NEWYORK-PRESBYTERIAN

Digestive Diseases

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Fall 2006

ROME III Help Physicians Treat Bowel Disorders

Columbia and Weill Cornell physicians at NewYork-Presbyterian Hospital are working to treat functional bowel disorders based on new guidelines released at the 2006 Digestive Disease Week (DDW) meeting.

"Functional bowel disorders are those for which no structural or chemical abnormalities exist to explain symptoms," said Susan Lucak, MD. "Two major conditions that fall into this category are irritable bowel syndrome [IBS] and functional dyspepsia."

The guidelines—ROME III criteria—are symptom-based and help to better define these conditions, said Dr. Lucak. The criteria help physicians study, assess and treat these patients in clinical practice and avoid a wastebasket diagnosis, she said. In the past, patients with gastrointestinal symptoms would undergo a workup, and if tests came back negative for specific gastrointestinal diseases, physicians would generally diagnose IBS or dyspepsia. "But people who have these disorders have their own specific symptoms," said Dr. Lucak.

"[IBS] has long been misunderstood and misdiagnosed," added Christine L. Frissora, MD, FACP. The first step toward treatment is to make an accurate diagnosis and to legitimize the disorder, she continued. The condition has been broadly defined as abdominal

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Researchers Make New Discoveries About Tumor Regrowth After Colorectal Cancer Surgery

Colorectal cancer (CRC) recurs in approximately 30% to 40% of patients who have clear margins after resection. Although this suggests that malignant cells were missed, there is increasing evidence that surgery itself may favor the growth of residual tumor cells. In work being performed at NewYork-Presbyterian Hospital, an increase in blood levels of vascular endothelial growth factor (VEGF), which promotes angiogenesis, has been identified as one of several molecular events that occur after CRC resection and may facilitate cancer recurrence. Targeting these factors may offer an opportunity to reduce the recurrence not only of CRC but also of other malignancies after surgery.

"It makes sense that surgery would stimulate angiogenesis because the wound needs a blood supply for healing, but to our surprise we found that blood levels of VEGF stay elevated for 3 to 4 weeks after surgery, and this is likely to be creating an environment conducive to cancer regrowth," said

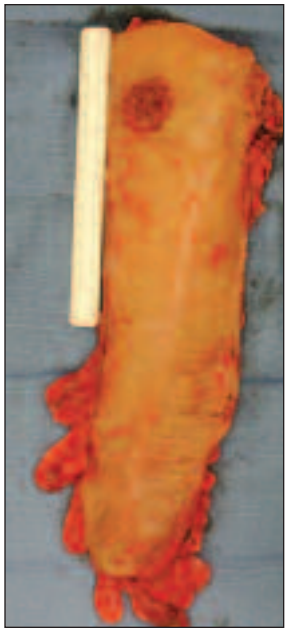

Photo courtesy of Richard L. Whelan, MD.

Rectal adenocarcinoma.

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XII International Celiac Disease Symposium. November 9-11, 2006. For more information, please visit www.celiacdiseasecenter.columbia.edu/symposium

The 23rd Annual Postgraduate Medicine Course, Update in Gastroenterology, Hepatology & Nutrition. December 1-2, 2006. For more information, please visit www.columbiacme.org

New York Annual Scientific Symposium on Colorectal Cancer. March 2, 2007. For more information, please visit www.monahancenter.org

Surgical Advances Are Paving Way for 'Incisionless' Colorectal Surgery and Perioperative Treatment

Imagine colorectal surgery with no incision. Imagine a novel presurgical treatment that decreases the risk for cancer regrowth.

These intriguing possibilities are fast becoming realities at the colon and rectal surgery sections of NewYork-Presbyterian Hospital/Weill Cornell Medical Center and NewYork-Presbyterian Hospital/Columbia University Medical Center. The institutions provide ideal settings in which to study and develop such surgical advances, according to Jeffrey W. Milsom, MD, and Richard L. Whelan, MD.

