

CLINICAL UPDATE

Managing Women's Digestive Health

Rectal Anatomy Is a Key Factor in Constipation

When it comes to idiopathic chronic constipation, anatomy can be destiny, according to Lawrence R. Schiller, MD, FACP, FACP.

The arrangement of the rectum and the anal canal is a problematic one. As the rectum winds around the curve of the sacrum and across the pelvic floor, it is actually heading in a forward direction. Thereafter, at the level of the puborectalis muscle, the rectum makes a 90-degree turn to the axis of the anal canal. The contracted puborectalis muscle maintains this sharp angle.

"This is a very important impediment to the passage of solid stool. If you have a solid fecal bolus...above the angle, it has a hard time getting around that corner.... In order to evacuate, we have to relax that muscle and straighten things out," said Dr. Schiller, Director of the Gastroenterology Fellowship Program in the Department of Gastroenterology at Baylor University Medical Center in Dallas.

Abnormal anatomy and disordered physiology play key roles in the three common problems that underlie the vast majority of idiopathic chronic constipation: slow transit, functional outlet obstruction, or irritable bowel syndrome (IBS).

Slow Transit Constipation

"Slow transit constipation is the most common type we see," noted Dr. Schiller. "Probably 80% of women who have chronic constipation have an element of slow transit. Presumably the problem is with colonic neuromuscular coordination, although this is not well established. There are some studies that suggest that nerve cells drop out of the myenteric plexus, but this has not been uniformly demonstrated.

you push things, you may get to a point where you can't push any more."

Another form of slow transit constipation is chronic intestinal pseudo-obstruction. This diffuse gastrointestinal dysmotility, Dr. Schiller suggested, "may be due to hollow visceral myopathy, where the muscle cells are shot. Or it may be due to enteric nervous system disorders, where the nerve cells are not functioning properly."

Functional Outlet Obstruction

Functional outlet obstruction is something that gynecologists see in their practices all the time, according to Dr. Schiller. This can take various forms:

- Intrarectal intussusception: Mucosa comes down and actually plugs the anal canal.
- Anterior rectal wall ulcer syndrome: An individual bears down to defecate and the anterior rectal wall is propelled into the anal canal, resulting sometimes in a solitary ulcer.
- Perineal descent: Weakness of the pelvic floor precludes effective evacuation.
- Hirschsprung's disease: In youngsters the enteric nervous system

Abnormal anatomy and disordered physiology play key roles in... chronic constipation.

— Lawrence R. Schiller, MD

"Slow transit constipation may develop secondary to functional outlet obstruction. If you tell someone not to defecate, say they are going up in the space shuttle or fighting a war somewhere, then they will develop slow transit as part of the accommodation mechanism to that."

"It may develop due to chronic stimulatory laxative use." Dr. Schiller noted that "the more

Continued on page 6

TOPIC HIGHLIGHTS

- Rectal Anatomy and Constipation
- Causes of Constipation
- Ob/Gyn: The Year in Review
- GI Disorders
- Treat Constipation Before Surgery
- Scientific Posters: Selected Summaries

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Focus Evaluation of Constipation on Two Causes: Medication and Function

The evaluation of a woman with constipation should focus on two possible causes: medication or a functional problem such as outlet obstruction or irritable bowel syndrome.

Gynecologists need to keep in mind that many women who have constipation suffer in silence. Embarrassment will prevent many women from mentioning the problem to their ob/gyn unless they are directly asked, according to Jack A. DiPalma, MD, FACP, FACC, Professor and Director of the Division of Gastroenterology at the University of South Alabama College of Medicine in Mobile.

Medications That Constipate

Case 1. A 32-year-old woman presents complaining that she has had constipation for the past 4 to 5 months. She has 4 to 5 hard stools daily; her evacuations are incomplete and difficult. Her stools are not loose. She started taking a calcium channel blocker for hypertension before the onset of constipation.

It pays to sit down with a constipated patient and review what prescriptions she is taking.

"The *Physicians' Desk Reference* lists more than 900 drugs that are reported by industry to cause constipation. And more than 100 of these medicines are listed as caus-

Constipation Causing Medications

Highlights from the list of 900 medications known to cause constipation include:

- Analgesics including nonsteroidal antiinflammatory drugs
- Anticholinergics
- Anticonvulsants
- Antihistamines
- Antihypertensives
- Chemotherapeutic agents
- Diuretics
- Metal ions
- Resins

Source: *Physicians' Desk Reference*, ed. 57th. Montvale, N.J.; 2003.

Colorectal Cancer Screening

"We should not lose the opportunity for colorectal cancer screening," stated Dr. Jack A. DiPalma.

Gynecologists are often women's primary care providers and thus may be the ones who screen them or refer them for screening, he noted.

