ASPIRIN AND COLORECTAL CANCER IN MEN
A prospective study of 47,363 male health professionals who were ages 40 to 75 years at enrollment in 1986 was conducted biannually. Data was collected on aspirin use, other risk factors and diagnoses of colorectal cancer. During 18 years of follow-up, 975 cases of colorectal cancer were documented over 761,757 person/years. After adjustment for risk factors, men who regularly used aspirin (2 or greater times per week), had a multivariate relative risk (RR) for colorectal cancer of 0.75, compared with nonregular users. However, significant risk reduction required at least 6 to 10 years of use and was no longer evident within 4 years of discontinuing use.

The benefit appeared related to increasing cumulative average dose, compared with men who denied any aspirin use. The multivariate RR of cancer for use were 0.94 for men who used 0.5 to 1.5 standard aspirin tablets per week, 0.80 for 2 to 5 aspirin tablets per week, 0.72 for 6 to 14 aspirin tablets per week and 0.3 for greater than 14 aspirin tablets per week.

It was concluded that regular, long-term aspirin use reduces risk of colorectal cancer among men. However, the benefit of aspirin necessitates at least six years of constant use, with maximal risk reduction at doses greater than 14 tablets per week. The potential hazards associated with long-term use of such doses should be carefully considered. (Chan AT, Giovanucci EL, Meyerhardt JA, et al. “Aspirin Dose and Duration of Use and Risk of Colorectal Cancer in Men.” Gastroenterology, 2008; Vol. 134, 21-28.)

Mucosal Atrophy in Celiac Disease
To study the macroscopic features in celiac disease by means of a magnified view of the intestinal mucosa utilizing wireless capsule endoscopy, evaluation of the following: (1) the distribution of atrophy in untreated celiac disease, (2) the correlation between extent of changes and clinical manifestations, (3) the accuracy and interobserver agreement of wireless capsule endoscopy assessment, and (4) the affect of gluten withdrawal.

Thirty-eight consecutive patients with untreated, biopsy-proven celiac disease underwent wireless capsule endoscopy (WCE). Each subject was invited to undergo repeat testing after at least six months of gluten withdrawal. The video images of each patient were reviewed independently by two investigators. Thirty-five (92%) subjects had visible atrophy detected by capsule endoscopy. Twenty-two (59%) subjects showed an extensive enteropathy. Twelve (32%) had enteropathy limited to the duodenum and only one had a jejunal enteropathy. No association was shown between the extent of the lesion and clinical manifestations. Capsule endoscopy had a better overall sensitivity for the detection of atrophy as compared with upper endoscopy (92% vs. 55%), with a specificity of 100%.

The overall interobserver agreement for the two reviewers was high (total agreement 86.5%). After gluten withdrawal, the extended pattern of atrophy improved both qualitatively and quantitatively.

It was concluded that celiac disease affects a highly variable portion of the small intestine, starting at the duodenum. The extent of visible enteropathy does not explain differences in clinical presentation. Most subjects with visually detectable villous atrophy showed a clinically significant improvement after gluten withdrawal. (Murray JA, Rubio-Tapia A, VanDyke C, et al. “Mucosal Atrophy in Celiac Disease: Extent of Involvement, Correlation with Clinical Presentation (continued on page 70)
and Response to Treatment.” *Clinical Gastroenterology and Hepatology*, 2008; Vol. 6, 186-193.)

**Aspirin and Folic Acid in Recurrent Colorectal Adenomas**

A multicenter, randomized, double-blind trial of aspirin (300 mg per day) and folate supplements (0.5 mg/day) to prevent colorectal adenoma recurrence was performed using a 2×2 factorial design. All patients had an adenoma equal to or greater than 0.5 cm removed in the six months before recruitment and were followed up at four month intervals with a second colonoscopy after approximately three years.

The primary outcome measure was a colorectal adenoma diagnosed after baseline.

A total of 945 patients were recruited into the study, of whom 853 underwent a second colonoscopy. In total 99 (22.8%) of 434 patients receiving aspirin had a recurrent adenoma, compared with 121 (28.9%) of 419 patients receiving placebo (relative risk 0.79).

A total of 104 patients developed an advanced colorectal adenoma (41) and 9.4% of these were in the aspirin group and 63 (15%) were in the placebo group (relative risk 0.63). Folate supplementation was found to have no effect on adenoma recurrence.

It was concluded that aspirin 300 mg per day but not folate 0.5 mg per day use was found to reduce the risk of colorectal adenoma recurrence with evidence that aspirin could have a significant role in preventing the development of advanced lesions. (Logan R, Grainge M, Shepherd V, Armitage N, Muir K, on behalf of the ukCAP Trial Group. “Aspirin and Folic Acid for the Prevention of Recurrent Colorectal Adenomas.” *Gastroenterology*, 2008; Vol. 134, 29-38.)

