with delayed GE of solids in patients with FD.

More recently OBT has been utilized to verify these clinical evidences. In 1998, Perri et al. have confirmed that a delayed GE was associated with postprandial fullness, nausea, and vomiting. On the contrary a successive study has showed that symptom prevalence and severity were similar in dyspeptic patients with and without delayed GE. Specific symptoms did not seem to be of predictive value for identifying alterations of GE.

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### Key Words:

Gastric emptying, 13C breath test.

### Introduction

Breath test using the nonradioactive isotope 13C bound to a digestible substance, has been validated for measuring gastric emptying (GE) of solids. The octanoate breath test (OBT) provides reproducible results that correlate with findings of gastric emptying scintigraphy.

The published peer-reviewed literature on OBT in functional and organic disease has been searched on PubMed using the key words 13C breath test, octanoic acid and gastric emptying. The more significant referenced articles from recent published manuscripts and abstracts from national and international meetings have been included in this review, apart from pharmacological studies which have been instead excluded.
showed that the presence of vomiting and postprandial fullness was associated with delayed solid emptying.6

Another interesting question has concerned the association of FD with irritable bowel disease (IBS). Gastric emptying of digestible solids in IBS patients has been evaluated in few studies. In a scintigraphic study, overlapping dyspepsia was diagnosed in 66% of 146 IBS patients. IBS patients without overlapping dyspepsia had normal gastric emptying of solids.7 A significant association was observed in IBS patients between delayed gastric emptying and overlapping relevant postprandial fullness and nausea. More recent reports using OBT have obtained conflicting results. Haag et al. have showed a GE significantly delayed both in dysmotility-like dyspeptic patients and in IBS subjects, although the sample size was small in both cases.

*Helicobacter pylori* status did not correlate with delayed GE. Conversely in a large series (309) of FD where the patients were divided in two groups (54% were FD alone and 46% FD with overlapped IBS), GE, accommodation to meal and *Helicobacter pylori* infection did not differ in the two populations. Association between FD and IBS was more frequent in female patients and was characterized by a greater symptom severity.

### Organic Disease

OBT has been successfully utilized in different pathological conditions (Table II). Numerous studies have evaluated gastric function in diabetes mellitus. Various reports have demonstrated similar results using OBT when compared to scintigraphy.10 These data have confirmed that solid GE was delayed in 30-50% of diabetics. Other studies have evaluated the relationship between GE and glycemic levels, autonomic neuropathy and gastric autoimmunity. In particular De Block et al.11 have showed that solid GE was delayed in 42% and liquid emptying in 36% of type 1 diabetics. Gastric motility did not correlate with symptoms and HbA1c level was the only risk factor for delayed solid emptying. Parietal cell antibodies did not correlate with GE while autonomic neuropathy correlated with liquid emptying only.

In other organic diseases most of reports have demonstrated a delayed GE. For instance in cirrhosis 75% of 80 subjects displayed a delay of GE.12 In another study where GE was also delayed, paracentesis did not influence gastric behaviour.13

As expected, in neurological conditions such as Parkinson and amyotrophic lateral sclerosis, GE was significantly slower that in control groups.14,15

These pathological evidences, compared to healthy controls, were confirmed in 16 obese women, in 30 critic ill subjects and in 5 post colectomy ileostomic patients.16-18

The OBT has also been employed to study the effects of renal failure on the gastric performance. Diabetic chronic renal failure patients have displayed lower gastric emptying rates than non-diabetic nephropatic patients. Even the non-diabetic patients had a significantly delayed GE rate compared to the healthy volunteers.19 In a successive report 66 hemodialysis patients, 58 predialysis patients and 28 on peritoneal dialysis patients were included. Gastroparesis was most prevalent in patients on peritoneal dialysis.20

Children with celiac disease have been studied by OBT before and after gluten free
diet\textsuperscript{21}, GE was significantly delayed when compared with healthy controls. After 6 months of gluten free diet, emptying values returned to normal range.

Although GE has commonly been considered altered in gastro-esophageal reflux disease (GERD)\textsuperscript{22,23}, infants with GERD did not have delayed GE using the OBT\textsuperscript{24}. In healthy preterm infants right-side positioning was associated with increased triggering of gastro-esophageal reflux, despite accelerating GE\textsuperscript{25}. In a physiological study, the gastric emptying rate for individual neonates was independent of milk amount\textsuperscript{26}. Also in duodenal ulcer disease OBT has showed normal emptying results\textsuperscript{27}. However, in some case, GE can be accelerated such as in distal gastrectomy\textsuperscript{28}, although in a recent report\textsuperscript{29}, in patients with post cancer distal gastrectomy, emptying rate was within normal range. No differences were found between symptomatic and asymptomatic Billroth II subjects.