The American College of Gastroenterology offers the following recommendations for screening patients who have an average risk of colon cancer:

- Begin screening at age 50.
- Offer annual fecal occult blood tests and flexible sigmoidoscopy every 5 years, or colonoscopy every 10 years (preferred).

Colorectal cancer screening is the standard of care for primary care physicians, Dr. DiPalma noted.

ing constipation more than 3% of the time," said Dr. DiPalma.

"Forty percent of our screened patients who met Rome II criteria for constipation were using medications known to cause constipation. Often, we have to treat through [the constipation] because the beneficial effects of the medicine prevent us from changing the medication," he said.

Obstructive Defecation

Case 2. A 45-year-old woman presents with a lifelong history of constipation. She notes that she has prolonged and excessive straining even to pass a soft stool. One clue to her diagnosis of obstructive defecation is that she reports she must apply digital pressure to the vaginal peritoneal area to pass the bowel movement. Standard laxatives have had no effect.

The physician, when examining the perineum and anus, should look for digital tenderness or a mass. Physicians may be able to recognize contractures of the puborectalis muscle and anal sphincter.

If her constipation is of recent onset and thus represents a change in her bowel habits, the physician might want to evaluate her for colorectal cancer. Routine screening should begin at 50 years of age in anyone with an average risk for colorectal cancer. The patient should be offered annual fecal

occult blood testing and either sigmoidoscopy every 5 years or colonoscopy every 10 years.

Anyone with a family history of colorectal cancer should begin screening at 40 years of age or 10 years younger than the youngest affected relative. Then, screening should be done by colonoscopy every 10 years when the family history involves a single first-degree relative more than 60 years of age. Screening should be done by colonoscopy every 3 to 5 years when the family history involves multiple first-degree relatives or someone less than 60 years of age, according to Dr. DiPalma.

Structural Evaluation

The findings from evaluation of structural function may give clues to whether the patient has outlet obstruction, slow transit, or other GI problems. Sitz colon markers can be used in a radiopaque study to evaluate the colon. In a colon marker transit study, the patient swallows a little capsule that contains 24 radiopaque rings. Five days later, an x-ray is done of the colon. In normal people, all the rings have passed through the colon and been eliminated. In patients with colonic inertia, these rings may be scattered throughout the colon. In

Ob/Gyn: The Year in Review

Three subspecialties of obstetrics and gynecology—gynecologic oncology, reproductive medicine, and maternal fetal medicine—have seen advances, promise, and controversy over the past year.

Gynecologic Oncology

Cervical Cancer

The American Cancer Society (ACS) issued guidelines in 2002 that call for changes in how Papanicolaou smears are done (*CA Cancer J Clin.* 2002;52: 342-362). The guidelines suggest looking for human papillomavirus (HPV) infection when doing a Papanicolaou smear for detection of cervical cancer cytology. In addition, the ACS guidelines specifically recommend that a woman have her first HPV/Papanicolaou smear done about 3 years after she first becomes sexually active, but no later than 21 years of age.

Conventional cytology should be performed yearly; but liquid-based cytology can be done every 2 years. In women older than 30 years of age who have had three normal tests in a row, where both HPV and Papanicolaou tests are negative, the testing can be done every 3 years. Women still need a yearly gynecologic exam for other reasons, but the interval between screening for cervical cytology can be longer.

The importance of laboratory testing for HPV has been improved by the U.S. Food and Drug Administration's approval in 2002 of a panel that tests for the 13 HPV types with the highest risk for causing cervical cancer. Although some type of HPV has infected an estimated 70% to 80% of women by the time they reach 30 years of age, only 20% have one of the high-risk types. The low-risk types of HPV are so ubiquitous and harmless that testing for them is of questionable value.

Gynecologists may be close to having a vaccine against HPV-16, the strain most closely associated

with cervical cancer. Data from a randomized, placebo-controlled study of 2,400 women showed that there were no cases of HPV-16 or cervical intraepithelial neoplasia (CIN) in the women given the active vaccine. The infection rate was 3.8 cases per 1,000 women-years in the women given the placebo vaccine, and there were some cases of CIN among them (*N Engl J Med.* 2002;347:1703-1705).

Ovarian Cancer

Proteinic patterns in serum are showing further promise in early screening for ovarian cancer. Findings (*Lancet.* 2002; 359:572-582) published in 2002 show that there are certain proteinic patterns in serum that can distinguish cancer from noncancer. When the patterns were used on the masked blood of 116 women, they correctly identified all 50 cases of ovarian cancer, including all 18 cases of stage I disease. Of the serum samples taken from 65 women without ovarian cancer, the patterns correctly identified 63.

