In the U.S., the incidence of esophageal adenocarcinoma has increased seven-fold during the past 30 years, which may partially be associated with a decreased frequency of *Helicobacter pylori* infection.

In the United States, the incidence of esophageal adenocarcinoma (EAC) has increased 7-fold during the past few decades, and in 2006, the incidence was 25.6 cases per million. This alarming increase is occurring at a rate far greater than that for any other cancer. We often presume that the reason for this increased rate is related to the increased prevalence of gastroesophageal reflux disease (GERD) and Barrett esophagus (BE). But epidemiologically, the frequencies of GERD and BE have increased only modestly during the past 30 years, not even close to the seven-fold increase seen for EAC. Other factors that might explain the tumor’s increased frequency include an increase in obesity (especially central obesity), a decreased frequency of *Helicobacter pylori* infection, and an increased intake of dietary nitrate. **Transition to Cancer:** The two important histological types of esophageal cancer are adenocarcinoma, which is associated with BE, and squamous cell carcinoma, which is the type that affects most of the world. The annual rate of transition from BE to EAC is decreasing. Based on the latest data, a reasonable estimate for the frequency of EAC development in BE is approximately 0.25% per year (1 in every 400 patients with BE). **Identifying BE:** BE is the condition in which any extent of metaplastic columnar epithelium (which predisposes to cancer development) replaces the stratified squamous epithelium that normally lines the distal esophagus. To identify the columnar-lined esophagus, we must be able to anatomically identify the gastroesophageal junction (GEJ), which is not an easy task. In the West, we traditionally define the GEJ as the most proximal extent of the gastric folds, but the GEJ can be a moving target during endoscopy. Not only is the anatomic identification difficult and somewhat controversial, but so is the histologic diagnosis. In the U.S., the histologic diagnosis of BE requires the presence of intestinal metaplasia, which means that goblet cells must be present in the mucosa. Other countries use different histologic parameters to diagnose BE. (Reviewer-).
Background: It is unclear how often we may miss abnormalities in the very distal terminal ileum.

Objective: To evaluate how often disease skipping the distal terminal ileum leads to negative results from ileocolonoscopy.

Methods: A search of all patients with a diagnosis of Crohn disease during 2009 at the Mayo Clinic in Rochester, Minnesota was conducted. Patients who underwent both computed tomography enterography (CTE) and colonoscopy were included. The presence of any small bowel inflammation was recorded as well as the length of terminal ileum examination at the time of endoscopy and the presence of inflammation both endoscopically and histologically.

Results: Of the 189 patients with Crohn disease, 153 (81%) had intubation of the terminal ileum at the time of colonoscopy. Of these, 67 had normal results. However, even though their ileoscopy was normal, over half of these 67 patients (36) had active small bowel disease on CTE. This disparity may be accounted for by disease skipping the distal ileum, disease involvement of the bowel wall or mesentery, or disease in the upper gastrointestinal tract.

Conclusions: A good number of patients may have disease in the small intestine that would be missed by ileocolonoscopy alone.

Reviewer's Comments: Up to 54% of patients with active small bowel of upper gut Crohn disease may have a normal ileoscopy as a result of skipping of the distal terminal ileum. Either we do not go in far enough with our scopes or there is skipping of disease lesions that are more proximal than anticipated. Involvement of the intramural portion of the bowel wall also would be missed on endoscopic exam. The authors do not suggest that radiography occur every time the patient has a colonoscopy, but it is important that to properly stage the disease, cross-sectional imaging occur during the initial workup or sometime early in the course of disease. Where available, MR enterography will be preferable for younger patients as there is no radiation exposure. Understanding disease location will help explain patient symptoms and decide on treatment strategies. For those with significant small bowel disease otherwise not seen, oral therapies may not be sufficient as there is not adequate absorption. Data regarding involvement of the upper small bowel suggest that stricturing occurs more frequently, and thus patients with what may be considered dyspeptic symptoms should be considered for obstruction or small bowel bacterial overgrowth. One of every 8 scans also revealed a condition that required further workup (pulmonary and adnexal entities). Occult extraintestinal manifestations (eg, sacroiliitis, nephrolithiasis, and thrombosis) can also be detected and would change management. This study was not perfect, but it points out that clinicians must examine the entire gastrointestinal tract for location, extent, and nature of Crohn disease irrespective of endoscopic and histologic findings in the very terminal ileum. (Reviewer-Sunanda V. Kane, MD).

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Keywords: Colonoscopy, CT Enterography, Crohn Disease, Intestine, Inflammation

Print Tag: Refer to original journal article
Herbal Remedy Found Effective vs Placebo in Mild, Moderate Ulcerative Colitis

Andrographis paniculata Extract (HMPL-004) for Active Ulcerative Colitis.
Sandborn WJ, Targan SR, et al:


Andrographis paniculata may represent a novel agent for mild to moderate ulcerative colitis.

Background: Alternative agents are needed to treat mildly to moderately active ulcerative colitis not responding to mesalamine.

Objective: To compare Andrographis paniculata extract with a placebo in patients with mild to moderate active ulcerative colitis.

Design: Multicenter, randomized, double-blind, placebo-controlled trial conducted in 52 centers in 5 countries.

Methods: Patients with a Mayo score of 4 to 10 were included. Those on steroids, immunomodulators, or biologics were excluded. A total of 224 patients were randomly assigned to oral capsules containing placebo or A. paniculata at doses of 1200 mg or 1800 mg given in 3 divided doses per day. The primary end point was clinical response at week 8. Endoscopy was done at study entry and at week 8. Other end points included clinical remission and mucosal healing.

Results/Conclusions: Overall, 52% of patients receiving the study drug had a response versus 40% of those receiving placebo. There was a dose response noted with 60% of those given the higher dose achieving response versus only 45% of those given the lower dose. For clinical remission, 34% of the 1200-mg group and 38% of the 1800-mg group achieved remission compared with 25% of those on placebo. In all, 44% of those receiving study drug achieved mucosal healing compared with 33% of those receiving placebo. This again became statistically significant for those on the higher dose versus placebo. Adverse events were similar among groups, with rash occurring in 8% of study drug patients versus only 1% of placebo patients. No patient discontinued therapy because of the rash.

Reviewer's Comments: This study represents the kind of research that combines anthropologic observations with basic science and clinical medicine. Agents that have been used for centuries to treat inflammatory conditions clearly have anti-inflammatory properties that are not toxic. Aspirin is probably the classic example of this. While mesalamine will most likely remain the first-line therapy for mild to moderate ulcerative colitis into the foreseeable future, other agents are needed to treat those not quite sick enough to merit immunosuppression. Well designed, thoughtful studies such as this one will help convince practitioners that "alternative" therapies can be safe and effective and warrant further discussion. Patients will appreciate that their health care provider now has an open mind about other therapies since this was an adequately sized, randomized, placebo-controlled trial. The strength of this kind of evidence cannot be surpassed. Whether this agent will eventually become mainstream has yet to be determined, as studies using phosphatidylcholine have essentially stalled in phase III, but the future certainly looks promising for novel agents to be tested. (Reviewer-Sunanda V. Kane, MD).