Surgeons are currently developing the techniques of endoluminal surgery—colorectal surgery that is performed via an endoscope inserted through the rectum. There is no abdominal cut, not even the small incision used for minimally invasive laparoscopic colorectal surgery. That means no incision pain, no scar, and no chance of infection at the wound site.

Dr. Milsom describes endoluminal surgery as a totally new approach that is being pioneered at NewYork-Presbyterian/Weill Cornell. "The surgeon will place the endoscope through the bowel, remove the diseased tissue, handle the blood supply, and extract the specimen—all through a rectal entry. And with no incision, this can be performed on an outpatient basis." Among the potential indications for endoluminal surgery are diverticulitis, ulcerative colitis, strictures, and inflammatory bowel diseases such as Crohn's disease. There may also be a few selected cases of colorectal cancer in which endoluminal surgery is indicated.

"In colorectal cancer, the surgeon wants to remove tissue with a large margin, to prevent recurrence, so that an endoluminal approach may not be appropriate in many cases," noted Dr. Milsom. "However, for elderly cancer patients who cannot tolerate other surgical procedures, endoluminal surgery might be an option."

Dr. Milsom contrasted endoluminal surgery with natural orifice transluminal endoscopic surgery (NOTES), another new, advanced incision-free surgical approach (Figure). In NOTES, which is still under development, a flexible endoscope is placed through the mouth into the gastric cavity and then into the peritoneal cavity through a puncture in the stomach wall. NOTES could conceivably be used for tubal ligation, appendectomy, cholecystectomy, or hysterectomy. However, the stomach perforation required for NOTES is considered a major complicating factor. Endoluminal surgery is a different type of procedure.

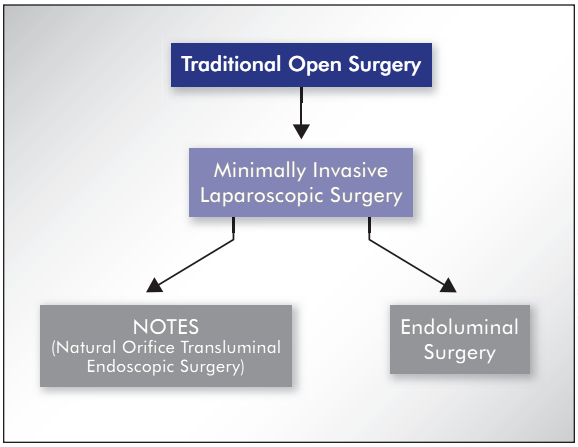

Figure courtesy of Jeffrey W. Milsom, MD.

Figure. Evolution of colorectal surgery.

Surgeons at NewYork-Presbyterian/Weill Cornell, said Dr. Milsom, are motivated to develop endoluminal surgery because "we are committed to finding the most advanced means to get people well quickly and with a lower risk of complications." Endoluminal procedures, he noted, are yet another example of his department's devotion to harnessing the power of today's endoscopic technologies. "We're big-time techies," said Dr. Milsom, "because technology keeps on improving outcomes."

At NewYork-Presbyterian/Columbia, the section of colon and rectal surgery is completing a study of granulocyte–macrophage colony-stimulating factor (GM-CSF). It is thought that this immunomodulator, when used perioperatively, may improve survival and decrease rates of disease recurrence in colorectal cancer patients; other immune system–modulating agents have been associated with decreased rates of tumor establishment and growth after abdominal surgery. The randomized, placebo-controlled Phase I trial will assess the safety of GM-CSF and its effect on a mediator of tumor blood supply—important information that is a prerequisite for conducting larger Phase II and Phase III studies to determine the efficacy of GM-CSF in suppressing cancer recurrence. Surprisingly, GM-CSF had no apparent effect on immune function during the study—a finding that may derive from the inclusion of patients who underwent minimally invasive, laparoscopic colorectal resection.

"Minimally invasive colorectal resection," said Dr. Whelan, "is less immunosuppressive than traditional open surgery. Therefore, it is difficult to demonstrate improvement of immune function with GM-CSF when you include this group of patients because

"We are committed to finding the most advanced means to get people well quickly and with a lower risk of complications. … We're big-time techies because technology keeps on improving outcomes."