Breakthroughs seem imminent in ovarian cancer prevention. One set of findings revealed the reason oral contraceptive use seems to reduce the risk for ovarian cancer: Progesterone produces apoptosis and interferes with ovarian cancer formation by transforming growth factors.

Other research on ovarian cancer prevention is being done through the Specialized Programs of Organized Research Excellence of the National Cancer Institute. There are some preliminary but exciting data showing that cyclooxygenase-2 inhibitors also interfere with ovarian cancer development.

Breast Cancer

There has been a major breakthrough over the past year in screening high-risk women for breast cancer through ductal lavage. Ninety-five percent of breast cancers begin in the ducts. This minimally invasive procedure provides a window to look into the breast. The

first step in ductal lavage is to make sure it is an appropriate procedure for the patient. In a noninvasive office procedure, the breast is massaged and the nipple is aspirated. If fluid is obtained, then the woman is a candidate for ductal lavage.

The patient returns to the office on another day for the 30-minute procedure, in which the physician places a cannula in the nipple, irrigates it with lidocaine, and then washes the duct with saline. White ductal fluid actually comes out. One is able to identify atypia by looking at the cells in the ductal wash.

Colorectal Cancer

Eyeballing stool is the new area of colorectal cancer diagnosis. Every case of colorectal cancer is genetic, involving mutated genes. That mutated DNA is shed continuously in feces, and the DNA is stable in the stool. There is already a test kit on the market for examining stool for the DNA mutations most commonly seen in colorectal cancer. The stool is purified before it is analyzed. If DNA mutations are found in the stool, then the patient is considered at high risk for colorectal cancer. There is at least one study that has looked at the sensitivity and specificity of this test versus colonoscopy. Those findings have not yet been published. At least for now, this test will not replace colonoscopy.

Source: Taken from a session presented by the Society for Gynecologic Oncologists at the 51st Annual Clinical Meeting of the American College of Obstetricians and Gynecologists, April 26-30, 2003, New Orleans.

Reproductive Medicine

Cloning has been the biggest and most controversial story in reproductive medicine in 2002 and 2003. The American Society for Reproductive Medicine has taken a position against reproductive cloning at the present time. Current cloning is inefficient and has a high malformation rate with high mortality.

Reproductive and therapeutic

cloning are the only types of cloning that might potentially involve human subjects. Most research on reproductive cloning has involved somatic cell nuclear transfer (SCNT), the method used to clone Dolly the sheep.

The process of SCNT begins with removing the nucleus from a haploid 22-chromosome oocyte. Then, the donor's somatic cell nucleus is deprogrammed to make it possible for expression of genes in that embryo. The 22-chromosome nucleus from the oocyte and the 22-chromosome nucleus from the somatic cell are returned to the oocyte shell and cultured. The resulting 44-chromosome blastocyst is placed in the uterus of a surrogate carrier.

SCNT has a very high embryonic wastage. The risks with this procedure arise in part from how quickly the genes must imprint. The result can be abnormal expression of the imprinted genes. The second area where things can go wrong is with mitosis and meiosis. Many motor proteins are damaged when the donor nucleus is transplanted into the oocyte shell. Motor protein gives structure to the process of mitosis and meiosis. Primates are particularly susceptible to such protein damage; the result is a large number of aneuploid embryos.

Source: Taken from a session presented by the American Society for Reproductive Medicine at the 51st Annual Clinical Meeting of the American College of Obstetricians and Gynecologists, April 26-30, 2003, New Orleans.

Maternal-Fetal Medicine

The big news in maternal-fetal medicine over the past few months has been the finding that progesterone prevents preterm birth. Women at high risk for preterm delivery, based on history, seem to benefit significantly from weekly injection with 17-alpha-hydroxy progesterone, a very potent relaxer of smooth muscle, according to

Continued on page 4

GI Disorders Often Present to Gynecologists First

Women with constipation, celiac disease, Crohn's disease, and even colorectal cancer are more likely to present to their gynecologists than to a gastroenterologist, says Christine L. Frissora, MD, FACC, FACP.

Ob/gyns need to be prepared to recognize gut-related problems in women. Gynecologists often are the only primary care physicians that most women see, said Dr. Frissora, Assistant Professor of Medicine in the Division of Gastroenterology/Hepatology at the New York-Cornell Medical Center in New York City.

Constipation

Estrogen and progesterone have been hypothesized to be involved in gut motility. Food that comes into the gastrointestinal (GI) tract disrupts villi, and this causes release of serotonin, which in turn stimulates contraction and relaxation of various muscles in the GI tract. Estrogen induces production of nitric oxide, which inhibits contraction of the intestine, and is thought of by Dr. Frissora as "the bloat peptide." Nitric oxide also is associated with constipation.