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Keywords: Ulcerative Colitis, Randomized Controlled Trial, HMPL-004

Print Tag: Refer to original journal article
Is Cyclosporin More Effective Than Infliximab for Steroid-Resistant Severe Acute UC?

_Ciclosporin Versus Infliximab in Patients With Severe Ulcerative Colitis Refractory to Intravenous Steroids: A Parallel, Open-Label Randomised Controlled Trial._

Laharie D, Bourreille A, et al:

**Lancet** 2012; 380 (December 1): 1909-1915

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Cyclosporin was no more effective than infliximab in treating patients with acute flares of ulcerative colitis who had failed IV steroid therapy.

**Background:** When patients with severe ulcerative colitis (UC) fail IV steroid therapy, the subsequent options are infliximab, cyclosporin, or colectomy. We have little information regarding whether cyclosporin or infliximab should be the next intervention.

**Objective:** To perform a multi-institutional randomized trial comparing these two agents.

**Design:** Parallel, open-label, randomized, controlled trial.

**Participants:** Adult patients (≥18 years of age) who had never received cyclosporin or infliximab and who were having an acute severe flare of UC (Lichtiger score >10) and did not respond to ≥5 days of ≥0.8 mg/kg per day IV methylprednisolone (or equivalent) were included.

**Methods:** Patients were centrally randomized to receive (1) cyclosporin (IV cyclosporin to maintain a serum level of 150 to 250 ng/mL; those who had a clinical response within 7 days were then switched to oral cyclosporin to maintain the same blood level) or (2) infliximab (one dose of 5 mg/kg; those who had a clinical response received further doses at days 14 and 42). A clinical response was defined as a fall in the Lichtiger score of at least 3 points to a score that was <10. The patients were followed for 14 weeks and then colonoscopy was repeated. The primary outcome was treatment failure at any time (lack of clinical response, subsequent relapse, increased Lichtiger score ≥3 points for ≥3 consecutive days, no steroid-free remission [defined as a Mayo score ≤2 with endoscopic subscore ≤1] at 98 days, or a severe adverse event, colectomy, or death). Secondary outcomes included clinical response rates, daily Lichtiger scores, time to clinical response, day 98 mucosal index activity score, colectomy-free survival, and safety. Assuming that use of cyclosporin would be 3.5 times as likely to avoid a treatment failure, 116 patients were needed. The trial was not blinded.

**Results:** Fifty-eight patients were randomized to cyclosporin and 57 to infliximab. The demographic features of the two groups were similar. By day 98, treatment failure had occurred in 35 cyclosporin patients and 31 infliximab patients (difference was not significant). There were no significant differences in any of the secondary outcomes.

**Conclusions:** Cyclosporin was not more effective than infliximab.

**Reviewer’s Comments:** Other than the lack of blinding (which could have been accomplished with blinded assessors), this was a methodologically well done trial. It should be remembered that the fact that no differences were seen does not mean that the two treatments are equivalent; the trial was powered for a substantial difference in efficacy, and a lesser difference in benefit has not been excluded. (Reviewer-Ronald L. Koretz, MD).

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Keywords: Steroid Resistant Flare, Infliximab, Cyclosporin

Print Tag: Refer to original journal article
Dogs May Be Able to Detect Clostridium difficile

Using a Dog’s Superior Olfactory Sensitivity to Identify Clostridium difficile in Stools and Patients: Proof of Principle Study.

Bomers MK, van Agtmael MA, et al:

BMJ 2012; December 13 (): epub ahead of print

A beagle dog can be trained to be able to detect the presence of Clostridium difficile using his olfactory sense.

**Background:** Dogs have been allegedly trained to detect various diseases such as cancer. 
**Objective:** To see if a dog could be trained to detect the presence of Clostridium difficile. 
**Design:** Prospective, blinded diagnostic challenge. 
**Participants:** A trained dog and patients with or without C diff diarrhea. 
**Methods:** Over a 2-month period, a 2-year-old male beagle dog was trained to recognize the odor of a toxigenic strain of C diff in or on various substances. The dog’s response was positive if he sat down, inconclusive if he showed excitement/took extra time without sitting down, or negative if he did not sit down. After the training period, the dog was presented with two sets of challenges. First, the dog was exposed 10 times to each of 50 positive and 50 negative stool specimens; if the same response was elicited >8 times, the test was called positive or negative. Second, on 30 different occasions, the dog was taken to 10 patient rooms, with one of those patients having C diff diarrhea. The dog did not make any direct contact with the patient but only smelled the room. The trainer was blinded. The outcome was the calculated sensitivity and specificity of the dog’s ability to sit at the appropriate time. An inconclusive result was considered to be negative in the primary analysis. 
**Results:** The dog correctly identified 50 positive stool specimens and 47 negative stool specimens (3 others inconclusive) (sensitivity 100% and specificity 94%). Twenty-five of the 30 positive patients and 265 of the 270 negative patients were also identified (sensitivity 83% and specificity 98%). 
**Conclusions:** The investigators believed that they had presented a proof of principle with regard to using canine olfaction to detect C diff. 

**Reviewer’s Comments:** Only one dog per trainer limits generalizability. We must also consider some potential trainer bias. For each of the 30 sets of rounds, the dog specifically identified 1 patient as positive, leaving us to wonder if some unconscious message was being transmitted, perhaps by the trainer, to not sit down any more times that day once the dog had identified a positive. Thus, the specificity numbers are somewhat misleading, since, if there was some bias to only identify 1 positive patient, the lowest possible specificity that could occur would be 89%. Furthermore, because of isolation policy, most of the C diff patients were housed in the same room. (Reviewer-Ronald L. Koretz, MD). 

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Keywords: clostridium difficile, olfactory detection

Print Tag: Refer to original journal article
CDC Recommendations for Screening Baby Boomers for HCV


Smith BD, Morgan RL, et al:

Ann Intern Med 2012; 157 (December 4): 817-822

Based on data-based evidence on hepatitis C virus (HCV) prevalence, natural history, treatment outcomes, and cost-effectiveness, the Centers for Disease Control and Prevention recommends one-time anti-HCV testing of individuals born from 1945 to 1965.

Background: Screening to identify hepatitis C virus (HCV)-infected individuals in the U.S. has been largely based on a history of risk factors, but this strategy has had important limitations and many infected individuals are not tested.

