Management and Surveillance of Dysplasia in Inflammatory Bowel Disease

by Veena Nannegari, Rachana Potru, Jesse Green

Surveillance for dysplasia and cancer should begin after 8 years of disease. This review will outline epidemiology, pathology, management of colon cancer in ulcerative colitis and Crohn’s disease and the evidence supporting a role for cancer surveillance.

Implications of the 2012 Centers for Disease Control and Prevention (CDC) Guidelines for Screening Hepatitis C Infection in the United States

by Patrick M. Horne, Rennie Mills

In the United States, the majority of patients with chronic Hepatitis C (HCV) contracted the virus as a result of contaminated blood product transfusions prior to 1992 or due to intravenous drug use (IVDU). Recent guidelines released by the Centers for Disease Control and Prevention (CDC) have addressed this issue. This review discusses risk factors for contracting HCV, potential implications of the CDC guidelines, the importance of screening and the impact these new guidelines will have on healthcare providers (HCP).

Regression of Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma of the Cecum After Eradication of Helicobacter Pylori

by Manish Prasad Shrestha, Tat-Kin Tsang

Meat And Cola: An Esophageal Bezoar Treated by a Novel, Inexpensive Approach

by Adam C. Adler, Cesar Cestero, Eddy A. Castillo
DEPARTMENTS

Book Reviews 50

Crossword Puzzle 62
by Myles Mellor

From the Literature 49
Murray H. Cohen, D.O., “From the Literature” Editor, is on the Editorial Board of Practical Gastroenterology.

From the Pediatric Gastroenterology Literature 52
by John F. Pohl, M.D., editor of “From the Pediatric Gastroenterology Literature” is on the Editorial Board of Practical Gastroenterology.

Medical Bulletin Board 54
News items of interest to the nation’s gastroenterologists.

Meetings Calendar 61
Meetings, events, courses, symposia, and their contacts.

Reader Request Fax Form 60
Readers may obtain additional information about products and services that appear in Practical Gastroenterology.
Nutritional Management of the Adult with Cystic Fibrosis – Part II

Medical advances, research discoveries, and an interdisciplinary healthcare environment have led to a dramatic improvement in the life expectancy and quality of life for individuals with cystic fibrosis (CF). Advanced age with CF can lead to complications, but it also means that individuals can develop careers, get married, and start a family. This is part II of a two part series, which serves to present the nutritional challenges of adults with CF and to provide tools to prevent or manage these nutritional concerns. Part II will address cystic fibrosis related diabetes, fertility, and pregnancy with cystic fibrosis.

INTRODUCTION

As the most common co-morbidity in people with CF, cystic fibrosis-related diabetes (CFRD) occurs in approximately 40-50% of adults. Although CFRD shares characteristics with both type 1 and type 2 diabetes, it is clinically distinct and thus requires a unique management approach. This additional diagnosis instills both a therapeutic burden on the patient while having a negative impact on survival and lung function.

With CF individuals living into the third, fourth, and even fifth decade, discussions regarding family planning are part of standard adult CF care. Ideally, CF patients should discuss pregnancy options with their adult CF team prior to conception. This allows the members of the health care team to provide guidance regarding the safety of conception for both the mother and the fetus and to discuss recommendations to optimize the health status of the mother prior to conception. Patients with CF who are pregnant benefit from nutrition counseling regarding appropriate weight gain, vitamin and mineral supplementation, and optimum blood sugar control.

Cystic Fibrosis-Related Diabetes

Due to the progressive destruction of the pancreas and specifically to insulin-producing β-cells, CFRD is primarily caused by progressive insulin deficiency. However, acute and chronic illness can cause some level of insulin resistance. CF patients also intermittently receive systemic glucocorticoids, which can further exacerbate hyperglycemia. The typical macrovascular complications seen in patients with uncontrolled type 1 and type 2 diabetes are not of primary concern for patients with CF. In fact, despite the increasing life expectancy for CF patients, there has yet to be a report of a CF patient dying from atherosclerotic cardiovascular disease. Declining lung function, weight loss, protein catabolism, and increased mortality are all
associated with the CFRD diagnosis thus warranting regular screening for CFRD among the CF population.²

In 2010, the Cystic Fibrosis Foundation (CFF), the American Diabetes Association (ADA), and the Pediatric Endocrine Society (PES) published clinical care guidelines for the screening, diagnosis, and medical management of CFRD.²

**Screening**

Classic symptoms of diabetes include polyuria and polydipsia, but these often go unnoticed in the CF population. Frequent respiratory treatments can cause dry mouth for CF patients, causing them to drink more, and subsequently urinate more frequently than the general population. Other symptoms of diabetes in the CF population include fatigue, unexplained decline in lung function, unexplained weight loss, or the inability to gain weight despite best efforts. Clinicians should evaluate for these symptoms and trends among their adult CF patients.

Starting at age 10, annual screening for CFRD should be performed on all patients, regardless of whether the patient is pancreatic sufficient or insufficient.² The gold standard for CFRD screening is the 2-hour 75-gram oral glucose tolerance test (OGTT). Using hemoglobin A1C or fasting blood glucose is not recommended since these are not sufficiently sensitive for CFRD diagnosis.²

Additional screening criteria have been established to assess for CFRD during acute illness, while a patient is on continuous enteral drip feedings, and during pregnancy. When CF patients are treated for a pulmonary exacerbation, they are placed on intravenous antibiotics and/or systemic glucocorticoids. During the first 48 hours of treatment, fasting plasma glucose levels and 2-hour postprandial plasma glucose levels should be checked.² If after 48 hours, glucose levels do not meet diagnostic criteria, testing is no longer necessary.² For CF patients receiving supplemental continuous enteral pump feeding, blood glucose should be monitored mid-feeding and immediately after the completion of enteral feeding.² Any elevated glucose level identified by self-monitoring of blood glucose (SMBG) should be confirmed by a certified laboratory.²

Women with CF who are pregnant should be screened for gestational diabetes at 12-16 weeks and again at 24-28 weeks gestation.³ For those diagnosed with gestational diabetes, further screening for CFRD should be done 6-12 weeks after delivery.³

**Diagnosis**

Similar to screening criteria for CFRD, diagnostic criteria for CFRD is delineated into categories of healthy patients, those being treated for acute illness, those on continuous drip enteral feedings, and those who are pregnant. These guidelines can be found in Figure 1.

Unfortunately, most CF patients, even those with normal 2-hour OGTT results and normal fasting glucose levels, have some degree of glucose abnormality. Individuals may demonstrate hyperglycemia in the middle of the 2-hour OGTT or may have elevated fasting glucose levels. These individuals are said to have indeterminate glycemia (INDET) or impaired fasting glucose (IFG), respectively.² Those whose blood glucose levels are between 100-199 mg/dL after the 2-hour OGTT are said to have impaired glucose tolerance (IGT). The clinical significance of these glucose abnormalities has not yet been defined, but CF patients who meet these criteria will often develop CFRD in the future. The diagnostic criteria presented in Figure 1 are based on the risk for microvascular complications for which patients with CFRD are also at risk.² Previous CFRD guidelines required a diagnostic distinction between those with fasting hyperglycemia (FH+) and those without fasting hyperglycemia (FH-). However, studies treating both FH+ and FH- patients with insulin therapy showed similar results and the 2010 guidelines state that distinguishing between FH+ and FH- individuals is no longer necessary.¹,²,⁴

**Management**

At this time, insulin is the only recommended medical therapy for the treatment of CFRD.² Studies comparing oral diabetes agents to insulin therapy in the CFRD population demonstrate that insulin is more effective in improving nutritional and metabolic outcomes.²,⁴,⁵ No specific insulin regimen has been established for CFRD patients and insulin therapy should be individualized. The majority of CFRD patients follow a basal-bolus insulin regimen requiring multiple daily subcutaneous injections of intermediate or long-acting insulin along with rapid-acting insulin at meal times. Insulin-infusion pumps are also gaining popularity among this population to provide the needed insulin without frequent injections. Patients with CFRD are counseled to perform SMBG at least three times per day and to monitor for signs and symptoms of hypo- and hyperglycemia. Guidelines for blood glucose
goals can be found in “Managing Cystic Fibrosis-Related Diabetes: An Instruction Guide for Patients and Families, 5th Edition” 6 This manual, released by the Cystic Fibrosis Foundation in 2011, is free in print or online from the Cystic Fibrosis Foundation website: www.cff.org 6 During times of pulmonary exacerbation, insulin needs may greatly increase and remain elevated several weeks after antibiotic and/or glucocorticoid administration ceases. Consequently, CFRD patients on elevated insulin regimens following illness should closely monitor for hypoglycemic events as the need for increased insulin tapers.

Exercise is an important component to the overall health of CF patients and is frequently encouraged. Patients with CFRD should be counseled about the hypoglycemic effects of exercise and that extra carbohydrate and/or decreased insulin doses prior to intense physical activity may be necessary. Adults with CFRD should also be counseled on the use of insulin with alcohol intake. Patients taking insulin should never drink on an empty stomach, are encouraged to consume adequate carbohydrates while drinking, and to monitor blood glucose while drinking. The hypoglycemic effects of alcohol, and the potential hyperglycemic effects of drinks that are commonly mixed with alcohol, should be discussed.

Unlike patients with type 1 or type 2 diabetes, patients with CFRD are not encouraged to follow a low-fat, low-salt, or low-calorie diet. Instead, they should continue to follow a high-fat, high-salt, high-calorie well-balanced diet and use a carbohydrate-to-insulin ratio to dose their rapid-acting insulin with meals and snacks. This diet prescription requires close coordination between the endocrinologist, the diabetes educator, and the multidisciplinary cystic fibrosis care team. CFRD patients must learn to accurately count carbohydrates and to monitor and document their blood glucose so that their basal insulin or their insulin-carbohydrate ratio can be adjusted if necessary.

