

# Academic Physician Quarterly

A DEPARTMENT OF MEDICINE BULLETIN



**UF** UNIVERSITY of  
**FLORIDA**  
College of Medicine  
Jacksonville

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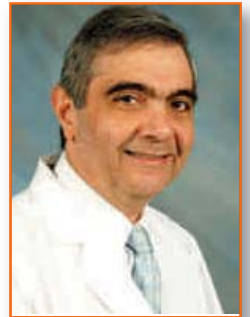
## NEWS AND NOTES

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## CHAIRMAN'S MESSAGE

Dear Colleagues:

The Department of Medicine continues to thrive through the exceptional clinical and scholarly productivity of the faculty. Our residency program once again was fully matched and had a new crop of young physicians joining our programs who had very high scores on qualifying examinations. The board pass rate continues to be one of the highest in the State of Florida. All these achievements are summarized in our annual report, which is now available through my office for your review.



In this issue of the Academic Physician Quarterly, we have a Focus topic on gastroparesis authored by members of the gastrointestinal (GI) diseases faculty and trainees. The GI division is continuing to expand through recruitment of highly talented and specialized faculty under the leadership of the divisional chief, Dr. James Scolapio.

I am proud to report that according to U.S. News & World Report's 2013-14 Best Hospitals rankings, UF Health Jacksonville was listed as high-performing in 11 specialties, including cancer; cardiology and heart surgery; diabetes and endocrinology; ear, nose and throat; gastroenterology and GI surgery; geriatrics; gynecology; nephrology; neurology and neurosurgery; pulmonology; and urology. It is notable that seven of our departmental subspecialties were included in this list.

Happy Thanksgiving.

Arshag D. Mooradian, MD  
Professor of Medicine  
Chairman, Department of Medicine

Bijo K. John, MD, Ann J. Lee, MD, Paul Sievert, MD and James Scolapio, MD, Division of Gastroenterology, Department of Medicine UFCOM-Jacksonville

## Gastroparesis

### INTRODUCTION

Normal gastrointestinal motor function is a complex, coordinated series of events that involves the sympathetic and parasympathetic nervous system and muscles of the stomach and the intestine. Any pathology or abnormality in any of these components can lead to delayed gastric emptying and produce symptoms of gastric retention in the absence of physical obstruction. It has a prevalence of 9.6 per 100,000 men and 37.8 per 100,000 women. Population-based studies have shown a higher incidence in patients with diabetes mellitus. In this article, we will provide an update on gastroparesis, focusing on clinical features, diagnostic evaluation and management.

### ETIOLOGY

Idiopathic (64%) and diabetic (31%) etiologies have been implicated in the majority of cases. Recently, with the increasing role of surgical treatment in the management of GERD and morbid obesity, postsurgical gastroparesis has become more widely recognized, and currently represents the third most common form of gastroparesis. Additionally, other causes have been identified, but represent only a minority of cases.

#### **Idiopathic gastroparesis**

Up to 64% of patients with delayed gastric emptying have no identifiable cause. In many of these patients, a prior history of a viral illness is reported, but a causative organism is rarely identified. Most of these patients are young or middle aged and predominately women. Oftentimes, clinical symptoms overlap with the diagnostic criteria for chronic idiopathic nausea, functional vomiting and functional dyspepsia.

#### **Diabetic gastroparesis**

Diabetes is commonly associated with gastroparesis in clinical practice. However, based on a recent population-based cohort study, the incidence of gastroparesis was low, with a significantly greater risk of disease reported in type 1 diabetes (5.2% in type 1 diabetes, 1% in type 2 diabetes and 0.2% in non-diabetic control).

Sustained hyperglycemia is thought to be the cause of autonomic dysfunction and/or enteric nervous system degeneration resulting in neuromuscular dysfunction. Several studies have also linked acute hyperglycemia

with delayed gastric emptying, although the pathophysiology remains poorly understood. In one study of normal subjects, gastric motility was markedly reduced at serum glucose concentration of 140 to 175 mg/dL, and nearly absent at a serum glucose concentration of 250 mg/dL.