—*Jeffrey W. Milsom, MD*

the placebo group shows fairly good immune function."

A key finding of the study is that patients treated with GM-CSF had significantly higher postsurgical concentrations of vascular endothelial growth factor receptor 1 (VEGFR-1). VEGFR-1 binds to vascular endothelial growth factor (VEGF). At elevated levels, VEGFR-1 decreases the ability of VEGF to promote the formation of new blood vessels (angiogenesis) in or near tumor microfoci, tiny fragments that remain undetected at the time a cancerous tumor is removed. "So far, our trial has shown that the safety of GM-CSF is quite good, so the drug holds promise as a well-tolerated means of combating tumor establishment and growth in the days and weeks after surgery," said Dr. Whelan.

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Researchers Study Promising New Treatments for Hepatitis B

"A major challenge in treating hepatitis B is that, with few exceptions, you can't eradicate it completely from the body," said Ira M. Jacobson, MD. "So the realistic goal of treatment in most patients is long-term viral suppression."

Five drugs are available to do just that. However, the question of which ones to use and how to use them is at the heart of some spirited debate right now, according to Dr. Jacobson.

His recent article in the *American Journal of Gastroenterology* looks in detail at 3 of the traditional medications for hepatitis B virus (HBV) infection—interferon (IFN), lamivudine and adefovir (*Am J Gastroenterol* 2006;101:S13-S18). Another article in the same issue examines the 2 newest agents—entecavir and peginterferon alfa-2a (*Am J Gastroenterol* 2006; 101:S19-S25).

Dr. Jacobson, who delivered the prestigious "State-of-the-Art Lecture" on hepatitis B at the 2006 Digestive Disease Week (DDW) meeting in Los Angeles, has been active, along with other Weill Cornell physician-researchers at NewYork-Presbyterian Hospital, in recent clinical studies of hepatitis drugs, including tenofovir, which currently is approved for HIV treatment but shows promise for patients with HBV.

There are a number of controversies currently engaging clinicians involved in the treatment of HBV. One centers on when to begin HBV therapy and in which patients. For example, in his lecture at DDW Dr. Jacobson raised the question, "Should patients with relatively mild disease be treated for the sake of suppressing their viral loads?" His view is that past treatment guidelines that rely on liver enzyme levels and outmoded thresholds for viral loads may be too restrictive to dictate current practice, and it may make sense to expand the treatment population and begin therapy earlier.

"In a setting in which several new drugs have come out and others are promising to follow soon, we are learning that we probably need to expand our thinking in terms of the spectrum of patients who are treatment candidates," said Dr. Jacobson.

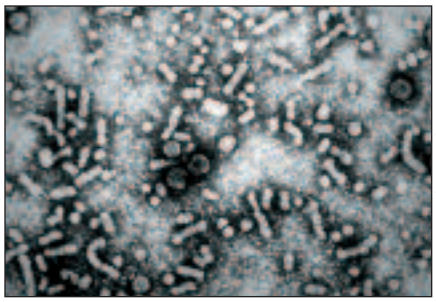

Photo courtesy of Centers for Disease Control.

This electron micrograph reveals the presence of hepatitis B virus "Dane particles," or virions. These particles measure 42 nm in their overall diameter, and contain a DNA-based core that is 27 nm in diameter.

Whether to use oral medications or injectables is another ongoing dispute. Three oral drugs—lamivudine, adefovir, and entecavir—are currently available, along with 2 injectables, IFN and peginterferon alfa-2a. The latter, however, has largely displaced IFN because it remains in the blood longer and can be administered once per week instead of 3 times. The use of IFN or its pegylated form has benefits and drawbacks.

"One advantage is that it is a finite course of therapy," said Dr. Jacobson. "You start it and stop it a year later. Whatever the patient's status is at the end of the year, you're done." Oral medications often need to be continued for years.