**Pregnancy and Fertility**

**Fertility**

Almost all men with CF struggle with infertility. Males with CF do not typically have issues with testicular
spermatogenesis, but bilateral absence or obstruction of the vas deferens is common. Consequently, although adequate sperm for fertilization may be present internally, it is not sufficiently present in the semen. Options for infertile men with CF include microsurgical epididymal sperm aspiration (MESA), percutaneous epididymal sperm aspiration (PESA), or testicular sperm harvesting. Extracted sperm is then used for in vitro fertilization.

Unlike men with CF, the majority of women with CF are able to conceive without issue. However, women with CF may reach menarche late and even after reaching menarche may experience stretches of amenorrhea or anovulation. These causes of infertility may be related to the CFTR mutation, poor health, or malnutrition. Women with CF can also have thicker cervical mucus, which leads to obstruction of the reproductive organs making it difficult for sperm to penetrate and subsequently fertilize. These obstacles

(continued on page 23)
can also be overcome using in vitro fertilization. Although in vitro fertilization is an option for both men and women with CF infertility, patients with CF are also turning to adoption and surrogacy as a means for having children.

**Medications During Pregnancy and Breastfeeding**

Adults with CF often spend their days juggling a complicated therapy schedule involving: oral and inhaled antibiotics, pancreatic enzyme replacements, insulin injections, and respiratory physiotherapy. In general, medications are not tested on pregnant women and information known about their safety during pregnancy or breastfeeding is established from animal studies, clinical experience, or known mechanism of action. Women with CF who are pregnant should discuss their entire medication list, both prescriptive and over-the-counter, with their CF physician, dietitian, and respiratory therapist. See Table I for a list of nutritionally relevant commonly used medications and their suggested use during pregnancy and breastfeeding.

**Weight: Before and During Pregnancy**

Concrete recommendations for pre-pregnancy weight in CF patients are not currently available. However, case series have demonstrated that CF women with higher pre-pregnancy BMIs deliver babies closer to full term. Additionally, those with a BMI < 20 kg/m² have an increased risk of adverse fetal outcomes. General CF guidelines advise a pre-pregnancy BMI of at least 19 kg/m². If patients cannot achieve this pre-pregnancy BMI goal with increased calorie intake and the use of oral supplements, it is not unreasonable to suggest gastrostomy tube placement for supplemental nocturnal feeding. In this population, a variable length gastrostomy tube rather than a fixed length balloon gastrostomy tube is preferred so that the feeding tube can remain in place as the abdomen stretches after pregnancy is achieved.

Guidelines for adequate weight gain for CF patients mimic those for the general population and are based on pre-pregnancy BMI. Malabsorption from pancreatic insufficiency and increased energy and protein requirements of CF patients can make what appears to be a modest weight gain quite challenging (see Table 2 for weight gain recommendations based on BMI).

An additional 300 to 800 calories per day may be required to support pregnancy for a CF patient. Importantly, this caloric requirement will vary from patient to patient, dependent on disease severity, degree of malabsorption, and sometimes results in needs greater than the general guidelines. It is often helpful to show patients their pre-pregnancy weight on a prenatal weight gain chart. This provides a visual for an appropriate weight gain goal and a copy of this chart can be sent home with the patient so that she can track her success.

**Vitamins During Pregnancy**

Vitamin supplementation during pregnancy with CF is similar to that of the general population. Due to chronic fat malabsorption, fat soluble vitamin levels (A, D, E and K) should be checked prior to conception and throughout pregnancy. Suboptimal levels should be corrected with additional supplementation (See Part I for “Vitamins Supplementation” guidelines). Folic acid deficiency can result in neural tube defects. Therefore, women with CF who are well nourished should take 400 mcg of folic acid daily while trying to get pregnant. Those at high risk for deficiency, or with a history of poor compliance, should take 4000 to 5000 mcg per day.
day prior to conception and during the first trimester. Iron deficiency anemia should be prevented or corrected prior to conception and throughout pregnancy. Iron stores should be assessed by checking serum ferritin levels each trimester and supplementing accordingly. Excessive vitamin A supplementation is often a concern during pregnancy since high doses of vitamin A can be teratogenic and standard CF multivitamins contain higher than recommended doses of vitamin A for pregnancy. However, low levels of vitamin A can also be teratogenic and some CF centers have continued high dose vitamin A supplementation throughout pregnancy without a resultant increase in serum vitamin A levels. Consequently, it is recommended to check vitamin A levels prior to pregnancy and if within normal limits, to continue routine high dose vitamin A supplementation. Vitamin A levels should be subsequently checked during each trimester with a decrease in dosage if serum levels become elevated.

Nutrition After Delivery

The delivery of a healthy baby, while maintaining a healthy mother with CF, is certainly a cause for celebration. However, the work to maintain maternal weight and lung function has just begun. Compound the work of new motherhood with the burden of CF therapy regimens and it is easy to understand how the mother may lose sight of her own health during those first few months with a newborn. Discussion about this challenging time should begin prior to delivery and follow-up with the multidisciplinary CF team shortly after pregnancy is helpful.

Similar to the general population, women with CF are encouraged to breastfeed and have done so successfully. As previously mentioned, information regarding the transfer of medications from mother to infant via breastmilk is often lacking and patients should review their entire medication list with the CF team when considering breastfeeding. Refer to Table 1 for a list of nutritionally relevant medications and their use during breastfeeding. A more extensive list of common CF medications and their use during pregnancy and breastfeeding can be found in the “Guidelines for the management of pregnancy in women with cystic fibrosis”.

Due to increased calorie and protein requirements, women with CF typically do not struggle to lose the weight gained during pregnancy and will often return to pre-pregnancy weight within one to two months after delivery. Breastfeeding increases calorie needs and women with CF who decide to breastfeed should be counseled to consume at least an additional 500 calories per day and to take 1200 mg calcium per day. Continue to routinely check fat-soluble vitamins (A, D, E and K) and replete to maintain normal levels (see Part I).

CONCLUSION

The advances in CF care have led to improved life expectancy, which can mean additional complications, but can also mean an enhanced quality of life. As a common co-morbidity of CF, CFRD must be diagnosed early and managed appropriately to minimize long-term consequences of inadequate blood glucose control. Healthy pregnancy is now a safe and feasible option for patients with CF. Practitioners can improve pregnancy outcomes by counseling patients before, during, and after delivery about the importance of nutrition and pregnancy. This is a challenging patient population, but the motivation and teamwork of the CF community make it equally rewarding.

References

11. Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines. 2009.
Patients with inflammatory bowel disease have an increased risk of developing colorectal cancer. Although surveillance is widely practiced, no large controlled trials have shown that it reduces mortality. Patients with longer duration and extent of colitis are at the highest risk. Surveillance for dysplasia and cancer should begin after 8 years of disease. Dysplasia associated with a non-adenoma-like lesion or mass and high grade dysplasia are indications for colectomy while adenoma-like lesions may be managed with complete polypectomy and frequent surveillance colonoscopies. This review will outline epidemiology, pathology, management of colon cancer in ulcerative colitis and Crohn’s disease and the evidence supporting a role for cancer surveillance. Newer techniques for colonoscopic surveillance and chemoprophylaxis will also be discussed though there may not be sufficient evidence to support widespread use of chemopreventive agents.

INTRODUCTION

Inflammatory bowel disease (IBD) places patients at increased risk for colorectal cancer (CRC). The risk is related to the anatomic extent, duration and severity of the disease. Although no large controlled trials have shown that surveillance decreases mortality, surveillance is widely practiced and recommended by all the major gastroenterological societies. This review will outline the epidemiology, pathology, natural history, surveillance and management of dysplasia in the setting of inflammatory bowel disease.

Veena Nannegari, M.D., Gastroenterology Fellow Rachana Potru, M.D., Gastroenterology Fellow Jesse Green, M.D., Professor of Medicine, Medical Director, DDC Endoscopy, Albany Medical Center, NY

Epidemiology

The risk of colorectal cancer is increased in patients with ulcerative colitis (UC) and Crohn’s disease (CD). A Swedish population-based study estimated that the risk of colorectal cancer in IBD was 95 cases per 100,000 population. The trend over the last 40 years has generally been of a decline in incidence of colorectal cancer. It is not clear if a gender difference exists in the risk. In another population-based study, males had a 60% higher risk of colorectal cancer than females though the effect of sex was seen only after ten years of follow-up. These gender differences could be explained by differences in the extent of inflammation or patient behavior leading to differences in medication or surveillance.
The risk of CRC in UC has been well-studied and depends on the extent and duration of disease. Patients with disease extending to the hepatic flexure or more proximally have the greatest risk of colorectal cancer. Compared to an age-matched population, the risk begins to increase eight to 10 years following the onset of symptoms.\textsuperscript{3,4,5} In one series, the absolute risk of CRC in patients with pancolitis was 30\% after 35 years of disease.\textsuperscript{6} Another study showed the presence of “backwash ileitis” (inflammation of the terminal ileum in the setting of colitis) as a risk factor for CRC, but other studies have not confirmed this relationship.\textsuperscript{7,8} The severity of inflammation may also be an independent risk factor as shown in a case–control study and later confirmed in a cohort study.\textsuperscript{9,10}

While patients with colitis confined to the left colon (i.e. distal to the splenic flexure) also have an increased risk of colorectal cancer, theirs is less so compared to patients with pancolitis. Many studies have shown that the risk of CRC increases after 15 to 20 years in patients with left-sided colitis, though rates of dysplasia are similar to patients with pancolitis.\textsuperscript{11,12} Patients with ulcerative proctitis and proctosigmoiditis are probably not at increased risk for CRC. Patients with UC complicated by primary sclerosing cholangitis do have an increased risk of colorectal cancer, particularly in the right colon.\textsuperscript{13} This suggests bile acids may play a role in the development of this cancer.