Many women report changes in the gut function, including a tendency to both bloat and experience constipation, in relation to the menses, at the onset of menopause, and afterwards as well. Changes in estrogen may be the reason why, according to Dr. Frissora. Untreated, constipation can cause hemorrhoids and fissures, she stressed.

Constipation is a common finding during pregnancy. However, the only perfectly safe treatment during gestation remains water and prunes and other high-fiber foods such as carrots, green peas, berries, and oatmeal. For women who are not pregnant, polyethylene glycol (PEG) powder can be helpful, as can a magnesium-hydroxide-based liquid lubricant laxative. "I avoid stimu-

lant laxatives," including herbal remedies such as senna and cascara. "They cause abdominal pain and dependence," she noted.

In women who have constipation after surgery, the best treatment is to get the patient moving. "If you can't move them, turn them. The chest-knee position helps them expel gas. Force the fluids. A stool softener is fine, then use an osmotic laxative such as PEG."

"Ob/gyns need to be prepared to recognize gut-related problems in women."

— Christine L. Frissora, MD

Celiac Disease

Consider the diagnosis of celiac disease in a very thin woman who tells you she eats like a horse, especially if she has low bone density. Other signs of celiac disease besides osteoporosis are infertility and anemia. These women usually complain of gas, bloating, diarrhea or constipation, and/or fatigue.

When sending such a woman for upper endoscopy, insist that the gastroenterologist biopsy the duodenum from six sites. "We cannot see celiac disease with our eyes," Dr. Frissora said. The diagnosis must be made by biopsy. Otherwise, many gastroenterologists will miss it.

Crohn's Disease

Crohn's disease is more common in women than men and is one type of inflammatory bowel disease. Onset usually occurs in the third decade of life. Women complain of pus and/or feces coming out of the vagina. Other signs of irritable bowel disease are malabsorption, osteoporosis, and anemia. There may be an abscess around the rectum and/or vagina. Constipation, abdominal pain, fever, fistulas, and/or diarrhea may occur in Crohn's disease. Strictures in the

colon caused by Crohn's disease as well as an enlarged cecum are easily visible on barium enema.

Colorectal Cancer

Women may have a higher incidence of right-sided colon lesions than do men. Thus, "although flexible sigmoidoscopy may be appropriate screening for a man, it may not be appropriate for a woman," said Dr. Frissora, who is also President of the Office of Women in Medicine and Science at New York-Cornell Medical Center.

The risk for colon cancer is increased in women with a number of GI disorders, including Crohn's disease, ulcerative colitis, and other forms of inflammatory bowel disease. A personal history of endometrial or ovarian cancer increases the risk for colorectal cancer.

Barium enemas are an inadequate way to screen for cancer of the colon and rectum. The point of colorectal cancer screening is to detect and remove the polyps that are the precursor lesions of the cancer. Findings from one study show that barium enemas miss detection of at least 50% of polyps that are visible on sigmoidoscopy (*N Engl J Med.* 2000;342:1766-1772).

Gynecologists have a duty to counsel woman about prevention of colorectal cancer. The medical literature contains a number of studies with data supporting specific approaches to prevention (see **box**). Obesity, low physical activity, and smoking all increase the risk for colorectal cancer. In addition, there are convincing data that daily low-dose aspirin and 400 mg/day of folate can reduce the risk for colorectal cancer.

Colon Cancer: Chemoprevention for Women

- 4-6 aspirin weekly for 20 years is associated with a relative risk for colon cancer of .56 in women. (*N Engl J Med.* 1995; 333:609-614)
- Folate in a daily dose of 400 mcg for 15 years is associated with a relative risk for colon cancer of .25 in women. (*Ann Intern Med.* 1998;129:517-524)
- Calcium in a daily dose of 1200 mg for 4 years is associated with a relative risk for colon cancer of .85 in women. (*N Engl J Med.* 1999;340:101-107)
- Hormone replacement therapy is associated with a relative risk for colon cancer of .65 in women. (*Ann Intern Med.* 1998;128:705-712)

Year in Review

Continued from page 3

findings presented in February at the annual meeting of the Society for Maternal-Fetal Medicine.

The findings involved a National Institutes of Health-funded study of 459 pregnant women with at least one prior preterm birth. They were enrolled between 16 and 20 weeks of gestation and randomized to receive weekly injections with either 17-alpha-hydroxy progesterone or placebo.

The incidence of preterm birth before 37 weeks, was 54.9% among

the 153 women in the placebo group and 36% among the 306 women given 17-alpha-hydroxy progesterone. The incidence of preterm birth before 35 weeks, was 30.7% in the placebo group and 20.6% in the group given active treatment. The incidence of preterm birth before 32 weeks was 19.6% in the placebo group and 11.4% in the progesterone group.