In the short term, IFN has also been shown to be more effective than oral drugs in inducing hepatitis Be (HBe) antigen seroconversion with 12 months of therapy. "If you reach this end point, you have a very nice suppression of viral replication for many years in the majority of patients," he said. In patients who lack HBe antigen because of certain mutations in the virus, IFN also has a greater chance of inducing sustained suppression of viral replication after a year of therapy than a comparable period of oral therapy, he added.

Over time, however, the rate of HBe antigen seroconversion increases with oral drugs, Dr. Jacobson said, and by the end of the second year the rates are comparable to those achieved after a year of IFN. What is more, he said, "at the end of year 3, with lamivudine or adefovir, the rate of HBe seroconversion climbs even higher." In patients negative for HBe antigen, very high rates of long-term viral suppression can be achieved, which correlates with reductions in liver scarring and with improvements in clinical outcomes. However, a stopping point associated with an acceptably low rate of viral reactivation after prolonged oral therapy has not been established.

Proponents of IFN therapy advance another argument: with a 12-month course of therapy, the drug is better at clearing every last trace of virus from the blood, as indicated by hepatitis B surface antigen conversion. The disadvantages of IFN are the higher risk of toxic side effects and the inconvenience of administering injections. Moreover, IFN is contraindicated in patients with cirrhosis because its immune properties may stimulate a dangerous flare of hepatitis in such patients.

A major advantage of oral medications is that they are better tolerated than IFN and do not require injections.

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Case Study: With Access to Key Research, Physicians Optimize Treatment in HBV

The Case

A 34-year-old Asian man presents to the Center for Liver Disease and Transplantation at NewYork-Presbyterian Hospital/Columbia University Medical Center for evaluation of his hepatitis B virus (HBV) infection. The patient was born in Hong Kong and immigrated to the United States in his teens. HBV was diagnosed about 2 years ago by his primary care physician after routine liver function tests (LFTs) proved to be abnormal. For 18 months, his disease has been under control with lamivudine therapy (100 mg/day), but his latest LFTs were again abnormal. At the Center, his aspartate aminotransferase (AST) and alanine aminotransferase levels are 130 U/L and 256 U/L, respectively. He is otherwise asymptomatic and his physical exam findings are unremarkable. He reports adherence to his antiviral regimen and says he has taken no herbal remedies or over-the-counter medications.

There are many reasons why a patient whose chronic HBV has been held in check with lamivudine develops a flare in LFTs, according to Robert S. Brown Jr., MD, MPH. They include a reactivation of the virus, worsening of liver disease, and the development of hepatocellular carcinoma or other complication. But the most likely scenario is resistance to the antiviral medication. In this patient, resistance was documented by viral rebound as well as genotypic analysis, Dr. Brown said.

"We always presume resistance because it is the most common explanation and it is the 1 condition you can easily treat," Dr. Brown said. "We added a second agent, but you also look for all those other things that could have led to worsening of this condition."

The second agent was adefovir dipivoxil, an oral nucleotide analog. Adefovir is the current "drug of choice" for patients with lamivudine resistance, according to Dr. Brown. On a combination of lamivudine and adefovir, the patient's viral load was reduced. Imaging showed no evidence of cancer. For the past 6 months, the patient has had normal liver enzymes and his HBV DNA has remained suppressed.

Discussion

HBV remains a significant health problem in the United States. Despite universal immunization of children as well as vaccination programs for health workers at risk for contracting the disease, some 100,000 cases are reported every year. Worldwide, an estimated 350 million people are infected with HBV. Anywhere from 15% to 40% of them develop serious complications, including HCC, cirrhosis, and hepatic decompensation.

Five therapeutic agents have been approved by the Food and Drug Administration for the treatment of HBV infection: interferon alfa-2b, pegylated interferon alfa-2a, lamivudine, adefovir, and entecavir. Each has its uses and limitations in clinical practice. Lamivudine, the oral nucleoside analog used initially in this case, has good tolerability and safety and has shown to be effective in reducing viral replication.