Objective: To develop screening recommendations to increase the identification of HCV-infected individuals and to add alcohol screening and intervention for those identified.

Methods: The Centers for Disease Control and Prevention (CDC), working with unnamed other federal agencies, health departments, and other groups, searched databases for information on HCV prevalence, natural history, treatment outcomes, cost-effectiveness, and the impact of brief alcohol screening and intervention in HCV-infected individuals. The authors studied the effect of birth cohort testing versus risk-based testing strategies, whether treatment is effective in reducing liver-related morbidity and all-cause mortality, and whether testing should be followed by alcohol intervention to limit or stop drinking in those identified.

Results: After peer review and public comment, as well as comments by unnamed hepatitis experts, the CDC strongly recommended, on the basis of “moderate quality evidence,” that adults born during 1945 to 1965 should be tested once for HCV antibodies. This cohort is expected to have a 3.25% prevalence of HCV antibodies. Further, treatment-induced achievement of a sustained virologic response (SVR) was with current therapy was associated with a reduction of both mortality and hepatocellular carcinoma (HCC). Treatment was also found to be cost-effective. The second strong recommendation based on moderate quality evidence was that HCV-infected individuals should be screened for alcohol consumption and receive counseling if indicated.

Conclusions: The CDC recommends one-time screening for HCV antibodies of all individuals born from 1945 to 1965, as well as continuing risk-based screening.

Reviewer’s Comments: Although the initial reaction of the leadership of the American Association for the Study of Liver Diseases and other organizations has been to endorse these recommendations, the response has not been uniform. In fact, the U.S Preventive Services Task Force, in its draft recommendations, has not supported age-based testing, suggesting only a moderate certainty of a small net benefit. They gave the recommendation a grade of C. Even screening of individuals known to be at high risk for hepatitis C (eg, injection drug users) was given a grade of B. As in 2004 when this Task Force did not recommend for or against screening for hepatitis C in asymptomatic individuals at high risk, a recommendation that sparked controversy and may have negatively impacted screening, their current assessment should, in my view, be ignored. Nonetheless, if the CDC recommendation is followed, 70 to 80 million baby boomers will need to be screened. This would be undertaken by primary care physicians who might soon be a little overwhelmed when an additional 30 million individuals are eligible for care under the Affordable Care Act. Did the CDC consider this or the difficulty of finding specialists able to take on the treatment of at least 1 million additional patients identified during screening? (Reviewer-Raymond S. Koff, MD).

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Keywords: Anti-HCV Testing, Birth Age Screening, CDC Recommendations, Alcohol Screening

Print Tag: Refer to original journal article
AIH – Is There a Risk of Relapse if Treatment Is Withdrawn?

Relapse Is Almost Universal After Withdrawal of Immunosuppressive Medication in Patients With Autoimmune Hepatitis in Remission.

van Gerven NMF, Verwer BJ, et al:

J Hepatology 2013; 58 (January): 141-147

Among patients with treatment-induced remission of autoimmune hepatitis lasting for at least 2 years, tapering or discontinuing therapy is highly likely to lead to relapse; hence enthusiasm for withdrawing treatment should be dampened.

**Background:** Immunosuppressive treatment-induced remission of autoimmune hepatitis (AIH) has been variably defined as normalization of serum alanine-aminotransferase levels (ALT), bilirubin, gamma globulin or IgG levels and improvement in liver histology to normal or mild portal hepatitis or in patients with cirrhosis, to no or minimal inflammatory activity. Histologic improvement lags behind biochemical improvement, and relapse occurs in a substantial number of patients on withdrawal of treatment within 2 years after remission is achieved.

**Objective:** To determine the risk of relapse upon drug withdrawal or drug taper in AIH patients in remission for at least 2 years.

**Design/Participants:** In this retrospective, multicenter study from the Netherlands, patients with AIH treated with prednisone, azathioprine, or the combination who achieved remission were followed.

**Methods:** Remission was defined as the absence of symptoms, normal ALT levels, and, when available, normal IgG levels, as well as the absence of inflammation, interface hepatitis, fibrosis, or cirrhosis. The frequency of relapse, defined as a three-fold increase or greater in serum ALT and/or an increase of IgG level to >2 g/dL, was determined. Loss of remission was defined as an elevated ALT level on 2 or more occasions at least 4 weeks apart, with or without symptoms, requiring re-starting immunosuppressive drug therapy.

**Results:** The median follow-up was 8.8 years. Among 131 patients in whom treatment had been discontinued or tapered after remission lasting for at least 2 years, 47% relapsed at 5 years, and 42% had loss of remission at 5 years. Approximately half had discontinued treatment, and in half, treatment was being tapered when relapse occurred. Re-treatment was necessary in 59% of patients 1 year after withdrawal, 73% at 2 years, 81% at 3 years, and 89% at 5 years. Factors associated with relapse included combination therapy versus monotherapy, age <45 years at the time of drug withdrawal, and the presence of another autoimmune disease. Among 32 relapsed patients in whom re-treatment resulted in remission, relapse reoccurred on drug tapering in all.

**Conclusions:** Relapse and loss of remission on discontinuation or tapering of treatment in AIH occurs in most patients in remission for at least 2 years and will require re-treatment. Enthusiasm for discontinuing or tapering treatment, even after prolonged remission, should be dampened.

**Reviewer’s Comments:** Several limitations of this retrospective study are apparent. Initial treatment regimens and protocols for tapering and treatment discontinuation were not standardized, and histologically confirmed remission was obtained in a minor proportion of patients. Nonetheless, these observations suggest that despite remission for at least a 2-year period, there is a high risk of relapse on drug tapering and withdrawal regardless of the duration of remission. Enthusiasm for discontinuing or tapering treatment, even after prolonged remission, should be dampened in this chronic disease in which few are cured. (Reviewer-Raymond S. Koff, MD).

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Keywords: Immunosuppressive Medication Withdrawal, Relapse, Remission, Re-Treatment

Print Tag: Refer to original journal article
Chemotherapy-Induced Reactivation and Exacerbation of Chronic Hepatitis C

Acute Exacerbation and Reactivation of Chronic Hepatitis C Virus Infection in Cancer Patients.
Mahale P, Kontoyiannis DP, et al:

J Hepatol 2012; 57 (December): 1177-1185

In this study, viral reactivations occurred in 36% and generally mild acute exacerbations were seen in 11% of HCV RNA-positive cancer patients after chemotherapy or immunosuppressive therapy.

Background: Reactivation of hepatitis B virus (HBV) infection associated with cancer chemotherapy, bone marrow transplantation, and treatment with immunosuppressive drugs such as rituximab is sufficiently common that prophylaxis with HBV antiviral drugs is now the standard of care. Reactivation of hepatitis C virus (HCV) also has been reported, but its frequency and severity are not well described.