#### **Postsurgical gastroparesis**

Postsurgical gastroparesis is the third most common cause of gastroparesis. Gastric stasis is often demonstrated following an intentional or accidental vagus nerve injury or after distal gastric resection. Postsurgical gastroparesis has been reported following bariatric surgery for morbid obesity, fundoplication for management of GERD, partial gastrectomy performed to correct complicated peptic ulcer disease, and after heart and lung transplantation possibly related to vagal nerve injury. Initial postoperative management of PSG should be conservative as most symptoms resolve with time.

#### **Other causes**

Rare causes of gastroparesis include, but are not limited to, prescription drugs (opiate analgesics, Exenatide and GLP-1 agonists, tricyclic antidepressants), connective tissue disorders (scleroderma, systemic lupus erythematosus, polymyositis), neurologic diseases (parkinsonism, stroke, multiple sclerosis, spinal injury), hormonal dysregulation (hypothyroidism, hyperparathyroidism) and paraneoplastic syndrome.

### LABORATORY TESTING

It is prudent to first rule out mechanical obstruction or mucosal disease in all patients presenting with vague upper abdominal symptoms. The choice of testing depends on the age, presentation and risk factors, including alarm symptoms. Clinicians may choose to order a barium follow through examination (upper GI series), computed tomography of the abdomen (CT scan) or upper endoscopy. If the above testing is essentially normal, a scintigraphic gastric emptying test, or commonly referred to as gastric emptying study (GES), is the next appropriate test.

### MANAGEMENT

Managing patients with gastroparesis requires a multidisciplinary approach. Treatment consists of four components: nutritional support, glycemic control in diabetes, pharmacologic therapy, and endoscopic and surgical treatment. Despite maximizing treatment options, clinical symptoms are often inadequately

managed. Therefore, long-term follow up with appropriate therapeutic modifications are required to optimize clinical needs and maintain quality of life.

### **Nutritional support**

Recurrent vomiting and poor oral intake can lead to protein-calorie malnutrition and deficiencies in vitamins and minerals. Maintaining an adequate nutritional state is an important goal of therapy. Reducing meal size and increasing the frequency of meals to four to six times a day is recommended to avoid gastric distention and exacerbating symptoms. Diet should also contain a low-fat and low-residue component, as lipids and fibers delay gastric emptying and can lead to the formation of food bezoars, especially in patients with severe gastric stasis. Additionally, patients are also encouraged to chew food well and take plenty of fluids throughout the meal, as gastric emptying of liquids is often preserved in most patients. In the subset of patients who are unable to tolerate solid meals, an alternative form of oral nutrition in the form of homogenized solids or



high-calorie liquid source may be required. Generally, poor tolerance of liquids is predictive of a poor outcome with oral nutrition and therefore, an alternative means for nutritional support may be required. When oral nutrition is unsuccessful, enteral alimentation should be considered (i.e., feeding jejunostomy tube). Total parenteral nutrition (TPN) is not commonly recommended, and clinical use is generally limited to cases with associated intestinal dysmotility.

### **Glycemic control in diabetes**

The affect of long-term glycemic control on improving gastric motility and clinical symptoms is controversial. Nevertheless, given the association between acute hyperglycemia and delayed gastric emptying, it is assumed that improving glycemic control may also

improve gastric motility and gastroparesis-related symptoms. Therefore, short- and long-term glycemic control is indicated as part of managing diabetic gastroparesis. The use of certain oral agents for treatment of diabetes, such as amylin analogs or GLP-1 analogs, have been reported to cause iatrogenic gastroparesis and should be avoided.

### **Pharmacologic therapy**

Pharmacologic therapy for gastroparesis consists of two classes of drugs: prokinetics and antiemetics.

Metoclopramide is a dopamine D2-receptor antagonist with both antiemetic and prokinetic properties. A short-term benefit in symptom reduction and accelerated gastric emptying have been supported by several comparator-controlled trials. However, the long-term efficacy is unclear and reported benefits were limited to small, open-label studies. Currently the FDA recommends a treatment duration of no longer than 12 weeks, but extended use is considered in patients who continue to experience benefit. Long-term use has also been limited by the potential for extrapyramidal side effects, including acute dystonia, parkinsonism type movements and tardive dyskinesia, which can lead to irreversible damage. Therefore, all physicians are legally obligated to discuss these adverse effects and document the discussion in the medical record.