**Fundic Gland Polyp Dysplasia in FAP**

Fundic gland polyps (FGPs) are common in familial adenomatous polyposis (FAP), but have been considered nonneoplastic. Gastric carcinoma rises from FGPs in FAP, presumably from a dysplasia/carcinoma pathway. To study the prevalence of FGPs and FGP dysplasia in FAP and identify endoscopic or demographic features associated with FGPs and dysplasia, a study was carried out.

Demographic and endoscopic information were obtained prospectively from 75 consecutive subjects undergoing upper endoscopic surveillance for FAP. Systematic biopsy specimens of FGPs, normal-appearance fundic mucosa and antral mucosa for *H. pylori* were obtained. Multivariable analysis assessed the association of demographic or endoscopic factors with the presence of FGP or FGP dysplasia.

FGPs were detected in 88% of subjects and were dysplastic in 41% (38% low-grade, 3% high-grade). *H. pylori* infection was rare in subjects without FGPs. In the multivariable analysis, larger FGP size (odds ratio/OR – 4), higher stage of duodenal polyposis (OR – 2.3), and antral gastritis (OR – 11.2) were associated with FGP dysplasia. Exposure to acid suppressive medication was associated with a marked decrease in dysplastic FGPs (OR – 0.14).

It was concluded that the majority of FAP patients have FGPs and nearly half will have dysplastic FGPs. There is an inverse relationship between *H. pylori* and FGPs. FGP dysplasia is associated with larger polyp size, increased severity of duodenal polyposis and antral gastritis. Acid suppressive therapy use appears protective against dysplasia in FGPs. (Bianchi L, Burke C, Bennett A, et al. “Fundic Gland Polyp Dysplasia is Common in Familial Adenomatous Polyps.” *Clinical Gastroenterology and Hepatology*, 2008; Vol. 6, 180-185.)

**Non-Polypoid Colorectal Neoplasms**

Data are limited on the significance of nonpolypoid colorectal neoplasm (NP-CRN) to determine the prevalence of NP-CRNs in a veteran hospital population and to characterize their association with colorectal cancer, a cross-sectional study was carried out with 1,819 patients undergoing elective colonoscopy from

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**Correction**

On page 33 in the February issue of *Practical Gastroenterology* in the article “Colorectal Screening in the Geriatric Population,” Gross, et al Reference number 75 is cited as finding that 90% of all deaths in a cohort of elderly patients with CRC were attributable to CHF. That proportion should be 9%.
July, 2003 to June, 2004. The endoscopic appearance, location, size, histology and depth of invasion of neoplasms were evaluated.

The overall prevalence of these neoplasms was 9.35%. The prevalence in the subpopulation for screening, surveillance and symptoms was 5.84%, 15.44% and 6.01%, respectively. The overall prevalence with in situ or submucosal invasion of carcinoma was 0.82%. In the screening population, the prevalence was 0.32%. Overall NP-CRNs were more likely to contain carcinoma (odds ratio 9.78), than polypoid lesions, irrespective of the size. The positive size/association/adjusted association of NP-CRNs with in situ or submucosal invasive carcinoma was also observed in subpopulations for screening (OR 2.01) and surveillance (OR 63.7).

The depressed type had the highest risk (33%), not polypoid, colorectal neoplasms containing carcinoma were smaller in diameter as compared with the polypoid ones. The procedure times did not change appreciably as compared with historical controls.

It was concluded that in this group of veteran patients, NP-CRNs were relatively common lesions diagnosed during routine colonoscopy and had a greater association with carcinoma, compared with polypoid neoplasms, irrespective of size. (Soetikno R, Kaltenbach T, Rouse R, et al. “Prevalence of Nonpolypoid (Flat and Depressed) Colorectal Neoplasms in Asymptomatic and Symptomatic Adults.” JAMA, 2008; Vol. 299, No. 9, 1027-1035.)

Narrow-Band Imaging Colonoscopy and Polyp Detection and Identification

To determine the detection rate of additional polyps by NBI after removal of polyps visualized by standard white light colonoscopy (WLC) and to correlate the surface mucosal and vascular patterns with polyp histologic diagnosis, a prospective pilot feasibility study was carried out among subjects referred for screening colonoscopy.

Colonic segments were sequentially examined initially with WLC, and NBI was calculated with removal of the polyps, followed by reexamination of the same segment with NBI. Additional polyps seen with NBI were photographed for their surface patterns and then removed. The total number of polyps visualized by WLC and NBI were calculated and the surface patterns were then correlated with polyp histologic features.