Objective: To assess the prevalence and characteristics of acute exacerbations and reactivation in HCV-infected cancer patients.

Methods: In this retrospective study from the M.D. Anderson Cancer Center, cancer patients with HCV antibodies who were treated with chemotherapy or immunosuppressive drugs over a 2-year period were analyzed using a standard case report form including demographic, clinical, and laboratory infection. Alanine aminotransferase (ALT) levels were determined before, during, and after chemotherapy. A greater than 3-fold increase in serum level of ALT in the absence of specified competing causes defined exacerbation. HCV RNA levels before and after chemotherapy were assessed when available, and increases ≥1 log_{10} IU/mL defined reactivation.

Results: A total of 308 patients with HCV antibodies at baseline also were HCV RNA positive, but only 22 of these also had post-chemotherapy viral loads measured. Viral reactivation occurred in 8 of these 22 patients (36%). The median increase in HCV RNA was 1.45 log_{10} IU/mL. Acute exacerbations occurred in 67% of episodes of HCV reactivation, and 80% were associated with use of rituximab. Acute exacerbations were found in 33 of the 308 patients (11%); in 42% of these, the ALT elevations exceeded the baseline by 10-fold or greater. Multiple logistic regression analysis revealed that hematological malignancies, mostly diffuse large B-cell lymphomas, and use of rituximab were significantly associated with acute exacerbations. Corticosteroid use was similar in those with and without exacerbations. Among patients with acute exacerbations, discontinuation of chemotherapy because of liver dysfunction was significantly more common at 45% than in patients without exacerbations (11%).

Conclusions: HCV reactivation and acute exacerbations may occur following chemotherapy and the use of rituximab in cancer patients. Although the course is often indolent, exacerbations often led to discontinuation of chemotherapy.

Reviewer's Comments: Although acute exacerbations of chronic HCV associated with chemotherapy and immunosuppressive drugs, as described here, were less severe clinically than those reported in HBV reactivation, they led to treatment discontinuation in nearly half of affected cancer patients. The true frequency of reactivation remains uncertain since only a minority of patients had viral load tests before and after chemotherapy. A larger, prospective study, with multiple HCV RNA and ALT measurements before, during, and after chemotherapy may better define the frequency of HCV reactivation. Until then, it would seem reasonable for oncologists to include HCV testing in addition to HBV, prior to beginning oncologic treatment. (Reviewer-Raymond S. Koff, MD).

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Keywords: Cancer, Chemotherapy, Immunosuppressive Drugs, HCV Reactivation, Exacerbation

Print Tag: Refer to original journal article
Aspirin Use Associated With Decreased Risks of HCC and Liver Death

Nonsteroidal Anti-Inflammatory Drug Use, Chronic Liver Disease, and Hepatocellular Carcinoma.

Sahasrabuddhe VV, Gunja MZ, et al:

J Natl Cancer Inst 2012; 104 (December 5): 1808-1814

Aspirin use is associated with a decreased risk of developing hepatocellular carcinoma and dying of chronic liver disease.

Background: Aspirin use has been strongly associated with a reduction in the development of colorectal cancer. The effect of aspirin on liver disease is less well studied.

Objective: To determine if there is an association between the use of nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin in particular, and a reduced risk of hepatocellular carcinoma (HCC) or death from chronic liver disease (CLD).

Design: Prospective cohort study.

Participants: Individuals enrolled in the National Institutes of Health-American Association of Retired Persons Diet and Health Study who had completed questionnaires in 1995 and 1996 providing demographic, dietary, clinical, and lifestyle information and did not have histories of, or current, cancer and were not dietary outliers were included.

Methods: 300,504 subjects were grouped into those who were aspirin and/or other NSAID users (separated into subgroups of those who took one agent, the other agent, or both) and those who were not taking these agents. Causes of mortality until December 31, 2008, were identified with death certificates; incident HCCs were identified via searches of several cancer registries. Hazard ratios were calculated for both outcomes, comparing various combinations of users to the nonuser control group after correcting for demographic differences.

Results: Users of aspirin, other NSAIDs, or both were significantly less likely to die from any chronic liver disease. On the other hand, an association between a decreased incidence of HCC was only seen for those who used aspirin. The various hazard ratios ranged between 0.50 and 0.74, suggesting a 26% to 50% reduction in incidences.

Conclusions: The use of aspirin and other NSAIDs was associated with a reduction in the subsequent mortality from chronic liver disease; the use of aspirin (but not other NSAIDs) was also associated with a reduction in the subsequent incidence of HCC.

Reviewer's Comments: With the single exception of when the investigators described aspirin as having a "protective effect," the term "association" was clearly used; it must be appreciated that observational studies can only demonstrate association, and that association cannot prove causation. Another confounding factor was that it was not established how many of the 300,000 subjects initially had known liver disease and, of that number, how many had been advised not to use aspirin or other NSAIDs because of the risk of bleeding. The initial questionnaires did collect information about hypertension and cardiovascular disease, so it must also follow that a future assessment of liver disease outcomes was not the primary reason for undertaking the prospective study in 1995 and 1996. Thus, this exercise only represents one of what are likely to be a number of dips into this data pool, which will provide ample opportunity for type I errors. (Reviewer-Ronald L. Koretz, MD).

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Keywords: Aspirin, Nonsteroidal Anti-Inflammatory Drugs, Chronic Liver Disease, Hepatocellular Carcinoma

Print Tag: Refer to original journal article
Supplemental Parenteral Nutrition May or May Not Benefit Patients in the ICU

Optimisation of Energy Provision With Supplemental Parenteral Nutrition in Critically Ill Patients: A Randomised Controlled Clinical Trial.
Heidegger CP, Berger MM, et al:
Lancet 2013; 381 (February 2): 385-393

Supplemental parenteral nutrition appears to improve infectious outcomes in a trial that had multiple risks of bias.

**Background:** A previous large, well-done randomized trial in critically ill patients suggested that, when enteral nutrition (EN) is not able to provide the required number of calories, the use of supplemental parenteral nutrition (SPN) resulted in net harm. Swiss investigators at 2 centers address this question in a somewhat different patient population.

**Objective:** To assess the efficacy of SPN in patients in the intensive care unit (ICU).

**Design:** Randomized trial.

**Participants:** Patients in the ICU in whom EN was not able to provide at least 60% of predicted caloric needs after 3 days and who were expected to be in the ICU for at least another 5 days were included.