Domperidone is also a dopamine D2-receptor antagonist similar to metoclopramide. It is as effective as metoclopramide, but the risk for extrapyramidal side effects are reported to be lower (particular tardive dyskinesia). The main concern with domperidone is its associated risk for QTc interval prolongation and the drug-drug interactions altering CYP2D6 function (antiemetic agents and antidepressants). Therefore, an electrocardiogram is recommended at the beginning of treatment and then monitored periodically during the treatment duration. This drug is currently not approved for use by the US Food and Drug Administration and only available through a FDA-sanctioned investigational new drug process.

Erythromycin is a motilin receptor agonist that stimulates gastric motility. This drug is often given as an infusion to treat acute episodes of gastric stasis. Prolonged use of erythromycin has been associated with tachyphylaxis and clinical response reportedly drops after four weeks of oral therapy. Despite this decrease in treatment response, a lesser but significant improvement is reportedly noted, thereby supporting longer therapy in select patients who continue to demonstrate clinical benefit. Similar to domperidone,



erythromycin is associated with the risk of prolonged QT syndrome and sudden cardiac death, particularly in patients taking medications that inhibit CYP3A4 function. Therefore, an electrocardiogram is recommended both at the beginning of treatment and then periodically during the treatment duration. Recently, azithromycin was recognized to have a similar prokinetic profile as erythromycin but with a reported longer duration of treatment effect. Additionally, azithromycin is a weak inhibitor of the CYP3A4, so reported drug-drug interactions and related QT prolongation has been less common.

In addition to prokinetics, antiemetic agents are used in conjunction to treat acute nausea. Several different classes of antiemetic drugs are available and include phenothiazines (prochlorperazine and thiethylperazine), antihistamines (promethazine), and serotonin 5-HT<sub>3</sub>-receptor antagonists. Currently, there are no studies that compare the efficacy between the different drug classes. Moreover, open label studies have also suggested that tricyclic antidepressants in low doses may decrease symptoms of nausea and vomiting and are considered in refractory cases.

### Non-pharmacologic therapy

Patients who fail medical therapy are considered for endoscopic and surgical intervention. These second-line treatments have not been well studied, so the clinical efficacy is not well established. Therefore, indications for treatment are often limited to cases of refractory gastroparesis.

Intrapyloric botulinum toxin injection therapy is aimed to treat the increased pyloric tone associated with gastroparesis. Several open-label studies reported improvement in gastric emptying and symptom response. On the contrary, no significant symptomatic benefit was noted in randomized, placebo-controlled trials. Therefore, intrapyloric botulinum toxin injection is currently not recommended for treatment of gastroparesis based on the available study evidence.

Gastric electrical stimulation is a FDA-approved humanitarian use device for refractory diabetic and idiopathic gastroparesis. Most of the data is from open-label clinical studies that suggest enhanced symptom control and improved oral tolerance of feeding. A recent meta-analysis also showed similar results, but additionally noted a greater clinical response for diabetic gastroparesis. Currently, there is no consensus guideline for treatment indication. Nevertheless, gastric electrical stimulation should be considered in patients with refractory diabetic and idiopathic gastroparesis.

Minimally invasive pyloroplasty is a very effective therapeutic modality that has shown excellent treatment outcomes. A recent study reported a significant improvement in symptoms with a reduction in mean gastric emptying time (320 to 112 minutes,  $p=0.001$ ) and the need for prokinetic therapy (from 89% to 14%). Other surgical options include subtotal and total gastrectomy, which are generally limited to patients with previous partial gastrectomy.