Finally during recovery from hyperemesis gravidarum, the patients have showed accelerated GE compared to no dyspeptic pregnant women\textsuperscript{30}.

**Discussion**

Several mechanisms concur to GE such as gastric accommodation and tone, antral contractility, antroduodenal coordination, pyloric function, entero-enteric reflex and probably digestive hormone modulation. By means of OBT, numerous attempts have been made to demonstrate some pathogenetic role on gastric function of various extrinsic factors. The concept that an inflammation of the stomach could compromise gastric function has been took often into account\textsuperscript{31}. However the majority of studies have excluded an association between Helicobacter pylori infection and gastric function, both in functional\textsuperscript{14,15} and organic diseases\textsuperscript{22,20,29}.

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**Table II.** The main published peer-reviewed literature on OBT in organic diseases.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Yrs</th>
<th>Journal</th>
<th>Pts</th>
<th>Cts</th>
<th>Methods</th>
<th>Results</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Diabetes</td>
<td>2003</td>
<td>Diab Care</td>
<td>42</td>
<td>/</td>
<td>AN+ &amp; Pcas -</td>
<td>40% delayed</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>and GERD</td>
<td></td>
<td></td>
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<tr>
<td>Preterm child</td>
<td>2003</td>
<td>Nutrition</td>
<td>16</td>
<td>/</td>
<td>vs milk</td>
<td>delayed</td>
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<tr>
<td></td>
<td>2004</td>
<td>J Pediatr</td>
<td>10</td>
<td>/</td>
<td>body position</td>
<td>phisiology</td>
<td></td>
</tr>
<tr>
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<td>Diab Ob Met</td>
<td>16</td>
<td>16</td>
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<td>9</td>
<td>9</td>
<td>Pre and post GFD</td>
<td>delayed</td>
<td>children</td>
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<tr>
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<td>80</td>
<td>/</td>
<td>H. pylori NS</td>
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<tr>
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<td>Gut</td>
<td>36</td>
<td>/</td>
<td>normal</td>
<td></td>
<td>children</td>
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<td>Ns</td>
<td>Distal gastrect.</td>
<td>accelerated</td>
<td>abstract</td>
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<td>Am J Gastro-enterol</td>
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<td>12</td>
<td>Post cancer</td>
<td></td>
<td>Billr II sympt. NS + barostat</td>
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<tr>
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<td>Ns</td>
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<td>22</td>
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<td></td>
<td></td>
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<td>Ns</td>
<td>H. pylori NS</td>
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<tr>
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<td>2001</td>
<td>Gastroenterology</td>
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<td>Ns</td>
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<td>Gastroenterology</td>
<td>Ns</td>
<td>Ns</td>
<td>vs no dyspeptic</td>
<td>accelerated</td>
<td>abstract</td>
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</table>

Abbreviations: yrs, years; pts, patients; cts, controls; AN, autonomic neuropathy; Pcas, parietal cell antibodies; GFD, gluten free diet; NS, not significant; ns, not specified; Billr, Billroth II symptomatic vs asymptomatic; PD, peritoneal dialysis; HD, hemodialysis.
Besides a few reports have evaluated the impact of the autoimmunity on GE and generally only in diabetes and with conflicting results\textsuperscript{11}.

Manometric antral hypomotility has been associated with scintigraphic gastric stasis\textsuperscript{32}. These data are consistent with the hypothesis that the delayed GE in gut dysmotilities occurs because of impaired antral peristalsis due to antral hypomotility or increased resistance to flow into the small bowel due to intestinal dysmotility. On the other hand, in a more recent work using OBT, there was no positive correlation between symptom scores, gastric half emptying times and motility scores\textsuperscript{33}.

Finally, always after OBT, half-time GE was delayed in 6 out of 12 patients with primary autonomic neuropathy (AN)\textsuperscript{34}. In diabetic patients another study concludes that the \textsuperscript{13}C-octanoic acid breath test represents a suitable measure of delayed GE, which is associated with the severity of gastric symptoms and with extrinsic cardio-vascular AN\textsuperscript{35}. Apart from diabetes it is however unlikely that an extrinsic AN can play a decisive pathophysiological role in gastro-intestinal disorders\textsuperscript{36}.

Although the published reports about OBT are numerous and qualified both in physiological and pathological conditions and confirm reliability, accuracy and safety of this test, more studies are needed to further demonstrate the real significance and utility of gastric function tests.

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