**Methods:** Patients who were believed to require artificial nutrition (EN or PN) were begun on EN shortly after admission. If they were not receiving ≥60% of their predicted caloric needs by day 3, they were randomized (computer generated in blocks of 4) into one of two arms—SPN (to receive the required amount of nutrients intravenously) or continued EN. The primary outcome was infections occurring from days 9 to 28. Secondary outcomes included antibiotic days, mortality, duration of ventilation and ICU/hospital length of stay, and various lab tests. Intention-to-treat analyses were done with the last value being brought forward. A sample size calculation indicated that 148 patients would be needed in each arm.

**Results:** A total of 153 patients were randomized into the SPN arm and 152 into the EN only arm. Between days 9 and 28, infections occurred in 27% of the SPN arm and 38% of the EN arms (P =0.04). The SPN group was on antibiotics for fewer days. No significant differences were seen in any other outcomes assessed.

**Conclusions:** SPN was beneficial in a patient population that was truly in need of artificial nutrition. These data differed from the previously reported trial because these patients had a better documented need for artificial nutrition and because a different PN solution was employed.

**Reviewer’s Comments:** There were methodologic problems that probably caused an overestimation of benefit. The trial was not blinded and the block design meant that at least every fourth subject did not have concealed allocation. The lack of blinding also may have allowed bias to neglect or overcall alleged infections. There were more dropouts in the SPN arm. Most importantly, infections that occurred in days 4 to 8 were not counted as part of the primary outcome, even though they would have occurred at a time when the PN was being administered. While the data were not presented as numbers of infected patients, there were more infections in the SPN arm (52) than in the EN arm (43) in days 4 to 8. The primary outcome provided in the trial registry included all infections in the first 90 days (subsequently revised to the first 30 days). (Reviewer-Ronald L. Koretz, MD).

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Keywords: Parenteral Nutrition, Enteral Nutrition, Critical Illness

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How Do We Lower the Risk of Recurrent Ulcer Bleeding in HPNBU Patients?

Gastroprotective Therapy Does Not Improve Outcomes of Patients With Helicobacter pylori-Negative Idiopathic Bleeding Ulcers.

Wong GL, Au KW, et al:

Clin Gastroenterol Hepatol 2012; 10 (October): 1124-1129

Objective: To determine the long-term clinical outcome of Helicobacter pylori-negative idiopathic bleeding ulcers (HPNBU) treated with gastroprotective agents (GPAs), such as proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RAs).

Design: Prospective 9-year cohort study of all patients with upper gastrointestinal (UGI) bleeding from 2002-2009 at the Prince of Wales Hospital in Hong Kong.

Methods: HP was ruled out with CLO tests and histological examinations of the antrum and corpus of the stomach. Exclusions included a recent history of aspirin, nonsteroidal anti-inflammatory drugs, or traditional Chinese medications. HPNBU patients were treated with 8 weeks of PPIs, while HP-positive patients received triple therapy plus a PPI for 1 week with re-endoscopy to determine healing of the ulcer. Prophylactic GPAs were left to the discretion of the attending physician. The primary end point of the study was recurrent GI bleeding and all-cause mortality in the HPNBU group.

Results: Of the 4827 patients with documented bleeding ulcers, 663 (13%) had HPNBU; 633 HP-positive treated, age- and sex-matched patients served as the control group. Pre-study characteristics noted that HPNBU patients had higher ASA scores and more UGI bleeding in the hospital. The HPNBU cohort had a significantly shorter follow-up (P <0.001) due to a higher mortality rate. Recurrent idiopathic bleeding was significantly higher in the HPNBU group versus the HP-positive treated group (43 vs 13 patients; P <0.001; HR, 2.7). Surprisingly, exposure to GPAs did not decrease rebleeding in the HPNBU group (2.7 per 100 person-years; HR, 0.7) and the rebleeding rate was not significant when compared to HPNBU patients not on GPAs. Mortality was significantly higher in the HPNBU group versus the HP-positive treated group (360 vs 172 patients). Independent risk factors for mortality included age >70 years, ASA grade ≥3, and ulcer bleeding during hospitalization. HPNBU alone was a risk factor for increased bleeding. During the GPA-exposed period, the incidence rate of death was 21.8 per 100 person-years, which was significantly higher than during the nonexposed period (13.8 per 100 person-years; P <0.001).

Conclusions: GPAs do not lower the risk of recurrent ulcer bleeding in patients with HP-negative idiopathic bleeding ulcers.

Reviewer’s Comments: The major weakness of this study was the unknown doses and regimens of PPIs and H2RAs and the fact that sicker individuals noted in the HPNBU group may require more antisecretory agents. A future study should maximize and standardize the PPI regimen for all HPNBU patients although in sick patients with comorbid diseases, acid may not play as significant a role in developing and treating ulcer disease. (Reviewer-Roy K.H. Wong, MD, FACP, FACG, AGAF).

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Keywords: Helicobacter pylori, Ulcer, Bleeding, Idiopathic, Gastroprotective Agents

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Increased Risk of Pancreatitis in Patients with Celiac Disease

Patients With Celiac Disease Have an Increased Risk for Pancreatitis.
Sadr-Azodi O, Sanders DS, et al:

Clin Gastroenterol Hepatol 2012; 10 (October): 1136-1142

Patients with celiac disease have a three-fold increased risk of developing pancreatitis, especially when diagnosed before the age of 40 years.

Objective: To determine the risk of pancreatitis (or subtype) in patients with proven celiac disease (CD).

Methods: From 28 Swedish pathology departments, biopsies dating from 1969 to 2008 identified 28,908 patients with a biopsy diagnosis of CD, which was defined as villous atrophy (VA) equivalent to Marsh grade 3. Each patient was matched with 5 persons in the normal population for age, sex, calendar year, and county of residence. A random chart sample of CD patients noted that 88% had positive serologies prior to intestinal biopsies. Two other cohorts were examined: individuals having small intestinal biopsy but no VA (inflammation, Marsh 12; n=13,306) and individuals with positive immunoglobulin (Ig)A/IgG gliadin or endomysium or tissue transglutaminase antibodies (n=3719; most were positive for IgA gliadin) but had normal mucosa. Pancreatitis and use of pancreatic enzymes was identified via diagnostic codes in the Swedish Patient Register and the Swedish Prescribed Drug Register. Pancreatitis was defined as patients with clinical pancreatitis plus those who received pancreatic enzymes. Pancreatitis subtypes included gallstone and non-gallstone etiologies, while smoking, diabetes and chronic alcohol use was identified.

