Advances in Diabetic Gastroparesis
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This review addresses the advances in our understanding of the epidemiology and mechanisms in diabetic gastroparesis and dyspepsia. The mechanisms discussed include: blood glucose levels at the time of presentation, “autovagotomy,” and the intrinsic innervation (particularly the interstitial cells of Cajal and nitrergic nerves). In animal models of diabetic gastroparesis, there is evidence that homeostatic mechanisms are activated in the enteric nervous system to compensate for the loss of extrinsic innervation. Understanding these advances is key to the development of novel therapeutic strategies and for making rational choices in the management of diabetic gastroparesis and dyspepsia. [Rev Gastroenterol Disord. 2002;2(2):47–56]

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Key words: Diabetes mellitus • Diabetic enteropathy • Gastroparesis • Dyspepsia • Autonomic neuropathy • Enteric neuropathy • Interstitial cells of Cajal • Pylorospasm • Nitrergic innervation

Gastrointestinal symptoms are frequently encountered in patients with diabetes mellitus. Diabetic enteropathy refers to all the gastrointestinal complications of diabetes and may include dysphagia, heartburn, nausea and vomiting, abdominal pain, constipation, diarrhea, and fecal incontinence. Although not generally considered important causes of mortality in diabetic patients, these symptoms can be encountered in up to 75% of diabetic outpatients evaluated at a tertiary referral center. However, the prevalence of gastrointestinal symptoms among community diabetic patients is lower and will be discussed under the heading of epidemiology.
Kassender recognized asymptomatic gastric retention in diabetics in 1958 and coined the term *gastroparesis diabeticorum*. Since the original report, the term has been used to reflect symptomatic as well as asymptomatic gastric retention, and more recently, the term *diabetic dyspepsia* has been used to reflect the spectrum of postprandial symptoms in diabetics attributable to upper gastrointestinal dysfunctions, including those associated with delayed gastric emptying. Thus, whereas nausea, vomiting, and early satiation after

<table>
<thead>
<tr>
<th>Symptoms/Syndrome</th>
<th>IDDM Patients (n = 138)</th>
<th>IDDM Controls (n = 170)</th>
<th>NIDDM Patients (n = 217)</th>
<th>NIDDM Controls (n = 218)</th>
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<tbody>
<tr>
<td>Irritable bowel syndrome</td>
<td></td>
<td></td>
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<tr>
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<td>Manning criteria</td>
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<tr>
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<td>13.5</td>
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<td>Symptoms and/or laxatives</td>
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<td>19.0</td>
<td>17.0</td>
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<td>0</td>
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<td>1.2</td>
<td>4.6</td>
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<tr>
<td>Nausea/vomiting</td>
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<td>10.6</td>
<td>6.0</td>
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</tr>
<tr>
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<td>20.6</td>
<td>13.4</td>
<td>17.4</td>
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<tr>
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<td></td>
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</tr>
<tr>
<td>Symptoms only</td>
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<td>22.9</td>
<td>19.8</td>
<td>24.3</td>
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<td>Symptoms and/or antacids</td>
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<td>36.5</td>
<td>24.0</td>
<td>36.2</td>
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<tr>
<td>P neuro symptoms (overall)</td>
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<td>65.9*</td>
<td>50.5</td>
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<td>34.8</td>
<td>28.2</td>
<td>41.5*</td>
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<td>33.3</td>
<td>31.2</td>
<td>54.4*</td>
<td>43.6</td>
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<tr>
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<td>5.9</td>
<td>7.8</td>
<td>7.3</td>
</tr>
<tr>
<td>Insufficient sweating</td>
<td>6.5*</td>
<td>1.8</td>
<td>5.5</td>
<td>5.5</td>
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<tr>
<td>Gustatory sweating</td>
<td>3.6</td>
<td>4.1</td>
<td>2.3</td>
<td>2.8</td>
</tr>
</tbody>
</table>

* P < .05 (univariate association, diabetes subgroup vs corresponding controls).

P neuro, peripheral neuropathy; A neuro, autonomic neuropathy; IDDM, insulin-dependent diabetes mellitus; NIDDM, non–insulin-dependent diabetes mellitus.

Note that people with IDDM have increased prevalence of constipation and/or use of laxatives and decreased prevalence of heartburn. Prevalence of dyspepsia is not greater in diabetics than in controls. Data from Maleki et al. 