The risk of dysplasia in CD has been less well-studied than that in ulcerative colitis. It may be similar to that of patients with UC but not all studies have reached this conclusion; the extent of risk is still debated. Most of these studies did not adjust for duration and extent of disease.\textsuperscript{14-16} An American population-based study found a significantly increased risk of small bowel but not colorectal cancer.\textsuperscript{17} A Swedish population-based study noted the overall relative risk of colon cancer was 2.5 in patients with CD though increased to 5.6 in those with disease restricted to the colon.\textsuperscript{14} The risk was even higher in patients diagnosed before age 30. Colorectal cancer in CD is observed at a similar age as that in UC with a median duration of disease prior to cancer diagnosis of 15 and 18 years, respectively.\textsuperscript{14,19} Despite this increased risk, however, the overall number of patients with CD who develop colorectal cancer is small.

**Pathogenesis**

The pathogenesis of colon cancer in IBD is not well understood but seems to be different than for sporadic CRC. Patients who develop CRC in IBD are usually younger (40s -50s) compared to sporadic CRC, who tend to be in their 60s at diagnosis.\textsuperscript{14} Dysplasia in UC is preceded by a long history of chronic inflammation and can be found at sites distant from the cancer. Dysplasia in sporadic colon cancer is usually associated with a polyp without inflammation.\textsuperscript{20}
Pathology

As in sporadic colorectal cancer, most cancers in IBD patients are adenocarcinomas. However, poorly differentiated, anaplastic and mucinous carcinomas are more common in colitis-associated CRC than sporadic. Neoplasms may appear polypoid, nodular, ulcerated or plaque-like. Colon cancer associated with UC is most common in the rectum and sigmoid colon whereas neoplasia in Crohn’s disease is evenly distributed between the right colon and the rectosigmoid. Cancer associated with IBD occurs in areas with chronic inflammation. Synchronous tumours occur in 12 percent of CRC in IBD cases compared to 3 to 5 percent in sporadic CRC.

It is generally accepted that colorectal cancer in IBD is preceded by dysplasia. Histologically dysplasia is categorized as negative, indefinite or positive; the positive category is divided into low grade and high grade dysplasia. Dysplastic areas may be difficult to recognize on endoscopy since they can be flat or only slightly elevated. Dysplasia may be difficult to distinguish from changes of chronic inflammation on histology and thus the presence of dysplasia should be confirmed by an experienced GI pathologist. The criteria for dysplasia emphasize the uniform nature of dysplastic changes affecting all parts of the crypt and surface epithelium. Other abnormalities seen in dysplastic epithelium include increased mitoses, back to back gland pattern, increased nuclear size, pleomorphism, and hyperchromaticity.

Detection of Dysplasia

Dysplasia is defined as unequivocal neoplasia of the epithelium confined to the basement membrane without invasion into the lamina propria. Unlike sporadic CRC in which dysplastic adenomas begin as raised polypoid lesions, dysplasia in IBD can arise in mucosa that is indistinct from surrounding mucosa. Flat dysplasia is thought to be endoscopically invisible and is conventionally thought to be detected only on random biopsy specimens. However, these lesions are in fact visible using newer generation colonoscopes with higher optical resolution. Elevated lesions that are endoscopically visible but not amenable to endoscopic resection are referred to as DALMs (dysplasia associated lesion or mass) a term that implies a high rate of synchronous malignant lesions. A newer term ALM (adenoma-like lesion or mass) describes a polypoid lesion resembling a sporadic adenoma found in an area of the colon not involved by chronic colitis and one that can be resected endoscopically. Low grade and high grade dysplasia was established with the presumption that low grade changes are early and less associated with imminent cancer.

Management of Dysplasia

One in 8 patients with UC will have dysplasia or cancer found on their initial screening colonoscopy, but those with a negative initial exam have a 3% chance of developing high grade dysplasia or cancer on subsequent surveillance colonoscopies. Nineteen percent of patients with LGD will already harbor concurrent CRC or HGD and an additional 29%-54% will subsequently develop advanced neoplasia over the next 5 years. HGD carries a 43% risk of synchronous malignancy and is an indication for colectomy.

Risk factors for the development of cancer in UC are duration and extent of colitis, early age of onset of colitis, family history of colorectal cancer and severity of microscopic inflammation. The duration and extent of colitis are well established risk factors for the development of cancer in UC. Patients with greater than 10 years of disease and those with extensive disease are at highest risk. The incidence rate increases with each successive decade of disease activity with approximate cumulative probabilities of 2% at 10 years, 8% at 20 years, and 18% at 30 years although recent data suggest that rates may represent an overestimate.
Some patients with ulcerative colitis develop dysplasia associated with a non-adenoma-like lesion or mass (DALM). These DALMs may harbor an underlying invasive carcinoma that may not be detectable by endoscopic biopsy and therefore requires colectomy. In a case-series of 12 patients with DALM that was resected, 60 percent had invasive carcinoma in the resected specimens. Malignancy was not detected prior to resection on multiple endoscopic biopsies.27

Unlike non-adenoma-like lesions, sporadic adenomas do not require colectomy and may be removed endoscopically even if they arise in an area of colitis. As a result, the two need to be distinguished to prevent unnecessary surgery. Patients with a non-adenoma-like DALM are more likely to be younger, have a longer duration of disease, more extensive disease and larger lesions. Lesions that appear endoscopically as pedunculated or sessile adenomas rather than flat, ulcerated or plaque-like even if located in an area of colitis have a favorable prognosis with endoscopic removal and close follow-up.28-30

Surveillance of Dysplasia

Screening and surveillance for dysplasia and cancer should begin after 8 years of disease. Patients with ulcerative proctitis are not considered at increased risk of CRC. Patients with left sided UC or those with more proximal disease are at higher risk than is the general population. Patients with Crohn’s disease (CD) are also at increased risk of CRC. CD patients with one third or more of the colon involved and with 8 years or more of chronic colitis should receive surveillance endoscopies.39 In Crohn’s colitis there is little data regarding screening and surveillance colonoscopy with biopsy. In one study, 259 patients who underwent examinations at least every 2 years, 16% were found...
Management of Dysplasia on Surveillance Colonoscopies in Ulcerative Colitis and Crohn’s of the Colon

<table>
<thead>
<tr>
<th>Society</th>
<th>Low Grade Dysplasia</th>
<th>Indefinite Dysplasia</th>
<th>High grade Dysplasia</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>American College of Gastroenterology</td>
<td>1. Confirm with second GI pathologist</td>
<td>1. Intensive medical therapy.</td>
<td>1. Confirm with second GI pathologist</td>
<td>1. If disease duration &lt; 20 years, repeat surveillance in 2 years.</td>
</tr>
<tr>
<td></td>
<td>2. Colectomy</td>
<td>2. Repeat surveillance in 3-6 months.</td>
<td>2. Colectomy</td>
<td>2. If disease duration is &gt; 20 years, repeat surveillance annually.</td>
</tr>
</tbody>
</table>

|                                              | 3. If the review is indeterminate, then repeat surveillance in 3 months using chromoendoscopy. | 3. If the review is indeterminate, then repeat surveillance in 3 months using chromoendoscopy. | c. *Higher risk – Surveillance every year. |

a. Lower risk – Extensive colitis with no active endoscopic or histologic inflammation, left-sided colitis, or Crohn’s colitis involving less than 50 percent of the colon.

b. Intermediate risk - Extensive colitis with mildly active endoscopic or histologic inflammation, post-inflammatory polyps, or a family history of colorectal cancer in a first-degree relative who was at least 50 years of age.

c. Higher risk - Extensive colitis with moderately active endoscopic or histologic inflammation, a stricture in the preceding five years, dysplasia in the previous five years that was not treated surgically, primary sclerosing cholangitis, or a family history of colorectal cancer in a first-degree relative younger than 50 years of age.

to have abnormal biopsies that comprised indefinite, LGD, HGD, and cancer. 

Although surveillance programs remain a popular management strategy in UC, some cancers will develop despite a surveillance program. The benefits of surveillance programs remain controversial particularly in light of estimates that about $200,000 is spent in surveillance programs for every carcinoma found or prevented.

Those who develop UC after the age of 70 may not need surveillance because the increased risk of cancer is small.

(continued on page 32)
will not then begin until the eighth decade, an age at which UC confers little or no additional risk above that in the general population.30, 35

In pancolitis the surveillance interval is generally recommended to be 1-2 years. Since the dysplasia-carcinoma sequence likely requires an extended period of time every 2 years would seem appropriate after two consecutive annual colonoscopies at which no dysplasia was detected. Screening is generally recommended to begin 8 years after onset of pancolitis since it is unusual for patients will develop carcinoma before 10 years of disease.34, 41

Left sided colitis is defined as disease distal to the splenic flexure. Colonoscopy with biopsies should begin 12-15 years after onset of disease. Surveillance procedures for dysplasia and carcinoma colonoscopy must be conducted to the ileocecal valve. To maximize the amount of tissue obtained endoscopists procure two to six biopsies per site using jumbo forceps usually from six to ten sites in the colon. Alternatively four quadrant biopsies every 10 cm can be performed. Rubin et al. published a detailed histology assessment of patients with UC who underwent colectomy. They reported that 33 biopsies were required to have a 95% sensitivity for any dysplasia to be present but up to 64 biopsies were required to find the highest degree. Because there is an increased risk of rectosigmoid cancer in UC an increased number of biopsies should be obtained from these sites.34, 41

Biopsy of obvious inflammatory polyps or pseudopolyps is to be avoided since they are less likely to contain dysplasia and are often difficult to interpret. However a lesion greater than 1 cm, or those with abnormal color or configuration from the usual inflammatory polyp should be sampled or removed completely. Strictures in UC are suspicious of carcinoma and should be sampled extensively since malignancy may be present in over one third of cases. Colonic strictures in Crohn’s disease must also be sampled since a significant proportion (5-11%) may be malignant.25,34,35,39