Source: Taken from a session presented by the Society for Maternal-Fetal Medicine at the 51st Annual Clinical Meeting of the American College of Obstetricians and Gynecologists, April 26-30, 2003, New Orleans.

Treat Constipation Before Gynecologic Surgery

Constipation should be treated before hysterectomy or other gynecologic surgery in the hope that presurgical treatment will reduce the rate of postsurgical constipation and complications, according to Marie Fidela R. Paraiso, MD, FACOG.

Although no data currently show that treating constipation presurgically will reduce its incidence postsurgically, none suggest that this management approach has negative clinical implications. "I want all my patients to have their constipation treated before I take them to surgery, so it doesn't bring my prolapse repairs down or predispose a patient to new onset prolapse," said Dr. Paraiso, who is Associate Fellowship Director of Urogynecologic and Reconstructive Pelvic Surgery and Co-Director of Resident Education at the Cleveland Clinic Foundation.

The lack of data on the effectiveness of treating constipation

presurgically to prevent postsurgical gut dysfunction has inspired Dr. Paraiso to develop a research protocol examining whether there is a strong case for pretreatment of constipation, she said.

The same approach can be used to treat constipation both

before surgery and when it develops as a postoperative complication; it has been effective in 90% of patients, in her experience. The first step is to have patients ingest foods that are high in fiber, including prune juice. The next step is to add fiber supplements to

the patient's regime, followed by a stool softener such as docusate sodium. The third step is to add an osmotic diuretic. Physicians need to keep in mind that patients often have strongly held but misguided beliefs about constipation that may interfere with treatment (**See box**), she added.

Dr. Paraiso said that she occasionally consults a gastroenterologist before she moves on to treating the patient with polyethylene glycol (PEG) powder, especially if the patient has not responded to first- and second-line therapy. Biofeedback has been shown to be effective in 50% to 60% of women with constipation. This modality corrects inappropriate pelvic floor contraction such as paroxysmal puborectalis or external anal sphincter contraction.

Following her review of the medical literature, Dr. Paraiso

Continued on page 6

Common Misconceptions

Based on the clinical experience of Marie Fidela R. Paraiso, MD, patients have many firmly held misconceptions about constipation that lead to delayed treatment, thereby potentially exacerbating the condition.

Unless physicians question patients closely about these mistaken beliefs about constipation, they cannot correct them and may undermine therapy for this problem. The following list includes the most common misconceptions:

- **Stool is toxic.**
- **Constipation can lead to cancer.**
- **Laxatives are harmful.**
- **Taking laxatives should be delayed for as long as possible to evacuate spontaneously.**

Scientific Posters: Selected Summaries

➔ Ultrasound

Pregnant women prefer that a female ultrasonographer perform a transvaginal ultrasound examination.

Transvaginal ultrasound is used toward the end of gestation to estimate cervical length. A total of 155 pregnant women were surveyed both before and after they underwent transvaginal ultrasound measurement of cervical length. Male ultrasonographers performed 54% of the transvaginal ultrasounds, and female ultrasonographers performed the remainder of the examinations, all of which were performed during the period May 1, 2002 to January 31, 2003.

Women whose transvaginal ultrasound examination was done by male technicians were signifi-

cantly more likely to describe the procedure as embarrassing than did those who were examined by females. However, women who had previously had a transvaginal ultrasound were less prone to embarrassment than women undergoing the procedure for the first time.

Transvaginal ultrasound and digital examination were equally accurate in assessing cervical length when the cervix was dilated. However, transvaginal ultrasound was more accurate when the cervix was closed.

Source: Tolaymat LL et al. "Transvaginal ultrasound and digital examination at term: Does the operator's gender matter?" Poster presented at the 51st Annual Clinical Meeting of the American College of Obstetricians and Gynecologists, April 26-30, 2003, New Orleans.

➔ Menopause

Women should be evaluated for osteoporosis and fracture soon after menopause.

This recommendation is based on findings from the National Osteoporosis Risk Assessment (NORA), in which bone density was measured in more than 200,000 women, aged 50 years or older, with no prior diagnosis of osteoporosis. Bone density was measured at the heel, forearm, or finger. One year later, more than 87,000 of the women, aged 50 to 64 years, completed surveys regarding their fractures over the past 12 months.

Bone loss occurred frequently in the women aged 50 to 64 years. Twenty-five percent of the women had T scores of -1.0 to -2.0 and 6% had scores less than -2.0.

During the first year of fol-

low-up, 904 women reported fractures of the wrist/forearm, rib, spine, or hip. There were 86 hip fractures that accounted for 37% of the fractures in this age group (50 to 64 years) and 21% of all the hip fractures for all the women studied. Peripheral bone density was highly predictive of fracture risk.