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meals were the classical symptoms of gastroparesis, the term dyspepsia in addition reflects bloating, fullness, and pain in the upper abdomen.1

Epidemiology of Gastrointestinal Symptoms in Diabetes

The first community-based epidemiological studies of symptoms in diabetics were performed in Germany and Finland by the groups of Enck and colleagues4 and Janatuinen and colleagues.3 These studies provided the surprising information that the only gastrointestinal problems with higher prevalence in diabetics than in controls were constipation, use of laxatives, and history of gall bladder surgery. The main findings were confirmed (Table 1) by a questionnaire-based study in Olmsted County, Minnesota.8 This showed that only constipation and use of laxatives were more prevalent in type I (not type II) diabetics than in controls matched for age and gender.8

The high prevalence of functional gastrointestinal disorders such as irritable bowel syndrome, constipation, and functional dyspepsia in Western civilizations confounds any estimates of the prevalence of diabetic enteropathy based on symptoms alone. Prevalence figures do not assess the impact or severity of the upper gastrointestinal symptoms suggestive of dyspepsia or gastroparesis. Thus, although Maleki and colleagues identified nausea, vomiting, or dyspepsia in around 11% of type I diabetics and around 6% of type II diabetics, these prevalence figures were not significantly different from age- and gender-matched nondiabetic community controls.8

Paradoxically, the Olmsted County study demonstrated a lower prevalence of heartburn among the participants with type I diabetes. Factors that may contribute to this finding are the possibility of vagal neuropathy reducing the sensation of heartburn and the strong recommendation by diabetologists to patients to avoid nonsteroidal anti-inflammatory medications to protect their renal function.

A more recent questionnaire-based community study in South Eastern Australia (Table 2) reported more diarrhea, fecal incontinence, dysphagia, and postprandial fullness among diabetics than among controls.7 In contrast to the three prior studies,4,6 which included at least 10% type I diabetics, in the study from Australia, 95% of the cohort were type II diabetics. Constipation (other than the symptom of “anal blockage”) was not significantly more prevalent in diabetics, in contrast to the three other epidemiological studies. The odds ratio for nausea was close to signifi-

Episodes of nausea and vomiting may last days to months or occur in cycles.

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feeding. Food ingestion may stimulate tension receptors in the nonaccommodating gastric wall, resulting in perception of bloating, early satiety, nausea, indigestion, or pain.

Pathophysiology and Mechanisms in Diabetic Gastroparesis

Diabetic gastroparesis is associated with abnormal motor and sensory functions. The factors involved in the development of abnormal sensory or motor functions of the upper gut in diabetes are shown in Table 3.