Colonoscopy
Dysplasia in IBD can be flat and multifocal and can be easily overlooked with conventional white light endoscopy. Random sampling throughout the colon has been the mainstay of conventional surveillance practice. However, obtaining at least 33 random biopsies throughout the colon is tedious, expensive and time consuming. There has been increased emphasis on targeted biopsies in surveillance colonoscopies because evidence suggests most dysplasia in UC is associated with visible mucosal abnormalities.32, 33 Subramaniam et al. found that high definition colonoscopy was associated with higher dysplasia detection rate in comparison to standard definition colonoscopy.33 There is growing evidence that the yield of surveillance can be improved by addition of newer endoscopic methods such as chromoendoscopy (CE) and autoflorescence with narrow-band imaging (NBI)38 that enhance the detection of subtle mucosal abnormalities. Chromoendoscopy with topicaly applied dyes such as methylene blue or indigo carmine facilitates the endoscopic detection of flat circumscribed colitis associated neoplastic changes in UC.42 Five controlled studies showed that the diagnostic yield for the detection of intra-epithelial neoplasia using CE is higher compared with conventional colonoscopy with random biopsy specimens.44 Although CE allows for identification of mucosal lesions, it is not suitable for accurate endoscopic diagnosis of intra-epithelial neoplasia in UC because of the lack of cellular resolution and subsurface imaging.42, 44 Recently, a miniaturized confocal microscope integrated into the distal tip of the conventional colonoscope was developed. 33 This new diagnostic technology in gastrointestinal endoscopy denoted confocal endomicroscopy enables histologic evaluation of the mucosal layer during colonoscopy. Because of the time required for examination of large surface areas, this technique is not suitable for screening of the entire colonic surface in UC to detect neoplasias in flat mucosa. In a study by Kiesslich, et al., CE was used to identify potential neoplastic lesions and was combined with endomicroscopy for the endoscopic diagnosis of colitis associated intra-epithelial neoplasia in UC. By using such chromoendoscopy-guided endomicroscopy, they were able to diagnose a 4.75 fold greater neoplastic detection rate in UC in comparison with conventional colonoscopy with random biopsy specimens and significantly (50%) fewer biopsy specimens were required. Endomicroscopy and chromoscopy prolonged colonoscopy for about 10 minutes on average, although this was not significantly different from the conventional colonoscopy group.42, 43

Chemoprevention in IBD
Sulfasalazine products have been investigated for their
chemopreventive effects and have yielded conflicting results. While Velayos and colleagues concluded that mesalamine is chemopreventive, other investigators have failed to demonstrate a meaningful protective effect. Given the disparity of results in studies, it remains unknown whether mesalamine-based medications are efficacious chemopreventive agents. However, given their utility in maintaining remission, their use is advocated in patients with UC.36,45

Data from observational studies suggest that long term use of 5-aminosalicylates may reduce the CRC risk by half in patients with long standing IBD while population based studies have been inconsistent and less convincing.36

Studies by Lashner et al. failed to prove a significant protective effect of folic acid in IBD. Their data however suggested the possibility of a chemopreventive effect. Given the low cost and low risk of adverse events at conventional doses of 400 ug per day and 1 mg per day, the administration of folic acid remains a common practice.36,45

Ursodeoxycholic acid (UDCA) has been suggested to decrease the risk of colorectal dysplasia in patients with PSC and UC. However, studies involving the usage of UDCA as a chemopreventive agent in patients with PSC and UC have yielded mixed results and are based on retrospective analyses with inherent limitations. Furthermore, high dose UDCA can be problematic in PSC patients. Therefore, UDCA cannot be recommended as a chemopreventative agent in PSC patients given the limited information available.48

The utility of immunomodulators in patients with steroid dependent and steroid refractory disease are well established forms of therapy in IBD. A single cohort study did not demonstrate a protective effect of 6-mercaptopurine and azathioprine yet Cessam study revealed a 3.5 time lower risk of CRC with thiopurines. The effect of methotrexate and anti-TNF agents as chemopreventive agents has not been studied.36,45

**CONCLUSION**

Patients with UC and Crohn’s disease have an increased risk of developing CRC although estimates of CRC risk are varied. Risk factors for development of CRC include younger age at diagnosis, extent and duration of colitis, severity of inflammation, family history of CRC, and coexistent primary sclerosing cholangitis. An initial screening colonoscopy should be performed in UC patients 8-10 years after the onset of symptoms. Thereafter, screening intervals are determined by the extent of colitis. Extensive biopsies should be obtained and the trend is toward targeted biopsies of suspicious lesions using enhanced imaging techniques such as high definition endoscopy and chromoendoscopy. With the exception of strictures screening and surveillance of CRC in patients with Crohn’s disease should be managed similarly to patients with UC. Current literature advocates the use of 5-ASA as a chemopreventive agent, but this remains inconclusive. The overall approach to cancer prevention in IBD includes intensive control of disease activity and close surveillance with colonoscopy.

**References**


Implications of the 2012 Centers for Disease Control and Prevention (CDC) Guidelines for Screening Hepatitis C Infection in the United States

Patrick M. Horne

Rennie Mills

In the United States (US), a large number of individuals are infected with chronic Hepatitis C (HCV). The majority of patients with chronic HCV contracted the virus as a result of contaminated blood product transfusions prior to 1992 or due to intravenous drug use (IVDU). Recent guidelines released by the Centers for Disease Control and Prevention (CDC) have addressed this issue by recommending the screening of baby boomers (those individuals born between the years of 1945-1965). This review discusses risk factors for contracting HCV, potential implications of the CDC guidelines, the importance of screening and the impact these new guidelines will have on healthcare providers (HCP).

INTRODUCTION

Hepatitis C, a viral infection of the liver, is usually an asymptomatic infection (up to 70% asymptomatic according to the CDC) and this leads to a low rate of diagnosis. Mild and nonspecific symptoms including fatigue, nausea, anorexia, myalgia, arthralgia, weakness and weight loss are often described in a patient that becomes symptomatic. Also contributing to the low level of diagnosis are transaminase levels that are normal in approximately one third of patients and fluctuating transaminases in another third.1 If left untreated, HCV can progress to cirrhosis and its complications including liver failure and development of liver cancer. The prevalence of a positive hepatitis C antibody (anti-HCV) in the United States was estimated to be approximately 1.6 percent or 4.1 million persons from 1999-2002 according to the 2006 National Health and Nutrition Examination Survey (NHANES) while the prevalence of a detectable hepatitis C viral load (HCV RNA) was 1.3 percent, equal to approximately 3.2 million people.2 However, since many groups known to have high prevalence of HCV were excluded from this analysis, including people who are homeless, incarcerated, hospitalized or institutionalized, these numbers are believed to be underestimated.3 As many as 85% of patients exposed to HCV will develop chronic infection.4 Of those 85%, approximately 20-30% of patients will develop cirrhosis over a 20 year period.
Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965*

- Adults born during 1945–1965 should receive one-time testing for HCV without prior ascertainment of HCV risk.

- All persons with identified HCV infection should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment services for HCV infection and related conditions.

Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

- HIV-infected patients should be tested routinely for evidence of chronic HCV infection. Initial testing for HCV should be performed using the most sensitive immunoassays licensed for detection of antibody to HCV (anti-HCV) in blood.

Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease

Routine HCV testing is recommended for:

- Persons who ever injected illegal drugs, including those who injected once or a few times many years ago and do not consider themselves as drug users.

- Persons with selected medical conditions, including persons who received clotting factor concentrates produced before 1987; persons who were ever on chronic (long-term) hemodialysis; and persons with persistently abnormal alanine aminotransferase levels.

- Prior recipients of transfusions or organ transplants, including persons who were notified that they received blood from a donor who later tested positive for HCV infection; persons who received a transfusion of blood or blood components before July 1992; and persons who received an organ transplant before July 1992.

Routine HCV testing is recommended for persons with recognized exposures, including:

- Health care, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood.

- Children born to HCV-positive women.
on average. The precise mechanism leading to the inability of most individuals to spontaneously clear acute HCV infection remains unclear, but it is likely multifactorial and includes genetic diversity of the virus and its tendency toward rapid mutation, allowing HCV to escape immune recognition. Current HCV therapy consists of pegylated interferon (PIFN) and ribavirin (RBV) for genotype 2, 3, and 4 and PIFN, RBV plus a protease inhibitor, either telaprevir or boceprevir, for genotype 1. While side effects continue to remain numerous, sustained virologic response rates (SVR) have significantly improved since therapy for HCV was first approved in 1991.

Recently, the CDC released updated and revised national guidelines for screening HCV in the US, in hopes of raising awareness of the prevalence of disease, improving the incidence of disease detection and positively impacting the healthcare system (Figure 1). However, these updated guidelines were met with some criticism and opposition. The US Preventative Task Force rejected these guidelines citing low prevalence of chronic HCV in the general population and a relatively low risk of developing progressive liver disease. Furthermore, they opined that screening does not lead to improved health care outcomes such as decreased cirrhosis, hepatocellular carcinoma (HCC) or mortality. However, since most individuals exposed to HCV develop chronic infection, and 20-30% develop cirrhosis and the potential complications associated with cirrhosis, the physical and financial burden on the current healthcare system is and will continue to be dramatic.

Importance of screening
While the number of individuals that were born between 1945 and 1965 only account for 27 percent of the U.S. population, these individuals account for 75 percent of all HCV infections in the US, 73 percent of HCV-related mortality and the highest risk of developing liver disease related complications including cirrhosis and HCC. This is illustrated in Figure 2 in an analysis by Razavi, et al. Therefore, proactively screening individuals born during this timeframe, independent of possible risk factors, yields early identification, diagnosis and access to treatment.