Source: Siris ES et al. "Low bone mass and fracture in women aged 50 to 64 years." Poster presented at the 51st Annual Clinical Meeting of the American College of Obstetricians and Gynecologists, April 26-30, 2003, New Orleans.

➔ Contraception

The women most likely to regret their tubal ligation are those who were younger than 25

Continued on page 7

Rectal Anatomy

Continued from page 1

fails to properly innervate the distal parts of the colon and rectum.

- Paradoxical puborectalis and external anal sphincter contraction during defecation: Spastic pelvic floor syndrome, or anismus for short.

Dr. Schiller cautioned the audience to “look beyond constipation and ease of defecation when dealing with patients with [spastic pelvic floor syndrome].” Most cases “have psychiatric overtones. Many of these women have had physical and sexual abuse in their background.” Their constipation may be part of a resulting somatization syndrome or anxiety. Other psychological causes of constipation are malingering, obsessive-compulsive disorder, and psychosis.

Irritable Bowel Syndrome

About 5% of the general population has constipation due to IBS. The condition represents an overlap of the problems associated with IBS and slow transit constipation.

In addition, patients with “constipation type” IBS have a similar psychologic profile to patients with regular IBS. “They have a similar hypersensitivity to pain,” Dr. Schiller said.

Constipation Research

Data from a study conducted at Baylor University Medical Center shed some light on the stool characteristics of people with constipation (*Dig Dis Sci.* 1998; 43:2353-2362).

The study compared weekly stool output from 20 normal subjects with those from 20 subjects with chronic constipation (**See box**). The constipated group averaged 1.7 bowel movements weekly, compared to 7.1 movements weekly for normal subjects.

To assess stool hardness, researchers modified a tool normally

used to assess bread freshness. When used as intended, the tool’s probe is inserted into bread, and the force required to compress the bread is used as a measure of freshness. In an off-label use of the machine, the researchers inserted its probe into stool. The hardness of bowel movements of the constipated subjects was about the same as that of normal subjects, with hardness levels of 39.3 g and 26.6 g respectively.

The stool weight per bowel movement did not differ significantly between the two groups.

The stool of the constipated group weighed an average of 90.3 g, while the stool in the normal subjects weighed an average of 84.5 g. “What this tells you is that the stroke volume of the rectum is about the same [in normal and constipated people]. It’s about 100 grams. That is how much the rectum wants to expel each day.”

The percentage of solids in the stools of constipated people was 31.7% versus 29% in unaffected people. “So people who have constipation make less stool per week. And they are not only absorbing more water in total, they are also breaking down the solids more, assuming that they are eating the same things [as people who are not constipated],” Dr. Schiller said.

Research has improved the understanding of the pathophysiology of constipation, but there is still a long way to go, Dr. Schiller said. It is impossible to achieve any true pharmacologic breakthroughs until the clinical significance of these various abnormalities is better understood.

While some drugs have been shown to have a beneficial effect on the colon and lessen constipation, more such drugs are needed, he emphasized.

Stool Characteristics		
	Normal Individuals (N=20)	Constipated Individuals (N=20)
Frequency	7.1±0.3 BM/wk	1.7±0.2 BM/wk
	~1 BM/d	~0.24 BM/d
Weight	589.4±60.2 g/wk	153.4±27.0 g/wk
	84.5±8.1 g/BM	90.3±12.3 g/BM
% Solids	29.0±0.8%	31.7±0.8%
Physical Hardness	26.6±3.9 g	39.3±7.0 g

Source: (*Dig Dis Sci.* 1998;43:2353-2362)

Treat Constipation

Continued from page 5

found only 11 studies evaluating the incidence and degree of constipation following gynecologic surgery, specifically hysterectomy. Notably, only one of these studies was a randomized, controlled trial. Overall, data showed that constipation was most common after hysterectomy and surgery for stage 4 endometriosis. Otherwise the results were inconsistent. Findings from a retrospective

study show that severe post-surgical constipation developed in 31% of 593 women after hysterectomy; another 11% had moderate constipation (*Dis Colon Rectum.* 1997;40:1342-1347).

In contrast, 56% of 236 women reported improvement in constipation following hysterectomy and 37% reported no change. However, they were interviewed 2-10 years after their surgery, which leaves a lot of room for recall bias (*Br J Obstet Gynaecol.* 1991;98:1129-1136).

Findings from a cross-sectional study of more than 1,000 women showed that 22% of those with prior hysterectomy complained of constipation while only 9% of women without hysterectomy reported constipation. (*Gut.* 1998; 34:1108-1111). In a second cross-sectional, case-control study, findings show only that decreased bowel function was “more likely” 2-8 years after hysterectomy (*Int J Colorectal Dis.* 1990;5:228-231).