**Table 3**

<table>
<thead>
<tr>
<th>Symptom/Symptom Complex</th>
<th>Controls</th>
<th>Patients with Diabetes</th>
<th>Unadjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain or discomfort</td>
<td>10.8</td>
<td>13.5</td>
<td>1.20 (0.97-1.73)</td>
</tr>
<tr>
<td>Early satiety</td>
<td>4.3</td>
<td>5.2</td>
<td>1.22 (0.79-1.91)</td>
</tr>
<tr>
<td>Postprandial fullness</td>
<td>5.2</td>
<td>8.6</td>
<td>1.72 (1.21-2.45)</td>
</tr>
<tr>
<td>Bloating</td>
<td>11.4</td>
<td>12.3</td>
<td>1.09 (0.81-1.46)</td>
</tr>
<tr>
<td>Heartburn</td>
<td>10.8</td>
<td>13.5</td>
<td>1.30 (0.97-1.73)</td>
</tr>
<tr>
<td>Nausea</td>
<td>3.5</td>
<td>5.2</td>
<td>1.51 (0.97-2.35)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.1</td>
<td>1.7</td>
<td>1.58 (0.73-3.44)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>1.7</td>
<td>5.4</td>
<td>3.33 (2.12-5.23)</td>
</tr>
<tr>
<td>Diarrhea or constipation</td>
<td>10.0</td>
<td>15.6</td>
<td>1.69 (1.29-2.21)</td>
</tr>
<tr>
<td>Anal blockage</td>
<td>5.0</td>
<td>7.7</td>
<td>1.60 (1.10-2.32)</td>
</tr>
<tr>
<td>&gt;3 bowel movements per day</td>
<td>5.3</td>
<td>8.4</td>
<td>1.64 (1.14-2.34)</td>
</tr>
<tr>
<td>&lt;3 bowel movements per week</td>
<td>3.6</td>
<td>4.3</td>
<td>1.19 (0.73-1.93)</td>
</tr>
<tr>
<td>Lumpy or hard stools</td>
<td>5.5</td>
<td>7.4</td>
<td>1.36 (0.93-1.98)</td>
</tr>
<tr>
<td>Loose or watery stools</td>
<td>5.4</td>
<td>10.0</td>
<td>1.95 (1.40-2.72)</td>
</tr>
<tr>
<td>Urgency</td>
<td>5.2</td>
<td>9.3</td>
<td>1.88 (1.33-2.65)</td>
</tr>
<tr>
<td>Fecal incontinence</td>
<td>0.8</td>
<td>2.6</td>
<td>3.39 (1.77-6.47)</td>
</tr>
<tr>
<td>Esophageal symptoms</td>
<td>11.5</td>
<td>15.4</td>
<td>1.40 (1.06-1.83)</td>
</tr>
<tr>
<td>Upper dysmotility symptoms</td>
<td>15.3</td>
<td>18.2</td>
<td>1.24 (0.96-1.59)</td>
</tr>
<tr>
<td>Any bowel symptom</td>
<td>18.9</td>
<td>26.0</td>
<td>1.51 (1.21-1.89)</td>
</tr>
<tr>
<td>Diarrhea symptoms</td>
<td>10.0</td>
<td>15.6</td>
<td>1.67 (1.27-2.19)</td>
</tr>
<tr>
<td>Constipation symptoms</td>
<td>9.2</td>
<td>11.4</td>
<td>1.26 (0.92-1.72)</td>
</tr>
</tbody>
</table>

Note higher prevalence of diarrhea, incontinence, dysphagia, and postprandial fullness, and of gastrointestinal symptom complexes in diabetics than controls. Note upper dysmotility symptoms just fail to reach significance. Reproduced, with permission, from Bytzer et al.7

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abnormalities of the small intestine observed in symptomatic diabetic patients\textsuperscript{12,13} are often indistinguishable from those seen in patients with other syndromes affecting postganglionic sympathetic function.\textsuperscript{14} Vagal dysfunction is probably critical in gastric stasis of solid food. Electrolyte imbalances due to diabetic ketoacidosis (eg, hypokalemia) and uremia may further aggravate impaired motor function in diabetic patients.

Vagal neuropathy was considered a likely cofactor preventing the gastric accommodation response.\textsuperscript{15-17} However, a recent study of patients with diabetes and vagal neuropathy showed normal postprandial change in gastric volume measured using single photon emission computed tomography imaging.\textsuperscript{18} This is consistent with the normalization of gastric accommodation in rats within 30 days after vagotomy.\textsuperscript{19} This normalization is suggestive of an adaptive response, which was inhibited in rats treated with tetrodotoxin, suggesting that enteric neurons are involved in the adaptation to chronic vagal denervation.\textsuperscript{19} In patients with prior gastric surgery that included vagotomy, the tonic response to a meal was maintained, whereas the phasic contractile response was reduced.\textsuperscript{20} The effect of glycemia on proximal gastric motor and sensory function is also controversial; Hebbard and colleagues\textsuperscript{21} showed significant disturbances in these functions. In contrast, other studies\textsuperscript{16,22} showed no reduction of gastric relaxation or inhibition of the volume increase postprandially, despite the diabetes being associated with hyperglycemia in the former study and chronic vagal neuropathy in the latter study.

Enteric (Intrinsic) Neuropathy

The enteric nerves have been studied most thoroughly in experimental animal models of diabetes. Immunohistochemical findings contrasted with the observations of Yoshida, Schuffler and colleagues,\textsuperscript{23} who used silver staining techniques to evaluate the myenteric plexus. These nerves appeared morphologically normal in patients with diabetes.\textsuperscript{23} In contrast, Belai, Burnstock, and colleagues\textsuperscript{24–28} documented disturbances in intrinsic nerves and the protective role of gangliosides in a series of elegant studies in the streptozotocin model of diabetes. For example, they showed reduced substance P (an excitatory neurotransmitter), increased VIPergic (an inhibitory neurotransmitter), and increased calcitonin gene–related peptide (sensory transmitter) intrinsic neurons in non-sphincteric muscle. Nitrergic neurons in the pyloric sphincter were also deficient.\textsuperscript{24} Neuropeptide Y and serotonin were altered in the same model, and these may contribute to abnormal fluid and electrolyte handling in the intestine.