Treatment resulting in SVR would prevent the progression of liver disease thereby decreasing the development of HCC, liver failure and the need for liver transplantation.
Implications of 2012 CDC Guidelines for Screening Hepatitis C Infection

(continued from page 38)

The incorporation of the CDC Hepatitis C screening guidelines would alleviate the burden of questioning all patients regarding history of illicit drug use or having received blood products. This also alleviates the risk of obtaining inaccurate information from the patient, whether it is intentional or unintentional.

According to the same analysis, the estimated lifetime cost of an individual infected with HCV is $64,490, significantly higher compared to non-infected individuals. The analysis also found that while HCV prevalence has declined, the prevalence of advanced liver disease will continue to increase, negatively impacting healthcare costs, as illustrated in Figure 3. Therefore, despite the low prevalence of infected persons as noted by the US Preventative Services Task Force, the cost per those infected dramatically impacts healthcare costs over an individual’s lifetime.

While the CDC guidelines have identified the population with the highest prevalence and HCV related mortality, it is important to also continue to screen those with known risk factors despite their age. Recent data from the Florida Department of Health (FDOH) reveals an overall decline in chronic hepatitis C in Florida between 2005-2011 yet the rates have doubled in young adults (18-30 years). Additionally, in Northern Kentucky, there has been a dramatic rise in HCV diagnosis in the 20-29 year old age group. 88% of these individuals had a history of IVDU and were tested while in transitional housing or treatment centers which has previously been not been a cohort fully reported.

Explanation of the CDC Birth Cohort

HCV is an RNA (ribonucleic acid) virus that is mainly transmitted through contaminated blood or blood products. The risks of exposure to HCV (Figure 1) include 1) individuals who received clotting factors prior to 1987 and/or blood transfusions or organ transplantation prior to July 1992 (the date that screening of blood products was improved), 2) illicit drug users (IVDU and nasal drug users), 3) chronic hemodialysis patients, 4) patients infected with human immunodeficiency virus (HIV) and, recently, 5) individuals in the US born between the years of 1945-1965.

With respect to the recent CDC guidelines, three different age cohorts, 1945-1965, 1950–1970 and 1945–1970, were evaluated and then stratified based on race, ethnicity and gender. The cohort of 1945-1965 was ultimately chosen as it was felt to have the best representative sample of patients encompassing...
all race and ethnicities. The prevalence of HCV in this cohort was found to be five times higher than the other cohorts, which, according to the CDC, “reflects the substantial number of incident infections throughout the 1970s and 1980s and the persistence of HCV as a chronic infection”. This particular time period has been associated with a high rate of HCV infection for many reasons including lack of available screening of the blood supply as well as the high rate of IVDU.

Although controversial, tattooing may also be a risk factor for contracting HCV. A recent article by Carney et al found a strong association between tattooing and HCV infection in a large cohort of patients. This association was noted even patients who lacked traditional HCV risk factors such as IVDU or blood transfusion prior to 1992.

Role of the Healthcare Provider

The release of new CDC guidelines will undoubtedly identify a vast number of individuals with chronic HCV that were previously undiagnosed. Inevitably this will lead to increased demand on medical services in primary care, and at least in the short-term, in the specialties of gastroenterology and hepatology. Currently the impact of the influx of newly diagnosed patients with positive anti-HCV antibody, whether to community gastroenterology practices or to academic health centers, is unclear. While the majority of individuals who have a positive anti-HCV antibody will later be confirmed to have chronic infection confirmed by HCV RNA, a small subset of patients with exposure history may spontaneously clear the virus or instead have a false positive result. Providers who are counseling individuals on test results should understand that a positive anti-HCV antibody is not necessarily a diagnosis of chronic infection. This is merely a reflection of prior exposure and further testing, specifically an HCV RNA, needs to be completed to confirm the presence of chronic infection. Misdiagnosis based on a positive anti-HCV antibody can lead to undue anxiety and stress and, in some cases, may impact the patient’s ability to qualify for healthcare or life insurance, lead to negative stigma associated with a false diagnosis and prevent the individual from ever donating blood.

CONCLUSION

The updated CDC Guidelines are an important step aimed at helping HCPs more easily identify individuals with HCV so that they may be referred for treatment if needed. In the not so distant future, new all-oral HCV medication regimens will be available that will be capable of curing more HCV patients, in less time, with less treatment-associated side effects. It appears that the medical field is rapidly moving forward to make HCV a disease of the past.

References

13. Florida Department of Health. Hepatitis C in Young Adults—Enhanced surveillance protocol
14. Northern Kentucky Independent Health Department District
Regression of Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma of the Cecum after Eradication of *Helicobacter pylori*

by Manish Prasad Shrestha, Tat-Kin Tsang

We report a case of 47-year-old female with mucosa-associated lymphoid tissue lymphoma of the cecum successfully treated by polypectomy and *Helicobacter pylori* (*H. Pylori*) eradication. Pathology of a 10mm cecal polyp removed during colonoscopy revealed a very dense lymphoproliferative infiltrate. Immunohistochemistry of the specimen supported a diagnosis of marginal zone lymphoma of the cecum. Histological and immunohistochemical examinations of gastric biopsy specimens taken during upper endoscopy revealed a chronic gastritis and *H. pylori* infection, but no gastric MALT lymphoma. The patient was treated with triple therapy consisting of lansoprazole, clarithromycin and amoxicillin, each given twice per day for two weeks for *H. pylori* eradication. Follow up colonoscopy performed 6 months later showed regression of the colonic MALT lymphoma. The patient has had no recurrence without any surgery, radiation or chemotherapy.

**INTRODUCTION**

Mucosa-associated lymphoid tissue (MALT) lymphoma is a marginal zone, peripheral B-cell lymphoma derived from marginal zone cells at extranodal and extrasplenic sites with low-grade malignancy potential. First described by Isaacson and Wright,¹ it arises in lymphoid tissue in response to chronic antigenic stimulation, chronic infection or autoimmune disease.² MALT lymphomas occur mainly in the gastrointestinal tract, in which the stomach is the most common site.³ 30% to 40% of MALT lymphomas occur at an extra-gastric site, such as the small intestine, colon, lung, skin, orbital soft tissue, salivary gland, breast and thyroid.

Most gastric MALT lymphomas arise in response to *H. pylori* infection.⁴,⁵ Several studies have confirmed the regression of gastric MALT lymphoma in a high proportion of patients treated by eradication of *H. pylori*.⁶,⁷,⁸,⁹,¹⁰ However, the role of *H. pylori* infection in extra-gastric MALT lymphoma is unclear. In the present report, we describe a case of cecal MALT lymphoma which responded to *H. pylori* eradication treatment, suggesting a possible role of *H. pylori* in the development of extra-gastric MALT lymphoma.

**CASE REPORT**

A 47 year-old Korean woman presented with a complaint of vague abdominal discomfort. She also had a positive fecal occult blood test without any further clinical signs. Her past history was significant for a partial hysterectomy (fibroids). Laboratory evaluation, including complete blood count and chemistries, were (continued on page 44)
Regression of MALT

A CASE REPORT

(continued from page 42)

within normal limits. Upper endoscopy was performed in July 2010. Histological and immunohistochemical examinations of gastric biopsy specimens revealed chronic gastritis and *H. pylori* infection but no gastric MALT lymphoma. The patient was treated with triple therapy consisting of lansoprazole, clarithromycin and amoxicillin, each given twice per day for two weeks. Colonoscopy performed in September 2010 revealed a 10 mm cecal polyp which was removed (Fig 1).

Histology of the biopsy specimens demonstrated a dense lymphoproliferative infiltrate (Fig 2). These lymphocytes immunohistochemically showed diffusely positive staining for CD20, findings compatible with marginal zone lymphoma (MALT lymphoma) of the cecum. CT-scan of the chest, abdomen and pelvis performed several weeks later showed no evidence of lymphadenopathy. Further treatment options were discussed with the patient. A “wait and watch strategy” was chosen by the patient. Repeat colonoscopy performed 6 months later showed no evidence of residual disease. The patient has had no recurrence without any surgery, radiation or chemotherapy.

DISCUSSION

MALT lymphoma is a marginal zone peripheral B-cell lymphoma derived from marginal zone cells at extranodal and extrasplenic sites with low-grade malignancy potential. It arises in lymphoid tissue in response to chronic antigenic stimulation, chronic infection or autoimmune disease.

Colonic MALT lymphoma is less common than gastric MALT lymphoma, therefore the optimal management of colonic MALT lymphoma has not been described. *H. pylori* eradication, surgery, chemotherapy and radiation therapy have been used in the treatment of colonic MALT lymphoma. In the present report, we describe a case of cecal MALT lymphoma which responded to the eradication therapy of *H. pylori*.

*H. pylori* is involved in the pathogenesis of gastric MALT lymphoma. It is found in approximately 80% of patients with MALT lymphoma. Chronic immune stimulation by *H. pylori* probably plays an important role in the development of gastric MALT lymphoma. *H. pylori* eradication therapy is currently widely accepted as an initial therapy in patients with low-grade gastric MALT lymphoma. In contrast, the role of *H. pylori* infection in colonic MALT lymphoma is unclear. Some reports have described the successful regression of colorectal MALT lymphoma after eradication of *H. pylori*. There is a possibility that *H. pylori* in the stomach may act as an antigenic stimulator for colonic mucosa via surface and/or vessel. *H. pylori* specific T cells in stomach and their products, such as cytokines may contribute to the growth of extra-gastric MALT lymphoma. Laboratory studies have shown that the growth of neoplastic B cells of gastric MALT lymphoma can be stimulated by *H. pylori* and that the effect is due...
to recognition of *H. pylori* by tumor-infiltrating T cells, which in turn provide help for tumor cell proliferation.²⁸

In a prospective study of 77 Austrian patients by Grunberger et al, *H. pylori* eradication was not effective for treatment of extra-gastric MALT lymphomas.²⁹

They suggested that *H. pylori* did not play a role in the development of these lymphomas. However, the major drawback of the study was patient selection. The majority of patients treated with *H. pylori* eradication had advanced disease. Presence of advanced disease may have affected the success of eradication therapy.