## GME CORNER



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## Constructing More Objective, Observable Evaluation Tools

As we enter a new age in resident/fellow education and the Next Accreditation System, we will be using new tools to evaluate our trainees. One new format

will be using Milestones and Entrustable Professional Activities (EPAs). Just what are milestones and EPAs? Here are a few definitions to get you started. Milestones are knowledge, skills and attitudes for each of the ACGME competencies that describe the development of competence from an early learner up to and beyond that expected for unsupervised practice. There are 22 reportable milestones that fall under the six existing competencies. All programs will be required to report their residents performance data on the 22 milestones. Examples: PC1 (Patient Care1) gathers and synthesizes essential and accurate information to define each patient's clinical problem(s). SBP2 (Systems Based Practice 2) recognizes system error and advocates for system improvement.

EPAs are the specific knowledge, skills and attitudes acquired over the course of training that society and our profession believe are critical to performing as a physician. They should describe an activity or task required of the resident for a faculty member/program director to entrust this activity to a trainee. Examples: Devise and implement insulin orders in a patient with new onset diabetes mellitus. This is a specific task that a faculty member would entrust a trainee to perform independently at the time of graduation.

EPAs are defined by milestones in each competency. For example, the above EPA example would require the following milestones: Clinical knowledge (MK1), responds to each patient's unique characteristics and need (PROF3) and develops and achieves a comprehensive management plan for each patient (PC2).

The future evaluation process for trainees will involve multisource evaluation tools (rotation evaluations, procedure evaluations, simulation evaluations, etc.) that are constructed with EPAs. These EPAs will then be mapped to ACGME reporting milestones. The ultimate goal will be a more objective evaluation process made up of observable developmental steps that describe progression from a beginning learner to

the expected level of proficiency at the completion of training.

This is a considerable amount of work to be done in the GME office to achieve this goal. We are building new evaluation tools with this new format and the logistics and technology present immense challenges. New Innovations does not always cooperate and sometimes things even get launched before we intend. At the same time, we continue to train residents and grade them on the old system until the new is up and running. In the end we hope to have a process in which trainees are evaluated in a meaningful way that satisfies both the teacher and the student.

In the meantime:



## A CLINICAL CASE

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### Streptococcal Pericarditis

#### CASE PRESENTATION

A 52-year-old man presented to the emergency department with progressively worsening shortness of breath and chest pain that was pleuritic in nature, associated with cough and expectoration (greenish-brown) but no history orthopnea/PND. He has had 8-10 pounds weight loss over two to three weeks, fevers, night sweats and chills.

Past medical history includes treatment for latent tuberculosis in 2008. He has 10 pack year smoking history, drinks six to eight beers a day and admits to occasional cocaine and marijuana use. No current home medications.

On examination, his vitals included HR: 120, BP: 134/80, RR: 18, O<sub>2</sub> sats: 90% RA. He was in mild to moderate respiratory distress, using accessory muscles of respiration. He had bilateral crepitations and rhonchi.

Tachycardic, friction rub present, S<sub>1</sub>, S<sub>2</sub> heard, no murmurs, no JVD.

Initial Lab test included: WBC : 20,000 (77% PMN), HB :14; troponin: 0.876, CK: 501, MB: 3 (0.7%); Na :127, K :5.4, Creatinine: 2.12, BUN :43, lactic acid:3.9; Bed side Ultrasound in ER: pericardial effusion. Other pertinent positive test results included: Positive urine streptococcal antigen; two out of two blood cultures positive for streptococcal pneumonia; sputum AFB negative times three and HIV test positive with CD4 : 331.

#### HOSPITAL COURSE

Pericardial drain placed and 2L of greenish fluid was drained over four days. Pericardial fluid analysis showed LDH 5040, albumin 2.3, protein 5.4 (exudative). Cultures of fluid were negative. Pericardial fluid cytology: Numerous neutrophils and few macrophages and lymphocytes. Following drainage of fluid, improvement in symptoms, ST elevation on EKG resolved. PICC line was placed and was discharged with antibiotics for total of six weeks.

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**DISCUSSION**

The potential causes of acute pericarditis are summarized in the table below.