Results: Of the 28,908 CD patients, 406 (1.2%) were identified with pancreatitis irrespective of etiology (62% females; median age, 30 years). This pancreatitis rate was 2.92 times the expected rate of n=139 (HR, 2.85; 95% CI, 2.53 to 3.21). When identifying subtypes of pancreatitis, all subtypes in patients who had CD carried an increased risk of pancreatitis: non–gallstone-related acute pancreatitis: 133 patients were identified, with an expected number of events (n) of 72 (HR, 1.86; 95% CI, 1.52 to 2.26), with the highest HR in patients diagnosed before age 40 years; gallstone-related acute pancreatitis: 30 patients identified with an expected number of events of 19 (HR, 1.59; 95% CI, 1.06 to 2.40). Interestingly, men were more likely to develop gallstone-related pancreatitis with a 2.21-fold increased risk (95% CI, 1.09 to 4.45). With regard to chronic pancreatitis, there were 49 observed cases with an expected n=15 (HR, 3.33; 95% CI, 2.33 to 4.76). Patients with CD had a 5.34-fold increased risk of receiving pancreatic enzymes (21 observed cases; expected n=4). There was also an increased risk of developing pancreatitis prior to the histological diagnosis of CD (HR, 2.59; 95% CI, 2.19 to 3.07). Interestingly, patients with CD had a lower risk of pancreatitis when compared to patients with inflammation only (HR, 0.73) and those with only positive serologies (HR, 0.71).

Conclusions: In celiac disease, there is a three-fold increased risk of developing pancreatitis.

Reviewer's Comments: Causes of pancreatitis related to CD may be the fact that VA is associated with pancreatic insufficiency and is reversed with a gluten-free diet. Malnutrition is known to cause acinar atrophy. Abnormal cholecystokinin release may cause pancreatitis, while duodenal and papillary inflammation may cause papillary stenosis. (Reviewer-Roy K.H. Wong, MD, FACP, FACG, AGAF).

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Keywords: Celiac Disease, Pancreatitis, Gallstone, Villous Atrophy

Print Tag: Refer to original journal article
An Analysis of Double-Balloon Enteroscopy

Changes Over Time in Indications, Diagnostic Yield, and Clinical Effects of Double-Balloon Enteroscopy.

Jeon SR, Kim J-O, et al:

Clin Gastroenterol Hepatol 2012; 10 (October): 1152-1156

In this study, the indication and outcomes for performing double-balloon enteroscopy did not change over time; however, the technique of the procedure tended to improve as there were fewer inadequate or failed procedures.

Objective: To determine changes in indications, diagnostic yield, clinical impact, and the use of double-balloon endoscopy (DBE) overtime.

Design/Participants: Single center, retrospective study of patients undergoing DBE between September 2004 and May 2011.

Methods: Data from September 2004 to August 2006; (stage 1; approximately a 2-year period; 117 DBE, 79 patients) versus September 2006 to May 2011; (stage 2; an approximately 5-year period; 64 DBEs, 54 patients) because of a significant decrement in DBE procedures after 2006. The entire small bowel (SB) was visualized by either 1 or 2 DBE procedures. The indications for DBE included occult GI bleeding (OGIB), abnormality in other modalities, Crohn disease, symptoms/signs only, therapeutic, surveillance, and other.

Results: No significant differences in patient characteristics between the 2 stages were noted except that more abdominal CT scans per patient were performed in the second stage (53% vs 81%; P <0.001). CT scans were performed for OGIB (51.1%), signs and symptoms (33.7%), and routine checkups (5.8%). A trend toward more capsule endoscopies (CEs) was noted (29% vs 44%; P <0.069). OGIB was the most common indication (59.4%) over the entire study period (nonsignificant trend) for each stage (65.8% vs 50%; P =0.06). However, DBE for abnormalities noted in other tests increased significantly (11.4% vs 29.6%; P<0.008). GI bleeding (32%) was the major reason for prompt DBE, followed by characterization of a mass (20%), enteropathy or enteritis (16%), SB stricture or obstruction (12%), and differential diagnosis of inflammatory bowel disease (10%). A slight increase in diagnostic yield was noted (89.3% vs 93.9%), with mucosal lesions the most common finding (56% vs 53.1%; P <0.686), followed by vascular lesions. The mean number of procedures per patient was significantly higher in the first versus second stage (1.51 vs 1.12; P <0.001), with fewer patients having a combined procedure during the second period (40% vs 11%; P <0.001). During the second stage, significantly fewer failures and inadequate studies, fewer combined approaches, shorter times to deepest insertion, and the use of more clips during therapeutic interventions were noted. Conclusions: Over time, the clinical indications to perform DBE and outcomes did not change. A higher selectivity of cases for DBE resulted from new diagnostic modalities.

Reviewer's Comments: Reasons for lower DBE studies in the second stage may be related to many patients undergoing abdominal CT scans first, few patients undergoing capsule endoscopy subsequently undergoing DBE, and more second-look endoscopies to identify a bleeding source. (Reviewer-Roy K.H. Wong, MD, FACP, FACG, AGAF).

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Keywords: Double-Balloon Enteroscopy, Indication, Diagnostic Yield, Small Bowel

Print Tag: Refer to original journal article
Postmenopausal Women May Be at Risk for Ulcerative Colitis

Hormone Therapy Increases Risk of Ulcerative Colitis but Not Crohn's Disease.


Exogenous estrogen may lead to an increased risk for ulcerative colitis.

**Background:** The data for the role of estrogen and inflammation are mixed.

**Objective:** To examine the association between postmenopausal hormone therapy and the risk of Crohn disease (CD) and ulcerative colitis (US).

**Methods:** The authors completed a prospective cohort study of 121,000 nurses enrolled in the national Nurses' Health Study. Information on postmenopausal women with documented hormone data was collected. The incidence of UC and CD was obtained. Adjusted hazard ratios to determine the relationship between hormone use and inflammatory bowel diseases (IBDs) were calculated.

**Results:** There were 138 incident cases of UC and 138 cases of CD diagnosed during the observed period. The hazard ratio for a woman using estrogen to develop UC was increased at 1.71 (1.07 to 2.74) for any current user and slightly decreased at 1.65 (1.03 to 2.66) for any history of use. Interestingly, there was no increased risk for women with CD (HR, 1.19; 0.78 to 1.82). Adjustments for body mass index, age, and smoking did not change these risks.

**Conclusions:** The risk for developing UC, but not CD, appears to be related to exogenous estrogen exposure, a fact that indicates that mechanisms for disease development differ between the two conditions.