Forty patients were enrolled, all men, 32 white. A total of 72 polyps were detected by WLC (43 tubular adenoma, 28 hyperplastic polyps), whereas NBI detected an additional 51 polyps, of which 29 were tubular adenomas and 22 were hyperplastic. Five different surface/vascular patterns were observed: Fine capillary network with absent mucosal pattern, circular pattern with dots, round/oval pattern, tubular pattern and gyrus pattern. The sensitivity/specificity and overall accuracy of the first two patterns for hyperplastic polyps were 86%, 96% and 92%, respectively and of the latter three patterns for tubular adenomas were 96%, 86% and 92%, respectively.

This pilot study demonstrated the feasibility of polyp detection and histologic correlation with NBI, but required confirmation in future randomized control trials. (Rastogi A, Bansal A, Wani S, et al. “Narrow-Band Imaging Colonoscopy—A Pilot Feasibility Study for the Detection of Polyps and Correlation of Surface Patterns with Polyp Histologic Diagnosis.” Gastrointestinal Endoscopy, 2008; Vol. 67, 280-286.)

EUS in Suspected Choledocholithiasis

To more precisely estimate the diagnostic accuracy of EUS in suspected choledocholithiasis, proposal of a less invasive means of diagnosing that entity to decrease the need for ERCP with its associated risk, MEDLINE and EMBASE databases were used to identify prospective cohort studies in which the results of EUS were compared with the results of an acceptable criterion standard, including ERCP, intraoperative cholangiography, or surgical exploration. Two independent reviewers extracted standardized data and assessed trial quality.
A random effects model was used to estimate the sensitivity, specificity, likelihood and diagnostic odds ratio (DOR) and a summary receiver operating characteristic curve was constructed. All three defined potential sources of heterogeneity were explored by subgroup analysis and meta-regression.

A total of 2,673 patients with suspected choledocholithiasis were reported in 27 studies that satisfied the inclusion criteria. EUS had a high overall pooled sensitivity of 0.94, a specificity of 0.95 and an area under the curve of 0.98. Three variables appeared to yield a higher DOR, a higher disease prevalence and adequate time interval between index tests and criterion standards, and the presence of verification by it.

It was concluded that EUS is a noninvasive test with excellent overall sensitivity and specificity for diagnosing choledocholithiasis. It was concluded that it therefore should be used to select patients for a therapeutic ERCP to minimize the risk of complications associated with unnecessary diagnostic ERCP. (Ctse F, Liu L, Barkun A, et al. “EUS: A Meta-Analysis of Test Performance in Suspected Choledocholithiasis.” Gastrointestinal Endoscopy, 2008; Vol. 67, 235-244.)

Optimal Band Imaging System in Early Gastric Cancer

The endoscopic diagnosis of depressed-type early gastric cancers is difficult because they manifested subtle changes of color and shape. The newly developed, optimal band imaging (OBI system) can reconstruct the best spectral images derived from ordinary endoscopic images and enhances the mucosal surface without the use of dyes and is based on narrowing the band width of conventional images arithmetically by using spectral estimation technology.

A prospective study to evaluate the usefulness of the OBI system for identifying the demarcation line of depressed type early gastric cancers was carried out in 27 cases with depressed type early gastric cancer. Demarcation of the depressed type early gastric cancer was easily identified by optimal band images without magnification in 26 of 27 cases (96%), because distinct demarcation was observed endoscopically between the reddish images of the cancerous lesion and the yellowish images of the surrounding, noncancerous area.

With forty-fold magnification of optimal band images, the demarcation was also clearly recognized in all cases.

In this small sample size, it was identified that the new contrasting images of the OBI system can delineate the depressed type early gastric cancer more easily than conventional endoscopy. (Osawa H, Yoshizawa M, Yamamoto H, et al. “Optimal Band Imaging System Can Facilitate Detection of Changes in Depressed-type Early Gastric Cancer.” Gastrointestinal Endoscopy, 2008; Vol. 67, 226-234.)

Argon Plasma Coagulation in Treatment of Gastric Vascular Ectasia

GVE is an uncommon etiology of GI bleeding, affecting patients with cirrhosis and a variety of chronic diseases. In order to compare the clinical and endoscopic patient characteristics and responses to treatment by Argon Plasma Coagulation (APC) of bleeding GVE between patients with cirrhosis and noncirrhotic patients, a retrospective study of consecutive patients between January 2001 and December 2005, including thirty patients treated with APC for bleeding GVE was carried out and clinical and endoscopic features of APC treatment success was compared between patients with cirrhosis (Group 1) and noncirrhotic patients (Group 2).