Estimates of postsurgical constipation range from 9% to 22% in

four prospective trials. Data from the one randomized trial showed no difference in rates of preoperative and postoperative constipation in 279 women randomized to either total abdominal or supracervical hysterectomy. Findings from that study showed both that hysterectomy in general does not increase the risk for constipation and that one type of hysterectomy is no better than the other in this regard (*N Engl J Med.* 2002;347: 1318-1325).

Focus Evaluation

Continued from page 2

patients with obstructed defecation, the markers are all hung up at one particular area of the colon.

“When I see obstructed defecation, I think outlet obstruction, cystocele, rectocele, intussusception, prolapse, and this whole group of disorders of pelvic floor dysynergia,” Dr. DiPalma said.

The patient in the case had pelvic floor dysfunction with close to normal transit. Findings from the Sitz marker study of the patient showed that her real problem was an inability to adequately evacuate. Other clues to the diagnosis were her excessive straining, even with soft stool, dyschezia, the need for digital manipulation, and failure to respond to standard laxative treatment.

Defecography that looked at the anorectal junction and anorectal angle showed that the puborectalis muscle did not relax during defecation.

Laxatives

Case 3. The patient is a 64-year-old woman who takes several cardiac medications that are known to cause constipation. Her thyroid-stimulating hormone test results are normal, her colonoscopy is negative, and she has tried bulk agents for her constipation, but they did not help.

Dr. DiPalma said that laxatives could be grouped into four categories: bulking agents, lubricating agents, stimulant laxatives, and osmotic agents. Each type of laxative has its benefits and drawbacks.

Fiber promotes peristalsis and reduces transit time. It is most effective when transit is normal. “Many of my patients have difficulty taking fiber for a long period of time,” Dr. DiPalma said. He noted that some authors recommend a trial of fiber before undertaking technical evaluations for constipation. Magnesium salts have a rapid onset of action. Their laxative action probably comes

from their hyperosmotic effects. Lactulose is not digested and is fermented by colon bacteria. Polyethylene glycol (PEG) is metabolically inert and obligates intraluminal water retention. “We use it once a day, and it has been effective,” said Dr. DiPalma.

Dr. DiPalma reported the results from his placebo-controlled, blinded, multicenter parallel study of 151 patients (131 women and 20 men) with fewer than three stools weekly (*Am J Gastroenterol.* 2000;95(2):446-450). Patients took either 17 g of PEG laxative or dextrose powder placebo daily for 14 days.

On average, by week 2 of treatment, PEG resulted in 4.5 bowel movements weekly, whereas placebo resulted in 2.7 movements weekly. A majority of patients reported that PEG relieved their constipation within 24 hours of the first dose. There were no clinically significant adverse side effects reported.

Laxatives

• Bulk Agents:

- Fiber, bran
- Psyllium
- Polycarbophils
- Methylcellulose

• Lubricating Agents:

- Mineral oil

• Stimulant Laxatives:

- Surface agents: docusate, bile acids
- Diphenylmethane: bisacodyl
- Ricinoleic Acid: castor oil
- Anthraquinones: senna, cascara sagrada

• Osmotic Agents:

- Magnesium and phosphate salts
- Sorbitol
- Glycerin suppositories
- Lactulose
- Polyethylene glycol

Scientific Posters

Continued from page 5

years of age when they had it done, who were in an unhappy marriage, and/or who underwent the procedure at their husband's request.

A total of 42 women, aged 18 to 42 years, completed surveys at the time they were seeking reversal of their bilateral tubal ligation. Their answers were compared to those of 45 other women of the same age who were not seeking reversal. Subjects completed a questionnaire on demographics and relationship characteristics at the time of their sterilization and at the present time.

Women who were younger than 25 years of age at the time of their tubal ligation were more likely than older women to request reversal. Women who

said the sterilization had been their husband's idea were significantly more likely to seek reversal. Of the women seeking reversal, 64% described their marriages as fair or poor at the time of the procedure. Only 33% remained married to the same spouse. In contrast, 75% of the women who were satisfied with their sterilization reported that their marriage was good at the time of the procedure and remain in that marriage.

Source: Moseman CP et al. "Identifying women who will request sterilization reversal." Poster presented at the 51st Annual Clinical Meeting of the American College of Obstetricians and Gynecologists, April 26-30, 2003, New Orleans.

➔ Gynecology

Episiotomy increases the risk for severe perineal lacerations in

women during spontaneous vaginal delivery but is protective in women having operative vaginal delivery.

A retrospective study was conducted in 177 women with third- and fourth-degree perineal tears, and 177 controls. Researchers used univariate analysis to identify a number of variables that were associated with severe perineal lacerations. Risk factors included nulliparity, induction, large size for gestational age, episiotomy, and prolonged second stage.