**Reviewer's Comments:** This intriguing study included a large number of patients followed over a long period of time (>100,000 women followed for >30 years), and incident, not prevalent, cases of IBD were identified. Gastroenterologists blinded to hormone exposure were reviewed the patient's records for accuracy of diagnosis. Prior literature on this topic relates to hormones in the form of oral contraceptives, with the risk of developing or exacerbating IBD. Only 1 prior study has examined the relationship between hormone replacement and IBD, and those investigators found that hormone therapy was protective of disease activity in women with IBD for the first few postmenopausal years. This present study examined a substantially large number of women and assessed risk for disease development based on hormone use. It is still unclear whether a woman who develops disease on hormone replacement will have a worse disease course than a woman not on hormones. This study suggests that the mechanisms for disease development between UC and CD may be different. Estrogen has effects on mainly Th2-mediated diseases, and UC falls into this category. Altered barrier function is thought to play a major role in UC versus CD, and estrogen has destructive properties to epithelium and disrupts normal barrier function. The practical aspects of these findings are in regard to counseling postmenopausal women about the use of exogenous estrogen. There are certain health benefits, but this may be another consideration in the discussion, and especially in women with a family history of IBD, hormone replacement would not be ideal. (Reviewer-Sunanda V. Kane, MD).

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Keywords: Estrogen, Postmenopausal, Ulcerative Colitis

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Perhaps Stress Does Play a Role in Causation of Crohn Disease

Association Between Depressive Symptoms and Incidence of Crohn's Disease and Ulcerative Colitis: Results From the Nurses’ Health Study.

Ananthakrishnan A, Khalili H, et al:

Clin Gastroenterol Hepatol 2013; 11 (January): 57-62

Screening for depression and mood disorders may just have a greater impact on long-term health than we thought.

**Background:** The relationship between depression and psychological stress and autoimmune diseases is uncertain.

**Methods:** Data from the Nurses’ Health Study were analyzed for depressive symptoms and the incidence of ulcerative colitis (UC) or Crohn disease (CD). Depression was assessed using a validated mental health index and UC or CD by self report and a review of records. The risk for UC or CD based on depression with adjustment for other factors was performed.

**Results:** Over 150,000 women were studied, and 170 incident cases of CD were found. Compared to women with recent normal depression scores, those with lower scores had a nearly 2.5 times greater risk for CD (OR, 2.39; 95% CI, 1.40 to 3.98). However, there was no increased risk in the incidence of UC.

**Conclusions:** Psychological factors may play a pathogenic role in CD but not UC.

**Reviewer’s Comments:** This is an interesting study as it provides incident data on a large number of CD patients from a population-based cohort. Depression was measured the same way in each subject and done repeatedly; therefore, the bias for the definition of depression would be minimal. Subjects who developed CD could be identified so that the "chicken-egg" question was not to blame. Prevalence studies and cross-sectional studies cannot identify that depression was not a result of getting a diagnosis of CD. The fact that depression was present before the CD suggests that stress on the immune system by depression could play a role in the development of CD. The fact that this was not seen in UC further strengthens the argument as the two diagnoses are felt to have different mechanistic pathways. These data suggest that we should be more proactive in screening our patients for depression and other mood disorders, as the effect these problems can have cumulatively on the immune system may contribute to the development of CD or other autoimmune conditions. (Reviewer-Sunanda V. Kane, MD).

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Keywords: Stress, Depression, Inflammatory Bowel Disease, Epidemiology

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Placing PEGs Into Patients With Advanced Cancer Provides Limited Utility

In-Hospital and Long-Term Outcomes After Percutaneous Endoscopic Gastrostomy in Patients With Malignancy.

Keung EZ, Liu X, et al:


The placement of a percutaneous endoscopic gastrostomy into patients with advanced cancer is associated with a generally poor prognosis that is likely related to the underlying malignancy.

Background: It is being recognized that the use of a percutaneous endoscopic gastrostomy (PEG) in a patient with advanced neurologic disease does not provide much clinical advantage. It is less-well understood how patients with cancer would fare after PEG placement.

Objective: To assess the outcomes in patients with malignancies who had PEGs placed.

Design: Retrospective cohort study.

Participants: Patients with cancer who had had PEGs placed between May 1, 2006, and May 1, 2011, were included.

Methods: Patients were retrospectively identified and their medical records reviewed. Information regarding demographics, disease state, procedure factors, comorbidity information, lab tests, treatment variables, nutritional care before and after the PEG placement, morbidity, and mortality was collected. Patients with head and neck or intrathoracic malignancies were excluded because feeding tubes were often routinely placed prior to medical or surgical therapy. The outcomes of interest were mortality, major and minor complications, and subsequent course. No control group was included.

Results: Of the 2270 PEGs placed during the 5-year period, 189 of these patients had cancer. The average age was 61 years, and 55% were male; 34% had hematologic malignancies and 44% had metastases. At the time of the PEG placement, >90% were being treated for their cancers; 94% of the patients were in the hospital and 37% were in the ICU. Only 2 of the 189 patients could not have the PEG placed successfully. In-hospital mortality was almost 20%; factors associated with these deaths (multivariate analysis) were admission to the ICU, earlier bone marrow transplantation, and treatment with steroids. Over half of the patients died within 1 year. Major and minor procedural complications were seen in 10% and 11%, respectively. Major complications were associated with thrombocytopenia, while minor complications were associated with lower aminotransferase levels and lower white blood counts. Most patients did not achieve their nutritional goals after PEG placement. For example, only 10 out of 44 patients who were on parenteral nutrition prior to the PEG were able to discontinue the IV nutrient infusions afterward. When the PEG was placed for drainage or obstruction so the patient could eat and the swallowed material drained, almost 60% remained null per os (npo) afterward. Forty-two of the patients changed their code status from full code to DNR or comfort measures only.

Conclusions: PEG placement was associated with a high rate of complications, frequent failure to improve nutritional parameters, and a substantial mortality rate.

Reviewer's Comments: It is impossible to know what the course of these patients would have been without the PEG placement. However, the outcomes after PEG placement were, in general, not very favorable. Given our limited resources, perhaps more thought should be given before such PEGs are offered to patients. (Reviewer-Ronald L. Koretz, MD).

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Keywords: Percutaneous Endoscopic Gastrostomy, Advanced Cancer

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Buspirone Relieves Some Symptoms of Functional Dyspepsia

Efficacy of Buspirone, a Fundus-Relaxing Drug, in Patients With Functional Dyspepsia.

Tack J, Janssen P, et al:

Clin Gastroenterol Hepatol 2012; 10 (November): 1239-1245

Compared to placebo, buspirone did relieve some symptoms of functional dyspepsia.

Background: One hypothesis for the cause of functional dyspepsia (FD) is a failure of the stomach to have normal postprandial accommodation (relaxation so the increased volume does not result in increased wall pressure).

Objective: To test the ability of buspirone, an anxiolytic agent that is known to facilitate accommodation, in relieving the symptoms of FD.

Design: Randomized, double-blind, crossover trial.