Endoscopic treatment efficacy was assessed on the recurrence of symptoms after APC. Seventeen patients were cirrhotic and 13 had no cirrhosis. Cirrhotic patients presented more frequently with overt bleeding (65% vs. 15%) and noncirrhotic patients with occult bleeding with iron deficiency anemia (35% vs. 85%). Endoscopy in noncirrhotic patients revealed more frequently a “watermelon” appearance (23.5% vs. 76.9%). Endoscopic treatment by APC was successful in 83.3% of patients. Patients from Group 2 required significantly more APC sessions to achieve a complete treatment (2.18 vs. 3.77).
It was concluded that APC treatment of bleeding GVE was efficient and safe in cirrhotic and non-cirrhotic patients in more than 80% of cases. Non-cirrhotic patients required significantly more APC sessions to achieve a complete treatment and endoscopic watermelon appearance and the use of antiplatelet drugs was associated with failure of APC. (LeCleir ES, Ben-Soussan E, Antonietti M, et al. “Bleeding Gastrovascular Ectasia Treated by Argon Plasma Coagulation: A Comparison Between Patients With and Without Cirrhosis.” Gastrointestinal Endoscopy, 2008; Vol. 67, 219-225.)

Narrow Band Imaging and Non-Neoplastic Gastric Pathology

In order to test the feasibility of Narrow Band Imaging (NBI), to predict gastric histologic diagnosis, a pilot feasibility study was carried out. Forty-seven patients undergoing upper endoscopy for various indications were prospectively enrolled. The gastric body and antrum were systematically examined by NBI before targeted biopsies. Images were graded according to the mucosal ridge/villous and circular and vascular patterns, and correlated with histologic findings in a blinded manner.

The final histologic diagnosis was based on this updated Sydney classification system.

Twenty-five patients (53.1%) had normal biopsy specimens, 13 (27.6%) had non-\textit{Helicobacter pylori} gastritis. Four (8.5%) had \textit{H. pylori} gastritis and five (10.6%) had intestinal metaplasia. The sensitivity, specificity and positive predictive value of a regular mucosal and vascular pattern for the diagnosis of normal mucosa/mild gastritis were 89%, 78% and 94%, respectively.

The sensitivity and specificity in an irregular pattern with decreased density of vessels for the diagnosis of \textit{H. pylori} was 75% and 88%, and that of the ridge/villous pattern for the diagnosis of intestinal metaplasia were 80% and 100%, respectively.

In this small study, it was concluded that NBI may help predict in vivo histologic diagnosis of gastric pathologic conditions with a “good” degree of accuracy. Further larger studies are required. (Bansal A, UluSarac O, Mathur S, Sharma P. “Correlation Between Narrow Band Imaging and Nonneoplastic Gastric Pathology: A Pilot Feasibility Trial.” Gastrointestinal Endoscopy, 2008; Vol. 67, 210-216.)

Certolizumab in Crohn’s Disease

Certolizumab pegol is a pegylated humanized fab fragment that binds tumor necrosis Factor a. In a randomized, double-blind, placebo-controlled trial, the efficacy of CP in 662 adults with moderate to severe Crohn’s disease was evaluated. Patients were stratified according to baseline levels of C-reactive protein (CRP) and were randomly assigned to receive either 400mg of CP or placebo subcutaneously at week zero, 2 and 4, and then every four weeks.

Primary end points were the induction of a response at week 6 and response at both week six and 26.

Among patients with a baseline CRP of at least 10 mg/liter, 37% of patients in the CP group had a response at week 6, as compared with 26 in the placebo group. At both week six and 26, corresponding values were 225 and 125, respectively. In the overall population, response rates at week six were 35% in the CP group and 27% in the placebo group. At both week six and 26, the response rates were 23% and 16%, respectively.

At week six and 26, the rates of remission in the two groups did not differ significantly. Serious adverse events were reported in 10% of the patients in the CP group and 7% of those in the placebo group. Serious infections were reported in 2% and less than 1%, respectively. In the CP group, antibodies to the drug developed in 8% of patients, and antinuclear antibodies developed in 2%.

It was concluded that in patients with moderate to severe Crohn’s disease, induction of maintenance therapy with CP was associated with a moderate improvement in response rates, as compared with placebo, but with no significant improvement in remission rates. (Sandborn WJ, Feagan BG, Stoinov S, et al for the PRECISE 1 Study Investigators. “Certolizumab Pegol for the Treatment of Crohn’s Disease.” \textit{NEJM}, 2007; Vol. 357, No. 3:228–238.)