Condition	Estimated incidence (%) <sup>a</sup>
Idiopathic	85-90
Infectious	
Viral	1-2
Bacterial	1-2
Tuberculous	4
Fungal	Rare
Parasites	Rare
Neoplastic disease	7
Systemic autoimmune disease	3-5
After cardiotomy or thoracic surgery	Rare (<1)
Aortic dissection	Rare (<1)
Chest wall trauma	Rare (<1)
Chest wall irradiation	Rare (<1)
Adverse drug reaction	Rare (<1)
Acute myocardial infarction	5-20 <sup>b</sup>
Myocarditis	30 <sup>b</sup>
Uremia	
Before dialysis	5
After initiation of dialysis	13

<sup>a</sup> Data on estimated incidence are adapted from references 1, 3, 4, and 5.  
<sup>b</sup> Percentage is related to the incidence of pericarditis in the specific population of patients.

For diagnosis of pericarditis, two of the following four should be present:

1. Chest pain (sudden in onset, retrosternal, pleuritic, positional)
2. Pericardial friction rub
3. Suggestive EKG changes such, as PR segment depression, ST segment elevation, electrical alternans if tamponade develops
4. New or worsening pericardial effusion

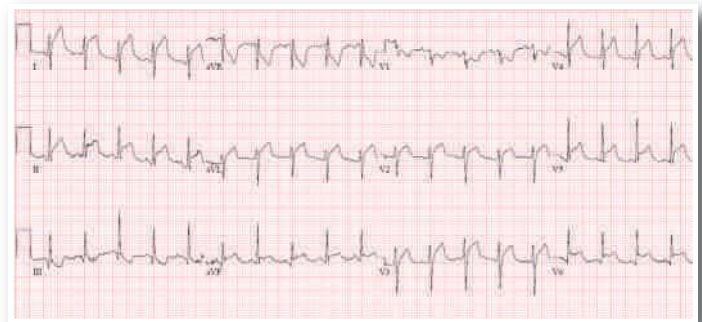
In case of tamponade, echo will show diastolic collapse of the anterior RV-free wall, RA collapse, increased tricuspid flow and decreased mitral flow during inspiration. Cardiac CT can be used to evaluate pericardial thickness and pericardial effusions.

Acute streptococcal pericarditis is a rare entity in adults in developed countries in the post-antibiotic era. It is always fatal if untreated. Mortality in treated patients is mostly due to tamponade, constriction and toxicity. Early treatment with antibiotics and surgical drainage can reduce mortality to 10-20%.

Etiological agent in bacterial pericarditis is usually staphylococcus. Streptococcus pneumoniae is a rare agent seen in about 9-10% of bacterial pericarditis. There were only 15 reported cases of S. pneumonia pericarditis from 1980 to 1988. A study by Leoncini et al. reported only five cases of purulent pericarditis in healthy adults from 1991 to 2005 and only two of those were due to S. pneumonia. It is usually a complication of infection originating elsewhere in the body, spreads by contiguous or hematogenous spread.



**Figure 1:** Chest x-ray showing large cardiac silhouette, bottle shaped heart and consolidation in the right upper lobe



**Figure 2:** Patient EKG on admission



**Figure 3:** Cardiac ECHO: EF of 45-50%, RVSP of 59, moderate to large circumferential pericardial effusion is seen. Respiratory variations of trans-aortic flow 35-40%. Strands and echo densities are noted, suggesting an exudative process.

Primary streptococcal pericarditis is rare entity reported in about eight cases.

Predisposing conditions include preexisting pericardial effusion, immunosuppression (HIV, immunosuppressive medications), chronic diseases (chronic alcohol abuse, RA), cardiac surgery and chest trauma. Predictors of poor outcome are fever greater than 38° C, sub-acute course, large effusion or tamponade, aspirin and NSAID failure. Treatment is both medical and surgical, with IV antibiotics and surgical drainage of the fluid.



Luke Miller, PharmD  
PGY-1 Pharmacy Resident

## Will Hydrocodone/Acetaminophen Become a Schedule II Controlled Substance?

*Reprinted from Drug Update Volume 30, Number 1; January-March 2013 with some editing with permission.*

On Jan. 25, 2013, the Food and Drug Administration's Drug Safety and Risk Management (DSaRM) advisory panel voted to recommend tighter restrictions on hydrocodone-containing products with a resounding 19 to 10 majority<sup>1</sup>. Tighter restrictions would move hydrocodone products (e.g., Vicodin®, Lortab®, Norco®) from Schedule III (C-III) to Schedule II (C-II) narcotics.