Methods: Patients with FD (Rome II criteria) were assessed off therapy for 2 weeks (run-in period), then randomized to either buspirone or placebo for 4 weeks, and then undergo a 2-week washout period followed by the use of whichever agent they had not received the first time. The primary outcome was improvement in a dyspepsia symptom severity score (DSS) in which each of 8 symptoms was graded as absent, mild, moderate, or severe on a 0- to 3-point basis (so the maximum score would be 24). Gastric emptying breath tests, meal-related symptoms, and gastric barostat data were other outcomes assessed. A sample size estimate indicated that the trial was powered to see a 30% difference in DSS scores.

Interventions: Buspirone 10 mg three times per day or matching placebo taken 15 minutes before meals.

Results: Twenty patients were entered into the trial initially, but 2 discontinued after the first week because of gastrointestinal symptoms and a third failed to complete the barostat studies; data were presented for the remaining 17 subjects. Before and after placebo treatment, DSS scores were 10.8 and 9.5, respectively (nonsignificant difference). Before and after buspirone DSS scores were 11.5 and 7.5, a significant difference. The individual symptoms that improved significantly were postprandial fullness, upper abdominal bloating, and early satiety. Meal-related symptoms also improved only with buspirone. Liquid emptying was significantly slower after buspirone, and no differences were seen for solid emptying. Gastric accommodation as measured by the barostat was significantly higher after buspirone.

Conclusions: Buspirone, when taken for 4 weeks, significantly improved symptoms of FD but did result in delayed gastric emptying of liquids.

Reviewer's Comments: There were a large number of analyses done and no correction was made for that; thus, some of the alleged significant findings may represent type I errors. While the DSS scores did improve, it was not clear how much actual relief these patients achieved; a difference of 4 points is consistent with 4 of the 8 symptoms improving 1 category each. (Reviewer-Ronald L. Koretz, MD).

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Keywords: Dyspepsia, Buspirone

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Hypomagnesemia Is a Drug Class Effect of Proton Pump Inhibitors

Systematic Review: Hypomagnesaemia Induced by Proton Pump Inhibition.
Hess MW, Hoenderop JGJ, et al:
Aliment Pharmacol Ther 2012; 36 (September): 405-413

Patients taking proton pump inhibitors for long periods of time should have magnesium levels checked.

**Background:** Since their introduction in the United States in 1989, proton pump inhibitors (PPIs) have become the mainstay for the treatment of acid-related disease. In recent years, there have been a growing number of reports purporting that long-term PPI use is associated with the development of hypomagnesemia.

**Objective:** To determine if the long-term use of PPIs is associated with the development of hypomagnesemia and to profile patients at risk of developing hypomagnesaemia.

**Methods:** A systematic review of all available case reports suggesting an association between PPI use and hypomagnesemia was performed along with statistical analysis of the extracted data.

**Results:** It was determined that after a median of 5.5 years, the development of hypomagnesemia is a drug class effect of PPI use. The onset of hypomagnesemia was broad and ranged from 14 days to 13 years. Discontinuation of the offending drug led to a fast recovery of magnesium deficiency, and re-challenge with the drug led to a recurrence within 4 days. The use of histamine-2 receptor antagonists were the preferred replacement for PPIs in cases of PPI-induced hypomagnesemia and prevented recurrence of this problem. There was no specific risk profile identified in those who developed hypomagnesemia associated with PPI use. There is little evidence found in the literature to suggest that the development of hypomagnesemia in patients on PPIs is associated with any damage to the renal epithelia.

**Conclusions:** Cases of PPI-associated hypomagnesemia demonstrated severe symptoms of magnesium depletion (neuronal, neuromuscular, cardiovascular, and metabolic) that reversed upon discontinuation of the PPI, which leads to normalization of magnesium levels.

**Reviewer's Comments:** It seems reasonably well established that patients taking PPIs for long periods of time (and sometimes even only after a short period of time) are at risk for the development of hypomagnesemia, which can lead to severe symptoms and problems if left untreated. Awareness of this potential problem should lead to testing for magnesium levels in patients whose symptoms suggest this problem and even in asymptomatic patients on long-term PPIs. (Reviewer-Michael M. Phillips, MD).

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Keywords: PPI-Induced Metabolic Problems

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Coffee Decreases Time of Postoperative Ileus in Patients Undergoing Colectomy

Randomized Clinical Trial on the Effect of Coffee on Postoperative Ileus Following Elective Colectomy.

Müller SA, Rahbari NN, et al:

Patients who are given coffee at 6 hours post-colectomy appear to have a shorter time to first bowel movement than those given water.

Background: It has been postulated that coffee might have a salutary effect on postoperative ileus after abdominal surgery.
Objective: To test this hypothesis in patients undergoing colectomy by either open or laparoscopic surgery for benign or malignant disease.
Design/Participants: A multicenter, parallel, open-label randomized study was conducted on 80 patients who had undergone colonic surgery both laparoscopic and open for both benign and malignant disease in several hospitals in Heidelberg, Germany.
Methods: Patients undergoing colectomy were randomly assigned preoperatively to receive either coffee or water following surgery (100 mL three times daily). The primary end point of the study was time to first bowel movement, with secondary end points being time to first flatus, time to tolerance of solid food, length of hospital stay, and perioperative morbidity.
Results: Eighty patients undergoing elective open or laparoscopic colectomy were randomly assigned to receive either water or coffee beginning 6 hours after surgery. Patients in both groups also received oral magnesium 1200 mg/day and macrogol (polyethylene glycol; 39.3 g/day), but no other laxatives or prokinetic agents were given. In an intention-to-treat analysis, the time to the first bowel movement was significantly shorter in the group receiving coffee than in those receiving water (60.4 ± 21.3 vs 74.0 ± 21.6 hours; P =0.006). The time to solid food was (49.2 ± 21.3 vs 55.8 ± 30.0 hours; P =0.276), and time to first flatus (40.6 ± 16.1 vs 46.4 ± 20.1 hours; P =0.214) showed a similar trend, but the differences were not significant. Length of hospital stay (10.8 ± 4.4 vs 11.3 ± 4.5 days; P =0.497) and morbidity (8 of 40 vs 10 of 39 patients; P =0.550) were comparable in the two groups.
Conclusions: Coffee consumption post-colectomy was safe and associated with a reduced time to first bowel movement.

Reviewer's Comments: This interesting article would appear to be of value to surgeons and those caring for postoperative patients who have undergone a colectomy. There was a significant reduction in time to first bowel movement as well as time to consumption of first solid foods. Therefore, it would seem logical that this would lead to a shorter period of postoperative hospitalization; however, in both groups, this time was quite long by American standards lasting 10 to 11 days. I can only guess that cultural differences lead to this discrepancy. It would appear that this relatively benign intervention may lead to a quicker road to recovery compared to those who are not treated in this manner. (Reviewer-Michael M. Phillips, MD).

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Keywords: Postoperative Ileus, Elective Colectomy, Coffee

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