Murray H. Cohen, D.O., editor of “From the Literature” is a member of the Editorial Board of Practical Gastroenterology.
New Scoring System Helps Predict Survival in Patients with Pancreatic Neuroendocrine Tumors

Researchers Analyze 20 Years of Data from National Cancer Database to Develop Reliable Predictions for This Tumor Type

A diagnosis of pancreatic cancer can be dire, but for a rare type of cancer known as pancreatic neuroendocrine tumors (PNET), survival rates are better than might be expected. “This is a less common form of pancreatic cancer, but it’s particularly interesting because it has a favorable prognosis—much more favorable than we typically think about for pancreatic adenocarcinoma, a more common variety,” according to Karl Y. Bilimoria, MD, American College of Surgeons Research Fellow, Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL and lead author of a new study on PNETs.

In a study just released in the *Annals of Surgery*, Dr. Bilimoria and associates studied this rare yet treatable tumor in order to develop a new scoring system to predict prognosis. Such scoring systems are used to predict outcomes, guide treatment decisions, and help classify patients into different groups for enrollment in clinical trials. “The goal was to come up with a simple score that physicians could easily use as part of their armamentarium to manage PNETs,” Dr. Bilimoria said.

To develop the scoring system, the research group analyzed 20 years of data from the National Cancer Data Base (NCDB), a joint program of the American College of Surgeons Commission on Cancer and the American Cancer Society. PNETs account for about 3%-5% of pancreatic tumors, and “generally, they are much less aggressive tumors,” Dr. Bilimoria explained. Dr. Bilimoria and his colleagues used NCDB data to help determine which factors affect survival in patients with PNETs. Studying this tumor is particularly important as studies have shown a 200 percent to 300 percent increase in PNETs over the past 16 years: “the incidence is probably increasing because more people are getting CT scans more often—it’s often an incidental finding discovered on a CT scan performed for another reason,” Dr. Bilimoria explained.

The researchers reviewed data on a large population of PNET patients (nearly 4,000 patients who underwent a surgical procedure from 1985 to 2004). “The large number of patients provided us with the ability to discriminate between the more and less important prognostic factors,” Dr. Bilimoria said.

The research group developed a final scoring system that included 3 levels (1, 2, and 3) based on a summation of three predictive factors: age (<55, 55–75, or >75); tumor grade (a factor based on the aggressiveness of the tumor cells); and distant metastases (none, liver, or other). Each factor was given a score, and the three scores were summed together to create a raw score. The raw score was then translated into a “prognostic score,” which provides an estimate of the five-year survival rate and can also be used to help guide treatment decisions.

As an example, a patient under 55 years of age (0 points) with a low-grade tumor (0 points) and no metastases (1 point) would have a raw score of 0. This raw score translates into a prognostic score of 1 (on a scale of 1 to 3) which has a five-year survival of 77 percent. Conversely, a prognostic score of 3 would be associated with a 5-year survival rate of 36 percent. Is this type of survival good or bad news for patients? “For adenocarcinoma, the same patient would have a 15 to 20 percent chance of survival at five years,” Dr. Bilimoria replied. “With these tumors, even people who have distant metastases at the time of presentation can have an excellent prognosis and may be surgical candidates.”

“There are three things that this new PNET scoring system really helps us with,” Dr. Bilimoria concluded. “First, it gives patients information about their prognosis that’s reliable and is based on a broad generalizable experience, across the country. Second, it gives you an idea of which treatments to choose. If they have a very aggressive tumor, we may think about getting them into a clinical trial or using an additional form of therapy, such as chemotherapy. And finally, it helps stratify patients once enrolled in a clinical trial.”

In addition to Dr. Bilimoria, contributing authors include Mark S. Talamonti, MD, FACS (Northwestern University); James S. Tomlinson, MD (Evanston Northwestern Healthcare); Andrew K. Stewart, MA (American College of Surgeons Commission on Cancer); David P. Winchester, MD, FACS (American Col-
Research Foundation for Tick-Borne Diseases to Fund Studies of Neurological and Immunological Mechanisms in Lyme Disease

The National Research Fund for Tick-Borne Diseases, Inc., the nation’s only non-profit organization dedicated primarily to funding scientific research in the rapidly expanding field of tick-borne infections, has announced the award of four grants totaling $344,000 for basic and translational research in Lyme disease. The two largest projects will focus on the pathogenesis of the illness. “Our goal this year was to fund research with maximum translational value to patients,” said Carl Brenner of the NRFTD’s Research Board. “Special emphasis was placed on proposals that showed particular promise for accelerating the transfer of findings to clinical application.”

Grant winners were selected following a rigorous peer-review process by the NRFTD’s distinguished Scientific Advisory Board using guidelines akin to those established by the National Institutes of Health.

Leo J. Shea, III, Ph.D., Chairman of the NRFTD Board of Directors said, “We take pride in knowing that our organization has funded more research grants at prestigious scientific institutions than any other non-government organization in the field of Lyme and other tick-borne diseases. The world-wide scientific community and our supporters have recognized the NRFTD’s unparalleled contributions to the field of scientific research and the goal of finding a cure for these dreaded diseases.”