Abnormal Interstitial Cells of Cajal

Two recent reports suggest that the pacemaker cells in the wall of the upper digestive tract are abnormal in experimental diabetes and in a single patient with diabetes mellitus. Thus Ordog and colleagues\textsuperscript{29} showed electrophysiological disturbances associated with long-standing diabetes, which was associated with reduced volume of interstitial cells of Cajal (ICC) in the antrum and fundus; at both sites, the nerve trunks in the wall of the stomach were rarely associated with ICCs, compared to control animals (Figure 1). A single case study reported by workers at Cleveland and Mayo Clinics showed a reduced ICC network in the jejunum, and this was also associated with reduced numbers of neurons staining for nNOS, VIP, and pituitary adenylate cyclase associated peptide (PACAP).\textsuperscript{30}

Effect of Changes in Blood Glucose

In recent years, it has been suggested that glycemic control alters several

\begin{table}
\centering
\caption{Pathophysiology of Diabetic Gastroparesis}
\begin{tabular}{|l|}
\hline
Autonomic (vagal) neuropathy \\
Intrinsic neuropathy: \\
Excitatory and inhibitory nerves \\
Interstitial cells of Cajal \\
Acute elevations of blood glucose \\
Psychosomatic factors \\
\hline
\end{tabular}
\end{table}

\textbf{Table 3}

Pathophysiology of Diabetic Gastroparesis

- Autonomic (vagal) neuropathy
- Intrinsic neuropathy:
- Excitatory and inhibitory nerves
- Interstitial cells of Cajal
- Acute elevations of blood glucose
- Psychosomatic factors

Figure 1. Networks of antral interstitial cells of Cajal are markedly damaged in diabetic compared to nondiabetic rats. Reproduced from Ordog et al,\textsuperscript{29} with permission from the American Diabetes Association.
Pathophysiological Mechanisms in Diabetic Gastroparesis continued

gastrointestinal functions, such as gastric emptying, gastric myoelectric activity, antral and duodenal motor activity, gastric visceral sensation, and the colonic response to feeding. Alterations in glucose control may also alter counterregulatory hormones, some of which directly affect gastrointestinal motility. These include glucagon, glucagon-like peptide 1, amylin, epinephrine, somatostatin, growth hormone, and cortisol. The effects of autonomic nerve damage on release of these hormones from the pancreas, intestine, and liver could also contribute to the motor dysfunction.

The magnitude of the changes in motor function related to glycemia deserves further evaluation. First, we need to consider the epidemiology of diabetic dyspepsia and gastroparesis and clinical studies of the association with current glycemia. In a clinic sample of diabetics, Bytzer and colleagues reported that gastrointestinal symptoms were associated with diabetic complications but not with current glycemic control measured by blood glucose and glycosylated hemoglobin levels. In contrast, another Australian study based on a community rather than a clinic sample suggested that, after adjusting for age and gender, there was an association between self-reported poor glycemic control and gastrointestinal symptom complexes.

The contribution of poor glycemic control on self report could not be documented for four specific symptoms: early satiety, vomiting, less than three bowel movements per week, and loose or watery stools.

Second, in physiological studies of clamped hyperglycemia in healthy controls, the magnitude of change in gastric emptying parameters was quite small (eg, a difference in t½ of around 15 and 5 minutes [median, respectively, for solids and liquids]). In diabetic patients, statistically significant though biologically unimpressive changes in gastric emptying of solids and liquids have been reported (Figure 2). More detailed study of postprandial antral contractile responses were described in healthy subjects exposed to moderate hyperglycemia. Work from our laboratory has suggested that non–insulin-dependent diabetes mellitus patients without evidence of autonomic neuropathy have normal gastric emptying of solids on scintigraphy and also normal gastric accommodation measured by barostatically controlled balloon, despite elevated glucose and HbA1c levels.

Moreover, we reported accelerated gastric emptying of nutrient liquids, confirming other observations in early diabetes. There is a positive correlation of glycemic response during the first 30 minutes postprandially and the percentage of glucose drink emptied in the first 30 minutes. One interpretation is that glycemia influences the rate of emptying; alternatively, the glucose levels may reflect the rate of emptying of liquids.