However, the development of resistance to lamivudine has become a significant clinical problem, with rates estimated to be 14% to 20% at 1 year and 69% after 5 years. The high rate underscores the importance of closely monitoring LFTs and HBV DNA levels in all patients on lamivudine monotherapy. Resistance is most commonly encountered in patients whose AST levels have flared after periods of stability on lamivudine. In fact, because of high resistance rates, some clinicians now avoid using lamivudine monotherapy and have switched instead to a combination of antivirals as the first-line response to HBV.

Only 2 drugs, adefovir and entecavir, have been tested in the setting of lamivudine resistance, according to Dr. Brown. "Entecavir in lamivudine-resistant patients appears to have a higher rate of developing entecavir resistance," he said. "So we didn't feel it would be the ideal choice. And it has never been studied in combination therapy with lamivudine. Adefovir has been looked at in combination therapy with lamivudine. We felt that until we had further data, we should stick with a drug combination where there is the most experience."

The decision in this case to retain lamivudine in the therapeutic regimen was based on evidence showing that the combination of adefovir and lamivudine can prevent replication of the wild-type virus as well as suppress resistant HBV. The combination may also help prevent the rare development of adefovir resistance.

Much of this important research was conducted at the Center for Liver Disease and Transplantation, which has been at the forefront of research into innovative treatment options to improve outcomes and quality of life in patients with liver diseases such as HBV. With its unique, multidisciplinary approach, patients benefit from the close collaboration of the hepatologists, gastroenterologists, hepatobiliary surgeons, diagnostic and pathology experts, advanced-care nurses, social workers, and patient support staff.

According to Dr. Brown, there is general agreement that the number of patients who would benefit from therapy is on the rise, at the same time that concern about the development of resistance is growing. This, he said, underscores the importance of implementing the optimal treatment regimen from the onset of therapy.

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CRC

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Richard L. Whelan, MD. "What we are finding is that after resection, remaining cancer cells, if present, are being literally "bathed" in a protein that improves the chances of a recurrent tumor developing."

An elevation of VEGF is not the only molecular event stimulated by surgery that may favor a return of malignancy. In a series of published studies, Dr. Whelan and his co-investigators demonstrated that circulating levels of the protein IGFBP-3, which has been shown to suppress tumor growth, fall precipitously after open surgery in most patients (*Surg Endosc* 2005;19:55-59). Other studies have shown a decline in immune function related to surgery. All of these changes give clinicians an opportunity to intervene and make the postsurgical environment less hospitable for cancer regrowth.

Although results from an initial clinical trial to assess the effect of pharmacologic stimulation of the immune system before and after surgery were disappointing, they did provide direction for future study. In a controlled study, 50 patients undergoing a laparoscopic CRC resection were randomized to receive granulocyte–macrophage colony-stimulating factor (GM-CSF) or saline solution. Although Dr. Whelan was able to show that immune function in the GM-CSF group was improved, there was little decline in the immune function of the control group, so the difference between the groups did not reach statistical significance. When the investigators measured the levels of soluble VEGF receptor 1 (sVEGFR-1) in the blood, a naturally occurring inhibitor of VEGF, they were dramatically increased among those randomized to GM-CSF.

"The results suggested that GM-CSF can be used to block angiogenesis. There was no difference observed in wound healing, so this approach appears to be safe," reported Dr. Whelan. He said that further controlled experiments in which blood was evaluated in endothelial cell culture before and after surgery demonstrated that the blood from patients who received GM-CSF was significantly less pro-angiogenic than the blood from the control patients, who received saline solution. He also observed that about 65% of patients treated with GM-CSF achieve a significant response in regard to elevation of sVEGFR-1 levels in the blood.

> "We may be able to pharmacologically alter the response to surgery so as to decrease the chances of tumor regrowth. We believe this is an exciting area of research."
>
> —Richard L. Whelan, MD

"The idea is that surgical removal of the primary tumor can set up an environment that helps residual tumor cells to survive and produce a recurrence," said Dr. Whelan. "We may be able to pharmacologically alter the response to surgery so as to decrease the chances of tumor regrowth. We believe this is an exciting area of research."