Further investigation is needed to clarify the use of antibiotics in extra-gastric MALT lymphomas, as well as the role of *H. pylori* in the pathogenesis of the MALT lymphoma. In our opinion, it may be reasonable to employ *H. pylori* eradication therapy as a first line therapy for patients with extra-gastric MALT lymphoma, especially those with early disease.

**CONCLUSION**

The role of *H. pylori* in the pathogenesis of extra-gastric MALT lymphoma is unclear. Further investigation is needed to clarify its role in the pathogenesis as well as the use of antibiotics for the treatment of the MALT lymphoma.

---

**References**

Meat And Cola: An Esophageal Bezoar Treated by a Novel, Inexpensive Approach: Case Report and Review of Literature

by Adam C. Adler, Cesar Cestero, Eddy A. Castillo

INTRODUCTION

Esophageal bezoars are seldom encountered. We report a case in which a 73 year old gentleman developed an esophageal bezoar secondary to dismotility from longstanding Parkinson’s disease. The patient was treated using cola washes through a nasogastric tube that proved efficacious and was both inexpensive and non-invasive. Few reports of this technique are found in the literature with most in relation to esophageal phytobezoars.

Report of Case

A 73 year old male, with multiple medical problems presented to the emergency department with worsening shortness of breath and subjective fever. The patient quickly developed respiratory distress requiring intubation and mechanical ventilation and was admitted under the pretense of a COPD exacerbation. Upon arrival to the ICU, multiple attempts to insert a nasogastric tube (NG) were unsuccessful. An NG tube was finally placed but became clogged. The gastroenterology consult team was able to advance an NG tube but removed it due to resistance. Upper endoscopy was performed and demonstrated a semi-solid mass of food products that coalesced to form a homogenous proteinaceous mass, which conformed to the shape of the esophagus (Image 1). The material had progressed though the lower esophageal sphincter and into the stomach. With the use of a snare, portions of the bezoar were sectioned and removed, however only a relatively small amount of the bezoar was removed. An oral esophageal tube was placed with recommendation for continuous irrigation with cola and water to soften the remaining bezoar. Repeat endoscopy 3 days later allowed for the removal of the remaining bezoar that had a proteinaceous appearance (Image 2). Esophageal biopsies taken at that time showed chronic inflammation with no evidence of esophagitis. The cola washes proved to be efficacious allowing complete removal of the foreign material. It was ascertained that the obstruction was most probably the meat-based meals that the patient was eating in the days prior.

Discussion

Esophageal bezoars are extremely rare with few reports available in the medical literature as most gastrointestinal bezoars occur within the stomach or below. Most of these reports are specific to phytobezoars that are composed of plant material and often times, a lead point may be identified.1 Esophageal bezoars are more commonly observed in: the critically ill, patients with esophageal strictures, underlying gastroparesis, achalasia, gastroesophageal reflux and following traumatic brain injury.2,3 Endoscopic evaluation with resection of the bezoar is the mainstay of treatment in most cases. Occasionally, attempts to dissolve esophageal bezoars using pancreatic enzymes or cola products have been reported and generally administered through an esophageal tube. Enteral feedings, especially feedings rich in protein are most often identified.1,4

(continued on page 48)
Meat And Cola

A CASE REPORT

(continued from page 46)

In our patient, attempts to completely remove the bezoar using endoscopic methods were unsuccessful. It was then decided to attempt dissolution using cola via an esophageal tube to dissolve the remaining clumps of proteinaceous material. The ability of cola to dissolve bezoars probably stems from its carbonic and phosphoric acid components with resultant PH of around 2.5-3.0. Dissolution was accomplished in our patient after 12 hours, corresponding to the timeframe reported in similar cases. After complete dissolution, the patient was evaluated for a PEG tube placement to avoid future events as his Parkinson’s disease has progressed. This method of treatment proved to be extremely cost effective and non-invasive. In patients where endoscopic resection proves impossible or ineffective it may be feasible to use such a method to achieve resolution.

References

Image 1. Endoscopic view of the proximal esophagus with large proteinaceous bezoar after partial resection.

Image 2. Upper endoscopy of the proximal esophagus 72 hours after dissolution of esophageal bezoar.
FIT to Evaluate Mucosal Healing in UC
To determine whether a fecal immunochemical test (FIT) can evaluate mucosal healing in ulcerative colitis (UC), feces collected from UC patients who underwent colonoscopy were examined by FITs and results were compared with colonoscopic findings. Mucosal status was assessed using the Mayo Endoscopic Subscore classification. Maximum score for the colorectum in each patient was recorded.

There were 310 colonoscopies performed in 152 UC patients. A large majority of patients with a Mayo 0 endoscopic score had negative FIT. Results (92%) and proportion of negative FIT results decreased with increases in the Mayo score (Mayo 1: 47%, Mayo 2: 13%, Mayo 3: 12%). When the negative FIT was defined as less than 100 ng/mL, the sensitivity and specificity of a negative FIT for mucosal healing (Mayo 0) were 0.92 and 0.71, respectively. In addition, a positive FIT greater than 100 ng/mL predicted mucosal inflammation (Mayo 2 or 3), with sensitivity 0.87 and specificity 0.60, respectively.

It was concluded that the FIT can effectively and noninvasively evaluate mucosal healing in UC.


H. Pylori-Negative Gastritis
To investigate the prevalence of H. pylori among individuals with histologic gastritis, subjects between 40 and 80 years of age underwent elective EGD at a VA Medical Center. Gastric biopsies were mapped from seven prespecified sites (two in the antrum, four in the corpus, and one in the cardia), and graded by two gastrointestinal pathologists, using the updated Sydney System.

H. pylori-negative required for criteria: Negative triple staining at all seven gastric sites, negative H. pylori culture, negative IgG H. pylori serology, and no previous treatment for H. pylori. Data regarding tobacco smoking, alcohol drinking, NSAID, and PPI use were obtained by questionnaire.

A total of 491 individuals were enrolled, 40.7% (200) had gastritis of at least grade 2 in at least one biopsy site for grade 1. In at least two sites, 41 (20.5%) had H. pylori-negative gastritis; 30 (73.2%), had chronic gastritis, 5 (12.2%) had active gastritis and 6 (14.6%) had both. H. pylori-negative gastritis was approximately equally distributed in the antrum, corpus, and both antrum and corpus. Past and current PPI use was more frequent in H. pylori-negative versus H. pylori-positive gastritis (68.2% and 53.8%).

Non-H. pylori gastritis was defined and found in 21% of patients with histologic gastritis. While PPI use is a potential risk factor, the cause or implications of this entity are not known.


Surveillance of Longstanding Achalasia
In early recognition of the need for retreatment in achalasia is of crucial importance to reduce morbidity and long-term complications. In order to decide which tests perform best for evaluation of same, a cohort of 41 patients with longstanding achalasia (median 17 years), underwent esophageal manometry, timed barium esophagogram and symptom evaluation. Patients were followed up to ten years, and were regarded as a therapeutic failure if Eckhardt score was greater than 3, or when retreatment was needed. Predictors of therapeutic failure were evaluated.

Seven patients had elevated LES pressure (greater than 10 mmHg) and 26 had esophageal stasis greater than 5 cm. on timed barium esophagogram. During follow-up, 25 patients had recurrence of symptoms and were considered therapeutic failures. Of the 25 patients, five had elevated LES pressure, whereas 22 had esophageal stasis on barium esophagogram. Hence, the sensitivity to predict the need of retreatment is higher for esophageal stasis (88%) compared with LES pressure (20%).

A total of 16 patients or 39% were in long-term remission, of which 12 patients (75%) did not have stasis at their initial visit.

It was concluded that in contrast to LES pressure, esophageal stasis is a good predictor of treatment failure in patients with long-standing achalasia. Based on these findings, timed barium esophagogram is preferable as a test to decide on retreatment.


Murray H. Cohen, D.O., “From the Literature” Editor, is on the Editorial Board of Practical Gastroenterology.
In the recently published text *Self-Expanding Stents in Gastrointestinal Endoscopy*, Editor Douglas G. Adler takes an evidence-based exploration of the use of self-expanding stents throughout the gastrointestinal tract. Each of the 14 chapters details the indications for use, available stent options, technical deployment methods, and potential complications and their management by leading authors in their field. The book is 264 pages and retails for $109.95. Throughout the book there are color figures, endoscopic photos, and fluoroscopic imaging that complement the practical descriptions and evidence reviews covered in each chapter. This collection of detailed reviews makes the book a valuable and highly relevant textbook to any gastroenterologist’s practice.

While each author thoroughly covers the entirety of the stent options available within their area of expertise, the dedication of four separate chapters to esophageal and biliary stenting and three chapters to colonic stenting leads to some redundancy when reading the text from cover to cover. Within the first 4 chapters each author mentions the potential complications in varying detail related to esophageal stent placement for benign, preoperative and unresectable disease. The fourth chapter then offers a dedicated chapter related to complications of esophageal stents. Likewise, chapters 5 to 8 review biliary applications, and there are some overlapping concepts. Each chapter has a slightly different format and subheadings which makes covering the entire text slightly more challenging for the reader. However, neither the redundancy nor formatting variation detract from Dr. Adler’s mission to collect a concise, highly focused review of self-expanding stent options in the gastrointestinal tract. The high quality images are plentiful and essentially allow the book to serve as an atlas of endoscopic stenting.

The final chapter written by Jeffrey L. Tokar, MD is particularly interesting as it offers insight into the future of endoscopic stenting outside the mechanical properties provided by stents. Dr. Tokar explores novel stent design approaches including: drug-eluting, biodegradable and radioactive stents in the gastrointestinal tract. The chapter covers what is currently known, where development of the technology is currently aimed and the potential clinical impact these innovative stents may offer patients with malignant and benign diseases. This aspect leaves the reader with a succinct review suggesting that the future of self-expanding stenting is promising.