Of the 354 women, 47 had an episiotomy during delivery. Episiotomy protected women who gave birth by operative vaginal delivery from severe perineal lacerations. Severe perineal lacerations occurred in 11 (36%) of the 31 women who had an operative vaginal delivery with episiotomy, compared with 82 (54%) of the

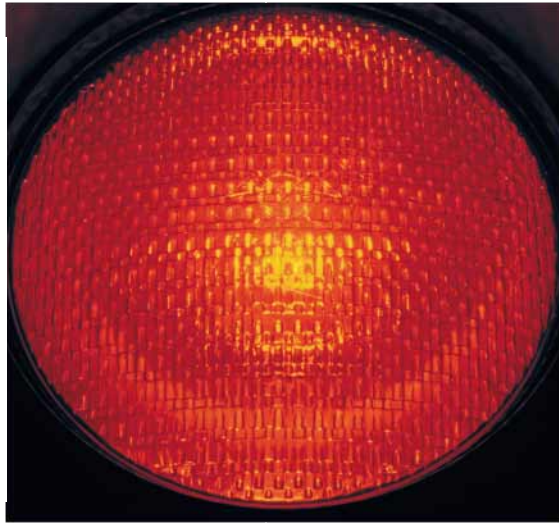
144 women who had an operative vaginal delivery without episiotomy.

In contrast, an episiotomy increased the risk for perineal laceration during spontaneous vaginal delivery. Severe perineal lacerations occurred in 20 (64%) of the 31 women who had spontaneous vaginal delivery with episiotomy versus 62 (36%) of 144 women who had spontaneous vaginal delivery without episiotomy.

Operative delivery was the only modifiable condition identified in this univariate analysis of factors associated with severe perineal laceration.

Source: Dunn TS et al. "Risk factors for severe perineal laceration: A case-control study." Poster presented at the 51st Annual Clinical Meeting of the American College of Obstetricians and Gynecologists, April 26-30, 2003, New Orleans.

If this is Constipation



This is MiraLax™



MIRALAX™
Polyethylene Glycol 3350, NF Powder for Solution

Works so well it's the #1 Rx laxative¹
Most-prescribed Rx by gastroenterologists²
Millions of scripts written¹

- No taste, grit, or residue • No sugar or sweetener
- Dissolves completely in water, juice, soda, coffee, or tea

An Effective Stool Softener

MiraLax is an osmotic laxative. Indications and Usage: For the treatment of occasional constipation. Most Common Adverse Events: Nausea, abdominal bloating, cramping, and flatulence. Contraindications: Patients with known or suspected bowel obstruction and/or allergy to polyethylene glycol. Warnings: Symptoms suggestive of bowel obstruction should be ruled out before initiating MiraLax therapy. Precautions: Patients should be evaluated for bowel obstruction or metabolic disorders.

Brief Summary: Before prescribing, see complete prescribing information. **INDICATIONS AND USAGE:** For the treatment of occasional constipation. This product should be used for 2 weeks or less or as directed by a physician. **CONTRAINDICATIONS:** MiraLax is contraindicated in patients with known or suspected bowel obstruction and patients known to be allergic to polyethylene glycol. **WARNINGS:** Patients with symptoms suggestive of bowel obstruction (nausea, vomiting, abdominal pain or distention) should be evaluated to rule out this condition before initiating MiraLax therapy. **PRECAUTIONS: General:** Patients presenting with complaints of constipation should have a thorough medical history and physical examination to detect associated metabolic, endocrine and neurogenic conditions, and medications. A diagnostic evaluation should include a structural evaluation of the colon. Patients should be educated about good defecatory and eating habits (such as high fiber diets) and lifestyle changes (adequate dietary fiber and fluid intake, regular exercise) which may produce more regular bowel habits. MiraLax should be administered dissolved in approximately 8 ounces of water, juice, soda, coffee, or tea. Safety and effectiveness in pediatric patients has not been established. MiraLax should only be administered to a pregnant woman if clearly needed. **ADVERSE REACTIONS:** Nausea, abdominal bloating, cramping and flatulence may occur. High doses may produce diarrhea and excessive stool frequency, particularly in elderly nursing home patients. Patients taking other medications containing polyethylene glycol have occasionally developed urticaria suggestive of an allergic reaction. **Rx only. STORAGE:** Store at 25°C (77°F). Distributed by Braintree Laboratories, Inc., Braintree, MA 02185

U.S. Patents No. 5,710,183; No. 6,048,901.

References: 1. #1 in prescription volume as reported in IMS Health. *National Prescription Audit, Therapeutic Category Reports*, January 2001-January 2003.
2. IMS Health. Custom Data, January 2001-December 2002.



For product samples and literature, call
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