Dr. Mark Wooten of the University of Toledo in Ohio has been awarded a two year NRFTD grant to examine the interactions between Borrelia burgdorferi, the causative agent of Lyme disease, and mouse skin cells. Dr. Wooten’s laboratory has developed a technique to directly assess these interactions in vivo. Because the B. burgdorferi bacterium is adapted to specific host organisms, studies performed in “test tubes” do not accurately reflect the true nature of this pathogen’s interplay with host immune cells. The studies will use novel fluorescent mouse strains, fluorescent bacteria and powerful microscopic techniques to visualize how B. burgdorferi interacts with immunological cells directly within the skin tissues of living mice and in real time. This innovative approach should help identify the critical events that allow the bacteria to escape immune clearance, thus providing a potential target for curative treatments.

Among the most devastating manifestations of Lyme disease are its neurologic complications. When invading the central nervous system (CNS), B. burgdorferi must first cross the blood-brain barrier, a specialized group of capillaries that act as the body’s first line of defense against CNS invasion. The barrier is comprised of specialized blood vessel cells called “brain microvascular endothelial cells,” or BMECs. Dr. Dennis Grab of Johns Hopkins University in Maryland has been awarded an NRFTD grant to study the mechanisms by which the pathogen evades these defenses. Dr. Grab and colleagues have evidence that B. burgdorferi causes BMECs to release enzymes that break down the connections holding the endothelial cells together, thus allowing the blood-brain barrier to be breached. This grant will allow Dr. Grab to discover which enzymes are released and the role they play in helping the bacterium cross capillaries and enter the brain. Armed with this knowledge, researchers may then be able to design therapies that prevent CNS invasion by the Lyme bacterium, thus significantly reducing the morbidity associated with Lyme disease.

Also receiving an NRFTD grant award is Dr. Linden Hu of Tufts-New England Medical Center, who

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will study the way *B. burgdorferi* responds and adapts to challenges posed by its different host environments. In nature, the Lyme organism is transmitted primarily between ticks and small mammals, and over millions of years has evolved to survive successfully in both. However, the mechanisms by which *B. burgdorferi* recognizes its environment and prepares for transition between the two types of hosts have not been well understood. Although it is known that the microbe shifts its outer surface proteins in response to changes in its environment, it has not been clear what signals the organism uses to trigger this change in protein expression. Dr. Hu has identified specific host hormones that appear to have a key role in this process, and will perform studies to elucidate the precise mechanisms that enable it. Understanding the elements critical to host adaptation may lead to new strategies for disrupting the ability of the organism to survive in its natural hosts, thus reducing transmission to humans.

NRFTD has funded an additional project focused on potentially reducing *B. burgdorferi* infection in the wild. There are several types of animals, including different rodents, shrews, and birds, that are reservoirs for *B. burgdorferi*. Dr. Alan Barbour of the University of California at Irvine has been awarded a grant by NRFTD to develop techniques for precisely identifying the sources of tick infection with *B. burgdorferi* in nature. Dr. Barbour is presently compiling a database of proteins associated with specific host species, and the NRFTD grant will help him determine the most informative and sensitive targets for further development of specific assays. Researchers will then be able to detect blood components in the tick and determine where they came from—that is, identify what animals a tick fed on months earlier. Once this is accomplished, disease prevention efforts that focus on natural reservoirs of infection can be initiated.

In addition to providing funds for these four projects, NRFTD also donated $3000 in support of the 2008 Gordon Conference on the Biology of Spirochetes, held in Venice, California on January 20–25, 2008. The Biology of Spirochetes conferences, which are held every two years, bring together international scientists from diverse research disciplines to exchange information, present findings and foster future collaborations in the study of spirochetal bacteria, which include the causative agents of Lyme disease and relapsing fever. Special emphasis is placed on new techniques for genetic manipulation, which aid in studies of the physiology, structure, pathogenesis and immunobiology of these microbes. NRFTD funds were used to support the attendance of several conference participants from remote locales.

The NRFTD was founded in 1999 to address the complex and critical research questions raised by thou-

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sands of patients afflicted with emerging tick-borne diseases, including Lyme disease, relapsing fever, anaplasmosis, babesiosis, and ehrlichiosis. The need for answers has grown markedly as Lyme disease continues to spread throughout the country and as other tick-borne infections have been recognized as public health threats.

For more information about the NRFTD, or to make a tax-deductible donation, please visit www.nrftd.org.