Third, more convincing data on the role of glycemia is provided by studies of gastric emptying in diabetic mice. In a series of elegant studies, Watkins and colleagues evaluated the gastric emptying of 20% glucose in a variety of mice: wild-type mice, non-obese diabetic (NOD) mice in prediabetic phase, NOD mice in the diabetic stage, and streptozotocin diabetic mice (Figures 3 and 4). Only the latter two groups (which were hyperglycemic) had delayed gastric emptying; in streptozotocin mice, gastric

Gastrointestinal symptoms were associated with diabetic complications but not with current glycemic control.
emptying was normalized 12 hours after insulin treatment. Moreover, pylori from the diabetic mice showed lack of nitric oxide–mediated relaxation and nNOS protein expression, which were reversed with insulin treatment. These are among the most convincing mechanistic data, but they pertain to the effect of glycemia on the emptying of liquids in mice. Further data on the emptying of solids would be helpful. Human studies at Mayo Clinic had previously shown that diabetic gastroparesis is associated with pylorospasm. These data suggest that inhibition of pyloric tone might be a novel approach to therapy of gastroparesis. This might be achieved by restoring nitrergic innervation, replacing the cellular effects of nitric oxide by enhancing intracellular cyclic guanosine monophosphate (cGMP) in pyloric muscle with a phosphodiesterase-5 inhibitor (eg, sildenafil), or blocking the excitation of pyloric tone, as has been preliminarily reported with botulinum toxin injection of the sphincter.

Psychological Factors
Lustman, Clouse, and colleagues have provided evidence that symptoms in diabetics are significantly influenced by psychological factors.

Treatment of Diabetic Gastroparesis and Diabetic Dyspepsia
General points in the management of diabetic enteropathy include optimal control of blood glucose and restoration of hydration, nutrition, and normal intestinal propulsion.

Medications
Patients with severe exacerbation of symptoms should be hospitalized and may require nasogastric suction. Intravenous fluids should be provided and metabolic derangements (ketoacidosis, uremia, hypo/hyperglycemia) corrected. Parenteral nutrition may become necessary in cases of malnutrition. Bezoars may be mechanically disrupted during endoscopy, followed by gastric decompression to drain residual nondigestible particles. Erythromycin at a dose of 3 mg/kg body weight intravenously every 8 hours appears to be effective in acute studies.

A week’s treatment with oral erythromycin, 250 mg, t.i.d., is worthwhile once patients start to tolerate oral intake of food. Erythromycin stimulates gastric motility, enhancing gastric emptying. It also affects postprandial symptoms in experimental hyperglycemia in healthy subjects. To date there have been no reports of its effects on sensory function, though two studies using invasive or noninvasive methods showed that erythromycin reduces gastric accommodation postprandially, an effect that may result in greater postprandial discomfort, which is often reported by patients receiving this medication.

Because both liquids and homoge-
nized solids are more readily emptied from the stomach than solids, liquid or blenderized food will be better tolerated. Frequent monitoring of blood glucose levels is essential during this phase. Rarely, it is necessary to bypass the stomach with a jejunal feeding tube if the motor dysfunction is limited to the stomach and there is no response to prokinetic therapy. This procedure should be preceded by a trial for a few days of nasoenteric feeding with infusion rates of at least 60 mL iso-osmolar nutrient per hour. Jejunal tubes may be placed by laparoscopy or mini-laparotomy or via percutaneous endoscopic insertion. Such tubes allow restoration of normal nutritional status, but they are not without adverse effects.

If the patient remains symptomatic, other prokinetic agents may be considered as adjuncts. Metoclopramide is a peripheral cholinergic (via activation of 5-HT4 receptors), antidopaminergic agent with central antiemetic activity. During acute administration, it initially enhances gastric emptying of liquids in patients with diabetic gastroparesis, but its symptomatic efficacy is probably related to its central antiemetic effects. However, its long-term use is also restricted by a decline in efficacy and by a troubling incidence of central nervous system side effects. Newer 5-HT4 agonists are being developed, and it is anticipated that these may have a greater benefit-risk ratio than previous agents that caused cardiac arrhythmias by their effects on the delayed rectifier potassium current in the heart. It is, however, important to recall that there are 5-HT4 receptors in cardiac muscle (eg, atria), and that 5-HT4 agonists that have no effect on the delayed rectifier potassium current may nevertheless induce tachycardia if given at high dose.