New studies with GM-CSF are being considered in which this growth factor will be started 3 days before patients undergo a surgical procedure and continued for the first two weeks after surgery to determine if the effects observed in the initial study can be enhanced. Dr. Whelan said that he and his team of investigators are also looking at the ability of other anticancer agents, such as the epidermal growth factor receptor inhibitor cetuximab, to reduce the tumor-stimulatory environment after surgery.

Chemotherapy is not generally considered to be appropriate until 4 to 6 weeks after surgery because of surgery-related immunosuppression and fears that the standard chemotherapy agents may impair wound healing and recovery. However, this practice may offer surviving tumor cells an environment that encourages tumor growth. An anticancer drug that is safe to administer during the early postoperative period could prevent recurrence, but the optimal intervention is not obvious. For example, aggressive blockade or inhibition of pro-angiogenic factors in this period could impair wound healing or otherwise compromise the surgical results. Initiatives like those in Dr. Whelan's GM-CSF study suggest that it may be possible to diminish the effects of VEGF while preserving wound healing and recovery.

"We have identified a potential problem and a possible solution, but we need more studies to demonstrate the benefits of intervening and to confirm that we are not introducing new complications," said Dr. Whelan. However, if an effective strategy to control postsurgical factors that favor recurrence can be shown to increase disease-free survival, it is likely to be relevant to a variety of cancers that recur after surgery in the face of disease-free margins.

"Altering the patient's response to surgery and minimizing the deleterious molecular events that promote cancer has implications for any type of malignancy," said Dr. Whelan. He said that further studies directed at attenuating the effects of surgery on promoting tumor cell proliferation, including clinical trials, are planned.

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Bowel

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pain and discomfort with altered bowel habits, primarily manifesting as diarrhea and constipation.

In the past, ROME criteria for IBS have focused on defining stool frequency for constipation and diarrhea, said Dr. Lucak. The newly released ROME III criteria focus on stool consistency. For example, a patient with IBS with constipation will have >25% hard and lumpy stools and <25% loose stools. In IBS with diarrhea, patients will experience >25% loose stools and <25% hard stools. A mixed pattern may also occur, with >25% loose and >25% hard and lumpy.

Prior to 2000, treatments for IBS consisted of multiple medications, including antispasmodics, laxatives, antidiarrheals, and antidepressants, said Dr. Lucak. Antidepressants tend to help with a patient's well-being, but studies have yet to show how they help relieve specific symptoms of the syndrome, she said.

Low doses of antidepressants are useful in some patients but may have side effects, including sexual dysfunction and weight gain, noted Dr. Frissora.

Newer treatments have helped address the multiple symptoms of IBS. In 2000, the U.S. Food and Drug Administration approved alosetron, an agent shown to be effective for the treatment of severe diarrhea-predominant IBS in women, said Dr. Frissora. The drug tegaserod became available in 2002 for women with IBS and treats the "ABCs" of the condition, meaning abdominal pain, bloating, and constipation, she explained.

The reason why these drugs were not approved for men is that not enough males enrolled in clinical trials, said Dr. Lucak. "This doesn't mean these therapies don't work in men," she added.

"For some patients, a combination approach to treatment is needed," said Dr. Frissora. For example, physical therapy for pelvic floor dysfunction, psychiatric counseling, which can sometimes help patients with contributing psychosocial problems, and nutritional counseling may be necessary.

In addition to current therapies, new treatments are on the horizon. A recent study presented at DDW showed that lubiprostone is effective in treating chronic constipation and may help alleviate IBS with constipation, said Dr. Lucak. The medication stimulates type 2 chloride channels in epithelial cells and increases fluid secretion in the small bowel, leading to increased motility.

Another agent, rifaximin, a nonabsorbable antibiotic that targets bacteria in the intestine, may help IBS when bloating is a major symptom. The drug is currently approved for traveler's diarrhea. It is being further investigated for the treatment of IBS.

"In my experience, rifaximin is excellent for treating patients with IBS symptoms who also have an overlap with fibromyalgia and chronic fatigue," said Dr. Frissora. "The reason for that may be that by decreasing intestinal bacteria, chronic inflammatory responses are suppressed."