New Blood Marker May Predict Prostate Cancer Spread

Information Could Lead to More Accurate Prediction of Cancer Metastasis Thereby Improving Patient Management

Researchers report finding a new blood biomarker that enables close to 98 percent accuracy in predicting the spread of prostate cancer to regional lymph nodes. Their study is published in the March 1 issue of *Clinical Cancer Research*.

When cancer spreads beyond a solid tumor, it often does so at a microscopic level that typically cannot be identified by conventional imaging methods such as CT scans. The new blood test measures levels of endoglin, a plasma biomarker that has been previously shown to predict the spread of colon and breast cancer. In this study, researchers concluded for the first time that endoglin could help predict whether a patient’s prostate cancer would spread beyond the solid tumor site into their lymph nodes.

Shahrokh F. Shariat, study author and chief urology resident, University of Texas Southwestern Medical Center and his colleagues observed 425 patients who had undergone surgery to remove both their prostates and associated pelvic lymph nodes. Researchers measured the levels of plasma endoglin using a commercially available blood test. Higher plasma endoglin levels were associated with an increased risk of cancer spread to the lymph nodes. Each 1 ng/mL increase of plasma endoglin increased the risk for cancer spread into the lymph nodes by 17 percent.

When researchers added endoglin levels to their usual methods of prediction, the accuracy improved from 89.4 percent without endoglin to 97.8 percent. Blood levels of endoglin may allow doctors to predict the risk of cancer spread at an earlier stage and with higher accuracy than currently available methods.

“Despite strides in the management of prostate cancer, approximately 25 percent to 30 percent fail primary curative treatment such as radical prostatectomy and radiotherapy. This is often due to spread of cancer cells beyond the original tumor site. Use of plasma endoglin could help identify patients at risk for lymph nodes metastasis who should undergo pelvic lymphadenectomy. In addition, it may spare patients at low risk of lymph node metastasis the potential morbidity of an unnecessary lymphadenectomy,” Shariat said.

The authors stressed that some limitations of this study should be noted. The retrospective study, the standard lymph node sampling, and the small number of events support the need for multicenter prospective studies before the clinical use of endoglin as a marker for predicting lymph node metastasis in patients with clinically localized prostate cancer.

“Ultimately endoglin will need to be combined with three of four other markers to predict risk with greater certainty. The problem with biomarkers is that there is a tremendous variability among patients, but this moves us forward from what we were able to do with imaging and with our other commonly used methods,” Shariat said. The study was funded through a grant from the National Institutes of Health.

IFFGD is Seeking Applications for 2008 Research Grants

IFFGD is seeking applications for research grants. Grant awards of $50,000 each are available to two investigators for research related to functional gas-
trointestinal and motility disorders, and neurogastroenterology. We are seeking proposals for research that will ultimately lead to improvements in the understanding of these disorders, their pathophysiology, and the care of patients. Applicants must have completed an MD, PhD, or equivalent degree. In evaluating the merits of an application, the Selection Committee will consider its scientific merit, its significance to the field, and its feasibility. A preference will be given to clinical research, as well as basic research that is translational in nature. The deadline for submitting applications is midnight, Monday June 2, 2008. The application must be uploaded via our online submission form.

Details are on our web page at: www.giresearch.org/site/gi-research/grants.

Due date for submitting applications Monday, June 2, 2008.

New Guidelines Update Recommendations on Colorectal Cancer Screening

Strong Preference for Tests That Can Prevent Colon Cancer, Including Colonoscopy

A new guideline on colorectal screening has been released by an expert group representing a broad spectrum of health care organizations. Included are the American College of Gastroenterology (ACG), the American Society for Gastrointestinal Endoscopy (ASGE) and the American Cancer Society. The guidelines offer recommendations for various alternatives for colorectal cancer detection and states a strong preference for screenings that can prevent colorectal cancer. The ACG and ASGE are members of the U.S. Multi-Society Task Force on Colorectal Cancer and were participants in the guideline development process.

“What distinguishes these new guidelines is an emphasis on the importance and value of preventing colorectal cancer, which physicians applaud,” said Amy E. Foxx-Orenstein, D.O., FACP, president of the ACG.

Several tests are among the recommended alternatives including stool tests that detect colorectal cancer but not its precursor, colon polyps, and structural examinations of the colon by endoscopic procedures such as flexible sigmoidoscopy and colonoscopy, as well as radiological examinations by either barium enema or CT colonography, also known as “virtual colonoscopy.” The new guidelines recognize that flexible sigmoidoscopy, barium enema and CT colonography require a follow-up colonoscopy if anything suspicious is discovered.