Erythromycin loses much of its stimulatory effect beyond the first few weeks of treatment, possibly due to downregulation of motilin receptor expression. The macrolide prokinetic, ABT-229, which has no antibacterial properties, proved ineffective in patients with diabetes and dyspepsia. It is regrettable that the patients evaluated included few with delayed gastric emptying at baseline, and gastric emptying responses were not checked at the end of the study.

Gastric pacing is also extremely controversial despite approval by the U.S. Food and Drug Administration. Diabetic gastroparesis has been attributed to impaired myoelectrical activity in the antrum. Antral contractile activity and propulsion are regulated by underlying electrical slow-wave activity that originates in the pacemaker region of the stomach (at the transition between fundus and corpus on the greater curvature) and migrates aborally towards the pylorus. Hence it has been postulated that gastric pacing could be able to correct and entrain gastric slow-wave activity and therefore improve gastric emptying. However, studies have produced conflicting results. Two approaches have been proposed: McCallum and colleagues have used stimulation with an attempt to capture the pacesetter potentials; in contrast,
a multicenter study used electrical stimulation rather than pacing and showed improved symptoms but no evidence of improved emptying. In the absence of positive control treatment, it is still unclear whether the stimulation is effective in treatment of gastroparesis.

**Conclusion**

Diabetic gastroparesis and dyspepsia remain important and frequent clinical problems. The intrinsic nerves (nitrergic and interstitial cells) are recognized as increasingly important mechanisms and potential targets for novel therapies. These novel approaches might include motilides (with less tendency to desensitize) to stimulate antral contractility consistently, phosphodiesterase-5 inhibitors which have the potential to increase intracellular cGMP and replace the deficient nitrergic innervation, or intrapyloric botulinum toxin injection to reduce pyloric tone. Formal placebo-controlled studies are needed to test these novel approaches as well as the efficacy of other prokinetics with improved benefit-risk ratio.

[Supported in part by grants RO1-DK54681 and K24-DK02638 from National Institutes of Health. I wish to thank Mrs. Cindy Stanislav for excellent secretarial assistance.]

**References**


43. Lustman PJ, Anderson RJ, Freedland KE, et al. Depression and poor glycemic control: a meta-


Gastroparesis can be connected to hypochlorhydria and be caused by chloride, sodium and/or zinc deficiency. As these minerals are needed for the stomach to produce adequate levels of gastric acid (HCl) to properly empty itself of a meal. On the molecular level, it is thought that gastroparesis can be caused by the loss of neuronal nitric oxide expression since the cells in the GI tract secrete nitric oxide. Pathogenesis of symptoms in diabetic gastroparesis include: Loss of gastric neurons containing nitric oxide synthase (NOS) is responsible for defective accommodation reflex, which leads to early satiety and postprandial fullness. "Recent advances in the pathophysiology and treatment of gastroparesis". Journal of Neurogastroenterology and Motility. Diabetic Gastroparesis/Gastropathy. Diagnosis of gastroparesis requires objective evidence of delayed gastric emptying. Patients should be evaluated for complications of vomiting and alternative causes of delayed gastric emptying, such as mechanical obstruction. Additionally, when advanced fibrosis is suspected, a liver biopsy or transient elastography may be performed. Management and Treatment of the Disease. Diabetic Gastroparesis/Gastropathy. Management of gastroparesis requires optimization of glycemic control both acute and chronically. Blood glucose levels >270 mg/dL prolongs gastric emptying time. Dietary Recommendations: Vitamin and mineral deficiencies may be seen in patient with gastroparesis due to food intolerance. Diabetic gastroparesis is the result of damage to the vagus nerve, which controls the movement of food through the digestive system. In a person with this condition, the stomach takes too long to empty its contents. Symptoms include heartburn, nausea, vomiting undigested food, and weight loss. In most cases, treatment does not cure the problem -- it is usually a chronic condition. What Is Diabetic Gastroparesis? Gastroparesis, also called delayed gastric emptying, is a disorder in which the stomach takes too long to empty its contents. It often occurs in people with type 1 diabetes or type 2 diabetes...