Overall, Dr. Adler’s book serves as a comprehensive, highly detailed, evidence-based review of the wide variety of applications for self-expanding stents in the gastrointestinal tract. This book would be highly beneficial to any gastrointestinal endoscopist interested in expanding their knowledge of self-expanding stents. It also would be an extremely valuable reference for all gastroenterology fellowship training programs as well as general, thoracic, and colorectal surgeons.

Kevin McNamara, MD
GI Fellow

William M. Tierney, MD
Professor of Medicine
Director of Endosonography
University of Oklahoma Health Sciences Center
Oklahoma City, OK

John Pohl, M.D., Book Editor, is on the Editorial Board of *Practical Gastroenterology*
Cow’s Milk Avoidance Alone for Treatment of Eosinophilic Esophagitis

Eosinophilic esophagitis (EoE) is likely exacerbated by both dietary antigens and inhaled aeroallergens. In order to induce remission of symptoms, many patients undergo a directed elimination diet to see if they will clinically improve with control of symptoms and decreased eosinophilic infiltration of the esophagus. The authors of this study evaluated the outcome of pediatric patients with EoE who underwent cow’s milk elimination as the sole dietary intervention.

This retrospective study evaluated 161 pediatric patients over a 5-year period with EoE defined as having esophageal biopsies greater than 15 eosinophils per high power field. Patients who underwent milk elimination alone from their diet had repeat esophageal biopsies after this intervention (17 patients), and they were compared to EoE patients who underwent a standard elimination diet, topical steroid treatment, elemental diet, or elimination diet with adjunct topical steroid treatment. The remission rate by simply eliminating milk was 65% (95% confidence interval, 42 – 88%) which was similar to the other treatment modalities. This patient group was younger (4.2 ± 2.2 years) compared to those patients receiving other treatment modalities. Dysphagia and vomiting were the most common symptoms in the patient group that underwent the single intervention of cow’s milk removal, and all patients in this treatment group had clinical improvement. Approximately 65% of the patients treated with cow’s milk avoidance underwent some type of allergy testing, and only one patient was positive for milk allergy based on patch testing. The majority of the patients with cow’s milk intervention had a history of atopy, including reactive airway disease, allergic rhinitis, or eczema. Repeat esophageal biopsy demonstrated that 7 children (41%) showed complete disease remission and 4 children (24%) showed partial remission. The authors noted that 6 children failed this treatment modality, but most of the patients who failed this therapy still had a reduction in esophageal eosinophils with repeat endoscopy.

This study suggests that removal of cow’s milk alone as a treatment for EoE may be an option, especially for younger children who cannot tolerate removal of many foods from their diet. Obviously, more studies, in particular prospective studies, are needed to validate these findings.

A Fecal Biomarker for Necrotizing Enterocolitis

Necrotizing enterocolitis (NEC) is a devastating intestinal disease seen in premature infants. It has a very high mortality rate, and its pathogenesis is unknown although bowel ischemia, intestinal bacterial translocation, and an impaired immune system may contribute to the disease. The diagnosis of NEC is often delayed leading to severe consequences, and the authors of this study attempted to determine if the fecal biomarker, S100A12 (calgranulin C), could be used to be a screening test for NEC. S100A12 is a type of damage-associated molecular pattern protein that is released when cells are damaged and is resistant to bacterial degradation.

Pre-term infants with a birth weight less than 1500 grams were recruited from 5 neonatal intensive care units (NICUs) in Germany over a one-year period. Stool samples were obtained every other day for at least 28 days, and infants were monitored for NEC throughout the study. NEC staging was performed using a modified Bell classification. Stool samples were tested for both S100A12 and calprotectin levels.

In total, 145 infants were recruited, of which 18 (12.4%) developed NEC. The rest of the infants had no gastrointestinal disease. Most patients with NEC required surgery, and NEC was associated with a 25% mortality rate. S100A12 levels decreased with increasing age in infants without NEC. However, infants who had suspected NEC and subsequently developed NEC had significantly higher fecal S100A12 levels. C-reactive protein and interleukin 6 levels did not differ between those infants with or without NEC. S100A12 levels were higher in those infants with NEC right at disease onset as well as in infants who eventually had a NEC-associated bowel perforation. S100A12 levels typically were elevated 4 to 10 days prior to NEC occurrence. Fecal calprotectin levels were elevated in patient with NEC although there was no significant difference in calprotectin levels prior to NEC in those infants who ended up having this disease. Fecal calprotectin levels also did not correlate with NEC severity.

Fecal S100A12 may provide a good screening test for those infants at risk of developing NEC in the NICU, and it appears to correlate well with disease severity.


John Pohl, M.D., Book Editor, is on the Editorial Board of Practical Gastroenterology
Oral Cancer Prevention International and CDx Laboratories Merge To Form CDx Diagnostics

New Company to Market Innovative Diagnostic Tools that Enable Prevention and Earlier Detection of Oral, Laryngeal and Esophageal Cancers - Strong Pipeline of New Tests for Liver, Pancreatic and Colon Cancer will Create Additional Value

SUFFERN, NY - January 8, 2013 -- Two companies which offer physicians advanced, clinically-proven diagnostic systems that can help prevent cancer by detecting pre-cancerous cells announced their merger today. Oral Cancer Prevention International, Inc. and CDx Laboratories, Inc. are joining to form a new entity known as CDx Diagnostics. The merger was facilitated by a new investment in CDx Diagnostics made by Waterbridge Capital, a New York City-based investment firm, which targets opportunistic equity investments in a number of areas, including promising companies focused on breakthrough diagnostic health technologies.

“Our goal in making this investment is to ensure that the newly merged company has access to the financial and human resources that it requires for rapid growth. It is very unusual for any medical device or diagnostic company to have successfully commercialized even one patented, clinically proven, FDA cleared, and reimbursed product independently, without the resources of a larger company,” said Joel Schreiber, CEO of Waterbridge Capital.

“We are pleased to be able to consolidate our oral, esophageal, and laryngeal cancer diagnostic assets into one company that can better leverage our investment in the proprietary computer algorithms and systems that we have developed to improve the detection of pre-cancerous cells. We welcome Waterbridge Capital as a board member and look forward to a mutually beneficial relationship,” said Mark Rutenberg, Chairman and CEO of CDx Diagnostics.

He continued, “This merger streamlines our capital structure and allows us to accelerate our strong pipeline of additional tests for liver, pancreatic, and Inflammatory Bowel Disease caused colon cancer. CDx Diagnostics will now fortify its leadership in developing advanced tools that deliver unparalleled information to doctors so they can rule out or confirm precancer while it is still easily treatable.”

CDx Diagnostics’ business model is based upon the recognition that detecting easily treatable pre-cancerous cells known as “dysplasia” can be the most effective method to prevent cancer. The Pap smear, which reduced cervical cancer from the most frequent cause of U.S. female cancer death in the 1950’s to the 14th largest by 1990, is an example of how availability of the right tool to detect dysplasia can stop cancer before it can actually start. While pre-cancerous cell detection has made cervical, skin and most colon cancer now largely preventable diseases, the detection of dysplasia in other body sites has been more elusive. CDx Laboratories was founded in 1997 to develop tools to detect dysplasia in tissues for which no practical and accurate tests were available. Its proprietary diagnostic platform consists of a patented minimally invasive brush biopsy method combined with a powerful computer-assisted laboratory analysis of the cells and tissue fragments obtained by the biopsy brush. Its tests are relatively quick and are covered by insurance.

In 2007, Oral Cancer Prevention International was founded to utilize the CDx technology platform to detect pre-cancerous cells in the mouth. Its OralCDx test is currently utilized by thousands of U.S. physicians and dentists to rule out the chance that a small common-appearing oral spot may contain pre-cancerous cells. For the last 20 years oral cancer has been rapidly rising in women, young people and non-smokers. OralCDx has already prevented over 10,000 U.S. oral cancers by detecting advanced precancerous cells in hundreds of thousands of patients with harmless appearing small oral spots.

Esophageal adenocarcinoma, the result of chronic heartburn, is the most rapidly growing U.S. cancer, quadrupling in white American men over 40 in the last 20 years. In 2011, two large clinical studies were published demonstrating that by using the EndoCDx WATS3D biopsy (Wide Area Transepithelial Sample with 3 Dimensional Analysis), provided by CDx Laboratories, during the routine upper endoscopy performed on millions of Americans with heartburn each year, gastroenterologists can quickly and easily increase their detection of its treatable pre-cancerous precursors -- Barrett’s esophagus and esophageal dysplasia -- by up to 40%. These studies show that WATS3D can detect cases of esophageal precancer that were missed by the standard random biopsy technique performed during upper endoscopy.

These results have been replicated in other studies of the WATS3D biopsy released during 2012. While expanded clinical trials continue since the WATS3D
method became commercially available in early 2012, it has already become a part of routine clinical practice in many of the largest academic and community gastroenterology centers in the United States.

“Based on almost six months of diligence, we have confirmed a remarkable level of enthusiasm among physicians for CDx’s computer-assisted biopsy approach for detecting still-harmless, but pre-cancerous cells. We believe that even fractional penetration for its two currently available tests in the U.S. market alone can prevent thousands of oral and esophageal cancers,” added Joel Schreiber.