The management of any findings from stool test, barium enema exams, CT colonography is an important part of a screening program using these tests:

• For any of the stool tests, a positive finding will require follow-up colonoscopy
• For flexible sigmoidoscopy, patients who have adenomas discovered at sigmoidoscopy should undergo colonoscopy, based on evidence suggesting that patients who have adenoma of any size in the distal colon (visible during the exam which only views part of the colon) are at increased risk for advanced neoplasia proximally (higher up in the beyond the reach of the sigmoidoscope.
• For CT colonography, the new guidelines reflect that the risk for patients whose largest polyps are smaller than 5 mm, but for polyps over 5 mm in size, a follow-up by colonoscopy is recommended.

IFFGD is Seeking Applications for 2009 Research Awards

IFFGD is seeking applications/nominations for research awards. The awards will be given to active investigators in six categories who have a record of research interest in basic mechanisms or clinical aspects of functional gastrointestinal and motility disorders, and neurogastroenterology. These awards of $7,500 each are intended to encourage the participation of clinicians and scientists in multidisciplinary efforts aimed at advancing the understanding of these basic mechanisms and clinical aspects in adults and in children. The individuals selected for awards will be recognized at IFFGD’s 8th International Symposium for Functional GI Disorders to be held in Milwaukee, WI on April 17–19, 2009. The deadline for receipt of applications is October 20, 2008.

Details are on our web page at: www.giresearch.org/site/gi-research/iffgd-research-awards/2009.

Due date for submitting applications Monday, October 20, 2008.
Acute Pancreatitis in Children

The pathophysiology of acute pancreatitis in children is poorly understood, and a paucity of large studies is available. Treatment options are even less well studied with physicians relying on correlations from the adult medical literature. This study from the Children’s Hospital of Pittsburgh evaluated the causes and outcomes of pancreatitis in young children (less than three years of age) over a 10-year period.

Children were retrospectively identified using ICD-9 coding for “acute pancreatitis” with the clinical definition including a three-fold or higher elevation of serum lipase or amylase, radiographic evidence of pancreatitis, surgical demonstration of pancreatitis, or a combination of these factors. The investigators found 87 children in this time period with a mean age of 20 months (51.7% male). The majority of children were Caucasian in ethnicity. None of the patients had an elevated serum amylase in the setting of a normal serum lipase, and either lipase or both amylase and lipase were elevated at initial diagnosis. Vomiting was the most common symptom although fever was noted in 40% of all patients. The most common association with acute pancreatitis was the presence of systemic disease, including respiratory disease, hemolytic uremic syndrome, shock, drowning, renal disease, and complications related to HIV infection or organ transplantation.

Most patients had a relatively mild course of acute pancreatitis that resolved with conservative management, including analgesic therapy, bowel rest, and intravenous fluid although eight patients had to undergo surgery which included choledochal cyst repair, annular pancreas repair, cholecystectomy, and sphincterotomy by ERCP.

The authors conclude that acute pancreatitis is a potential complication in any hospitalized child who presents with abdominal pain and vomiting. A low threshold for the evaluation of pancreatitis should be considered in any child who has these symptoms in the setting of systemic disease. Future prospective studies could evaluate for CFTR mutations in children with acute pancreatitis. (Kandula L, Lowe M. “Etiology and outcome of acute pancreatitis in infants and toddlers.” J Pediatric, 2008; Vol. 152:106-110).

Endoluminal Gastroplication Results in Children

Gastroesophageal reflux disease (GERD) is a common gastrointestinal problem in children. Although pharmacologic therapy is available, surgical intervention is necessary for recalcitrant cases. Unfortunately, fundoplication can be associated with significant postoperative complications, and other options, including endoscopic endoluminal gastroplication, should be evaluated.

This study from England evaluated 17 children (mean 12.6 years, range 6.5–15.9 years) over a three-year period that underwent endoluminal gastroplication using the EndoCinch device (Bard Endoscopic Technologies, Billerica, MA). Patients were evaluated for symptom persistence, quality of life, and medication usage during time periods consisting of six weeks prior to the procedure and one and three years after the procedure.

No major complications occurred after the procedure, and all symptoms related to minor complications resolved in 24 hours. Many symptoms, including heartburn frequency were significantly reduced after endoluminal gastroplication. Quality of life and pH probe parameters improved after endoluminal gastroplication as well. The study demonstrated that 88% of patients remained off antisecretory medication one year after endoluminal gastroplication while 56% of patients remained off such medications after three years.

This small study shows that endoluminal gastroplication is a safe procedure and appears to reduce the symptoms of pediatric GERD. Larger studies are necessary to prove the long-term safety and efficacy of this endoscopic technique. (Thomson M, Antao B, Hall S, Afzal N, Hurlstone P, Swain C, Fritscher-Ravens A. “Medium-term outcome of endoluminal gastroplication with the EndoCinch device in children.” J Pediat Gastroenterol Nutrit, 2008; Vol. 46: 172-177).