The other major functional bowel

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Table. Bowel Disease "Red Flags"

History

- Onset in older patients (>50 y)
- Family history of colon cancer or inflammatory bowel disease
- Unintentional weight loss of ≥10 pounds
- Hematochezia
- Symptoms of underkying disorders such as hypothyroidism

Physical Exam

- Abnormal findings on rectal exam
- Abnormal mass

Laboratory Findings

- Hemoglobin (Hgb)
- White blood cell count
- Guaiac positive stool

Sources: *Gastroenterology.* 1997;112:2120-2137
CMAJ. 1999;161:154-160
Aliment Pharmacol Ther. 1997;11:3-15
Emerg Med. 2001;Apr:57-64

HBV

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Their downside is the potential development of resistance, particularly with lamivudine. Combining medications is one way to defeat resistance. "We've learned that lamivudine and adefovir are very effective in a combination that seems to minimize resistance," Dr. Jacobson noted, "because the minute the virus tries, in effect, to outwit one drug by developing a mutation, the other drug is there to suppress the mutant."

The newest oral medication, entecavir, suppresses the virus more effectively than either of the other oral drugs, said Dr. Jacobson, and has "an unblemished resistance track record" after nearly 2 years of use in patients who have not had previous therapy.

However, Dr. Jacobson noted the belief among some clinicians that it is unrealistic to think that any one drug will ever be enough to treat the disease and that it is just a matter of time before resistance surfaces in patients treated with entecavir. The countering argument, he said, is that 3 different mutations need to occur at the same time for the virus to outwit entecavir—a mathematical improbability, according to the drug's proponents.

"It's a very lively controversy in the field right now," Dr. Jacobson said.

"Should we still be using monotherapy," Dr. Jacobson said, "and if we do, when should we go to combination therapy or switch to another drug?"

"More and more," he said, "the pendulum is swinging to earlier switching or adding another drug in patients who are likely to develop resistance as measured by excessively high viral levels at 6 to 12 months of treatment."

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Bowel

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disorder, functional dyspepsia, is a diagnosis that patients often receive if they undergo upper endoscopy and physicians cannot find a structural explanation for epigastric pain such as ulcers or esophagitis, said Dr. Lucak. Other symptoms include early satiety, bloating, nausea, and vomiting.

ROME criteria have further described the condition using subcategories, explained Dr. Lucak. For instance, patients with functional dyspepsia related to eating have postprandial distress syndrome. The condition occurs in about 32% of functional dyspepsia cases. Other subcategories include epigastric pain syndrome, seen in 39% of cases, and chronic idiopathic nausea, occurring in about 7% of patients with functional dyspepsia. Cyclical vomiting syndrome is another subcategory, but is rare and occurs more often in children than adults. Overlap of the first 3 subcategories can occur, said Dr. Lucak.

Generally, patients with functional dyspepsia do not respond to treatment with proton pump inhibitors such as esomeprazole or lansoprazole. Researchers are evaluating tegaserod for the treatment of functional dyspepsia. The drug may stimulate motor function of the upper gastrointestinal tract, said Dr. Lucak. Subdepressant doses of antidepressants have been found to be helpful in some patients with functional dyspepsia.

Overall, functional bowel disorders may overlap. IBS may overlap with functional dyspepsia, gastroesophageal reflux disease or chronic constipation. "Researchers and clinicians are asking themselves if these disorders are separate diseases or are they part of a continuum of disorders in which gastrointestinal motility and sensitivity are altered," said Dr. Lucak.

Some studies have shown that many of the upper gastrointestinal symptoms reported by patients with functional dyspepsia overlap with those reported by some IBS patients, noted Dr. Frissora. However, the nature of a patient's abdominal pain is one distinguishing feature that differentiates the 2 conditions. In functional dyspepsia, the pain is centered in the upper abdomen, while it is centered in the lower abdomen for IBS, she explained.

"Clearly, more studies need to be done to validate and further tease out these conditions," said Dr. Lucak. "Researchers need to look at the subcategories specifically and evaluate specific treatments."

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NEWYORK-PRESBYTERIAN Digestive Diseases

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