Schedule II substances are defined as products with a "high potential for abuse which may lead to severe psychological or physical dependence," where Schedule III substances have less potential abuse than those in Schedule II but may lead to physical or psychological dependence<sup>2</sup>. Similar to other Schedule II medications (e.g., oxycodone, morphine, fentanyl), tighter restrictions on prescribing and dispensing would result. Prescriptions for Schedule II controlled substances must be printed, signed in ink, and cannot include refills. Authorizations for renewal may not be made by telephone and a new prescription must be issued. Also, partial filling of C-II prescriptions is unlawful. Typically, if a Schedule II prescription is filled for less than the quantity written, the balance is forfeited. A petition to reschedule these medications was originally filed by the Drug Enforcement Agency (DEA) in 1999.

Although the Advisory Panel has voted in favor of the tighter restrictions, the FDA is not required to follow these recommendations. A timeline for the FDA's response to these recommendations has not been publicly announced; however, several U.S. senators have stressed the urgency of rescheduling these medications to the commissioner of the FDA.

Individual state efforts to reschedule hydrocodone have met variable success. Past efforts to reschedule hydrocodone as a Schedule II drug failed in Florida in the 2000s<sup>3</sup>. However, effective Feb. 23, 2013, all strengths, formulations and combination products of hydrocodone became Schedule II drugs in the State of

New York<sup>4</sup>.

Overall, prescription drug abuse has reached epidemic levels in the United States and is considered to be the nation's fastest-growing drug problem. Prescription medications are the second-most abused category of illicit drugs in the United States. Of people who used illicit drugs for the first time in the past year, almost one-third of them began their abuse with non-medical



use of prescription drugs<sup>1</sup>. In 2009, more than 2 million adults age 50 or older reported abuse of prescription drugs (i.e., ingestion for non-medical uses)<sup>5</sup>. Clearly, new strategies are needed to address this problem. It remains to be seen whether the FDA will find that reclassifying hydrocodone products is one of these necessary actions.

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## NEWS & NOTES

### **UF Health Jacksonville Listed as High-Performing in 11 Specialties**

I am proud to inform you that according to U.S. News & World Report's 2013-14 Best Hospitals rankings, UF Health Jacksonville was listed as high-performing in 11 specialties, including: cancer; cardiology and heart surgery; diabetes and endocrinology; ear, nose and throat; gastroenterology and GI surgery; geriatrics; gynecology; nephrology; neurology and neurosurgery; pulmonology; and urology. It is notable that seven of our departmental subspecialties were included in this list.

Out of approximately 5,000 facilities considered for inclusion in the 2013-14 Best Hospitals rankings, only 3 percent of hospitals were nationally ranked in any of the 16 specialties. In addition, only 15 percent of hospitals are listed as high-performing.

The rankings take into consideration the reputation of each hospital, patient survival rates, and a set of care-related factors such as nursing and patient services. Medical centers are also assessed for competence providing complex care for patients who are high-risk.

Our goal is to have all our subspecialties eventually achieve Best Hospital rankings.

U.S. News & World Report's 2013-14 Best Hospitals listings are available online at [www.usnews.com/besthospitals](http://www.usnews.com/besthospitals).

I want to thank our faculty, house staff and the ancillary staff for achieving this honor.

Congratulations to all.

### **Ted Bass, MD, Cardiology Chief Leads Updates for Clinical Competencies**

The chief of cardiology at the University of Florida College of Medicine-Jacksonville, Ted Bass, MD, has recently been cited in a large number of professional journals and online news feeds within his field for a paper for which he was vice chair of the writing committee and one of the lead authors. Dr. Bass was inducted as president of the Society for Cardiovascular Angiography and Interventions at the society's annual meeting in May.

The updated statement, which features input from the American College of Cardiology, American Heart Association and Society for Cardiovascular Angiography and Interventions, highlights new and adjusted benchmarks to assist with measuring and evaluating operator and institution performance of coronary-related procedures.