**About CDx Diagnostics and WATS3D Biopsy**

CDx Diagnostics (www.cdxdiagnostics.com) is the world’s leader in the prevention of cancer of the oral cavity, pharynx, larynx and esophagus through early detection of their easily treatable, pre-cancerous precursors.Clinicians use CDx patented WATS3D biopsy instruments to collect, through minimally invasive procedures, a wide area, disaggregated tissue specimen of the entire thickness of the suspect epithelium. This unique tissue specimen is then subjected to specialized, computer-assisted laboratory analysis. In clinical trials, CDx Diagnostics’ WATS3D biopsy significantly increased the detection rate of Barrett’s esophagus in GERD patients as well as precancerous changes in esophageal tissue (dysplasia) by up to 40%. The high sensitivity of WATS3D is due to the large tissue area sampled, and the proprietary 3-Dimensionial computer imaging system that is based on an algorithm developed as part of the U.S. Strategic Defense Initiative missile defense program.

**About Barrett’s Esophagus and Esophageal Cancer**

Many cases of esophageal adenocarcinoma (EA) are preceded by chronic heartburn. Some heartburn patients develop altered cell patches in their esophagus. A condition known as dysplasia occurs as Barrett’s esophagus progresses to Barrett’s-associated cancer. Dysplasia is considered a precancerous condition and should be monitored very closely to ensure the cells do not become cancerous. Dysplastic cells are very similar to cancer cells but have not yet acquired the ability to invade into tissue or metastasize. Esophageal cancer is now the fastest growing form of cancer in the United States.

**About Oral Precancer and Oral Cancer**

Oral cancer kills about as many Americans as melanoma, twice as many as cervical cancer, and is now rapidly increasing in the formerly low risk groups of women, young people, and non-smokers. Oral cancer can be prevented if it is detected in its precancerous (dysplastic) stage. Oral precancer typically appears as a visible, small, innocuous appearing white or red tissue spot. While the vast majority of these routine oral spots are harmless, the only two ways to rule out the presence of precancerous cells are a scalpel biopsy, or a painless, computer-assisted, transepithelial brush biopsy (OralCDx) of the oral spot. For additional information contact: CDx Diagnostics

Sharon Golubchik T: 845-369-7096
E: gsharon@cdxdiagnostics.com
ZA201 is a double-blind, active-controlled Phase 2 study of the safety and efficacy of Zoenasa Rectal Gel and will be conducted at 25 centers in approximately 120 adult patients with left-sided (distal) ulcerative colitis. The study’s Principal Investigator is Dr. Philip B. Miner, Jr., of the Oklahoma Foundation for Digestive Research in Oklahoma City, one of the foremost clinical research investigators for IBD. ZA201’s first patient was enrolled at Digestive Health Specialists of the Southeast in Dothan, AL, under Dr. Jeffery Crittenden.

About Altheus Therapeutics, Inc.
Altheus was founded in 2006 by Dr. Richard Harty at the University of Oklahoma Health Sciences Center to develop Zoenasa, a novel therapy for Inflammatory Bowel Disease (IBD). Altheus has completed a Phase 1 study of Zoenasa Rectal Gel and recently began a 120 patient Phase 2 proof-of-concept clinical trial.

For more information about Zoenasa, ulcerative colitis or the Phase 2 clinical study, visit www.altheustherapeutics.com
The ZA201 Clinical Trials.Gov entry can be found at: http://clinicaltrials.gov/ct2/show/NCT01586533

Surgeons at Sun Coast Bariatrics are the first in the Tampa Bay area to offer a single-incision sleeve gastrectomy procedure for patients seeking to lose weight.

ST. PETERSBURG, FLA. – Dr. Tiffany Jessee, a nationally recognized leader in bariatric surgery, and her colleague, Dr. Robyn Ache, are using the SPIDER® Surgical System to perform the weight-loss procedure through a small, single incision made near the patient’s belly button – resulting in a virtually invisible scar.

According to Ache, “The sleeve gastrectomy is the nation’s fastest growing option for surgically supported weight loss because of its appealing patient benefits. Unlike other weight-loss operations, there is no re-routing of the body’s natural pathway for food, or implantation of a device that requires frequent adjustments.”

During a sleeve gastrectomy, the surgeon removes about 80 percent of the stomach, leaving a small tube or sleeve to serve as the patient’s new smaller stomach. A smaller stomach means patients feel satisfied after consuming much less food. Ache reports that her patients are losing 30 to 50 percent of excess weight within six months to a year.

“The sleeve gastrectomy proves to be a safe and extremely effective operation for weight loss,” Jessee stated. “By using the SPIDER Surgical System, we now can perform the procedure with fewer incisions, which means patients have a better cosmetic outcome.”

Last year, the New England Journal of Medicine – one of the world’s most respected peer-reviewed medical journals – published studies demonstrating that sleeve gastrectomy was more effective in treating Type 2 diabetes than medicine, diet and exercise alone. Read the article at http://tinyurl.com/d2zdwjg

The SPIDER Surgical System by TransEnterix completely changes the state of single-incision surgery. Using it, the surgeon makes a small incision, inserts the device and opens it inside the patient’s abdomen like an umbrella. SPIDER’s expansion allows the surgeon to comfortably and precisely manipulate 360-degree-rotating, flexible instruments at angles that enhance her access and dexterity at the operating site. When the procedure is completed, the surgeon closes the system and removes it through the same incision.

Sun Coast Bariatrics offers a comprehensive and compassionate bariatric surgery program that includes patient education and support, nutritional therapy, and individual physical activity consultations and recommendations for patients. To learn more about Sun Coast Bariatrics and its fellowship trained surgeons, visit http://www.suncoastbariatrics.com

The SPIDER Surgical System’s expansion ability and flexible instruments are proprietary technologies created by TransEnterix; they won’t be found in any other system. Surgeons worldwide are using the system to successfully treat obesity and a variety of general surgery conditions. To see how it works, visit http://www.spidersurgery.com

TransEnterix is a cutting-edge medical device company that develops pioneering technologies to advance minimally invasive surgery. To learn more, visit: http://www.transenterix.com
For additional information about products and services that appear in Practical Gastroenterology, check the appropriate boxes on this coupon, fill in your name and address and send it to:

PRACTICAL GASTROENTEROLOGY
99B Main Street, Westhampton Beach, NY 11978
Or send your form via fax to: (631) 288-4435

Although every effort has been made to ensure the accuracy of this index, we cannot absolutely guarantee against the eventuality of last minute changes or omissions.

NAME
HOSPITAL/COMPANY
ADDRESS
SUITE/APT #
CITY
STATE
ZIP
PHONE

PLEASE PLACE ONE LETTER OR NUMERAL IN EACH BOX PROVIDED.
**MEETINGS CALENDAR**

May 17–22, 2013 SGNA 40th Annual Course
Austin, Texas—Celebrating 40 years of Annual Course education, The Society of Gastroenterology Nurses and Associates brings together the best and brightest GI/endoscopy professionals to drive the future of our field. SGNA is the leading organization of nurses and associates dedicated to the safe and effective practice of gastroenterology and endoscopy nursing. SGNA advances the science and practice of gastroenterology and endoscopy nursing through education, research, advocacy and collaboration, and by promoting the professional development of its members in an atmosphere of mutual support. Our membership spans across the United States and 16 other countries with a full range of members from Registered Nurses, Licensed Practical/Vocational Nurses, Associates (assistants and technicians) and Advance Practice Nurses. For more information visit: www.sgna.org

May 18–21, 2013 Digestive Disease Week
Orange County Convention Center, Orlando, FL. Digestive Disease Week® (DDW) is the largest and most prestigious meeting in the world for the GI professional. Every year DDW attracts approximately 15,000 physicians, researchers and academics from around the world. Choose from over 400 sessions, including clinical and research symposia, state-of-the-art lectures and research and topic fora, covering a wide array of topics and presented by a world-renowned faculty unsurpassed in their field. For more information visit: www.ddw.org

September 21-24 2013 GASTRO 2013 APDW/WCOG SHANGHAI, Asian Pacific Digestive Week 2013, World Congress of Gastroenterology
Shanghai Expo Center, Shanghai China. A World Congress in Asia! Submit your abstract and register today and take advantage of Early Bird Registration fees. The Early Bird Registration deadline is April 15, 2013. The Regular Registration deadline is August 15, 2013. For further information regarding the upcoming Congress, visit the Gastro 2013 APDW/WCOG Shanghai website at www.gastro2013.org

October 24–26, 2013 Annual Probiotic Symposium
Probiotics: Current Perspectives and Controversies
San Antonio, Texas. Attend the 7th Annual Probiotic Symposium for a unique opportunity to learn about the current perspectives and controversies in probiotics research and use in clinical practice. CME Credit for Physicians and other Healthcare Professionals will be available. Save $100—Register before October 6, 2013 For more information visit: www.ProbioticSymposium.com
ACROSS
1 A glucagon-like peptide 2 analogue which may restore
intestinal structure
7 Make an incision
9 Complete exon content of an
organism
10 Inflammation of the rectum
11 Before, to a poet
13 Less obese
15 Saclike structure
18 Self-abnegation
20 Intestine related
22 1st cervical vertebra
23 ___larged
24 Get older
26 It may be divided into
foregut, midgut and hindgut
27 Standard used for
measuring
28 Lower esophageal
sphincter
29 Well-liked
30 Heredity unit
32 Fistulas, ____ between cavities
35 Measure of acidity
36 Emotional intelligence, for short
37 Having an abnormally
high temperature
38 Anal tear
41 Fatty liquid
42 Diminished in size due
to disease or injury

DOWN
1 Medical procedures
2 Pair
3 Looking pale
and unhealthy
4 ____ gastrointestinal tract
5 Anemia, ____ deficiency
6 Abnormal position
of an organ
7 A biomarker of mucosal
mass
8 Trademarks, for short
12 Secretion from the kidneys
14 Difficult to manage
16 Cereal grain
17 It supports a parasite
19 Units of power
21 Involuntary retention of
urine and faeces
24 Acetic acid, for short
25 Brain scan
28 Lower esophageal
sphincter
29 Well-liked
31 Protective covering
33 Colon cleaner
34 Less risky
35 For each
37 Moving to and ____
39 Deplete
40 Prefix meaning single

(Answers on page 50)