

COMMENTS AND RESPONSES

Echinacea for the Common Cold

TO THE EDITOR: Barrett and colleagues (1) are to be lauded for their efforts to scientifically examine the commonly used phytomedicinal agent echinacea. However, while they have successfully debunked the advisability of use of oral unrefined echinacea, it is highly likely that the preparation used in their study was inadequate and the route of administration was suboptimal to appropriately test the efficacy of the herb in the treatment of upper respiratory tract infections. Although echinacea is a native American plant, the best research on it has been done in Germany, where in 1992 Commission E (the equivalent of an herbal Food and Drug Administration) approved the use only of alcoholic root extracts of *Echinacea pallida* (narrow leaf coneflower) or juice pressed from *E. purpurea* (common purple coneflower) (2). Because all *Echinacea* species are endangered, the latter preparation from cultivated sources is preferred. (Individuals who are concerned about conservation are urged to visit United Plant Savers at <http://plantsavers.org/>.)

Many prominent herbal references (3–5) emphasize an important point about echinacea administration: Because echinacea may act locally on oropharyngeal lymphoid tissue, best results accrue when a tincture is held in the mouth or gargled before swallowing. Although anecdotal, the experience of roughly 100 of my patients supports the finding that oral capsular echinacea preparations yield no useful results, while the gargling technique yields noticeable prophylaxis and attenuation of upper respiratory tract infections and influenza, as well as rapid healing of aphthous ulcers. Although the unique taste and mild local anesthetic effects of echinacea tinctures make true blinding procedures more difficult, it is likely that another trial employing this technique with a tincture of pressed *E. purpurea* aerial parts (for example, EchinaGuard Liquid Extract, Nature's Way, Springville, Utah) will have much more encouraging results.

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TO THE EDITOR: Influenza would have been a better subject for Barrett and colleagues to examine (1). Unfortunately, many manufacturers market echinacea as a preventive agent (2), but this has not been my experience. I have found echinacea drops to be the most effective preparation, but this method of use is unusual and not

familiar to many practitioners of traditional medicine. The preparation I use is marketed in Israel as ProtecPlus (Altman Natural Chemist Ltd, Cholon, Israel) and contains additional ingredients besides echinacea. According to instructions, the patient should mix 30 drops with a little water and use it as a mouthwash for at least 30 seconds, then swallow. The patient should ingest no food or drink for 5 minutes before or 10 minutes after the treatment and should repeat the treatment every 4 hours. When improvement is noted, the patient should reduce the dose to 20 drops 3 times per day until he or she is better. The medicine is absorbed by the mucous membranes of the mouth and bypasses the liver.

Echinacea works by acting as a decoy. The influenza virus secretes a protein enzyme called hyaluronidase, which breaks down hyaluronic acid, a major component of the intracellular cement that holds body cells together. Hyaluronidase allows the influenza virus to enter a cell by opening and immediately closing a "trapdoor." Once inside, the virus replicates, causing the person to get sick. Echinacea interferes with secretion of this enzyme, stops it from entering the cell and the immune system, and kills the virus before it can do any harm (Jacobs A. Personal communication). Echinacea, therefore, attracts the virus to attack it, allowing the body to heal itself naturally. It's always worked for me.

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TO THE EDITOR: Barrett and colleagues' study (1) of an unrefined echinacea product, while elegant, was limited by poorly chosen and inadequately characterized source material. Clinical trials should begin with botanically identified raw material, with sources and processing described and representative voucher specimens of the whole plant or samples of the raw material preserved in a publicly accessible herbarium, unless a defined commercial product is to be studied. Shaklee Technica (Pleasanton, California) distributes an echinacea-containing product through multilevel marketing, but it is not the formulation provided to Barrett and colleagues.

The product used by Barrett and colleagues was chemically analyzed only after unblinding, when moderate levels of echinacea-specific compounds provided the first evidence that the capsules contained some *Echinacea* species. Contrary to Turner's suggestion in the accompanying editorial (2), this does not qualify as "standardiz[ation] by measuring specific components," which would have confirmed minimum levels of those components before the study began.

The choice to include 2 species is also strange, since it is not the rule in commerce. If 1 species was more potent, or if the differing active metabolites of the 2 species did not combine in an additive manner, neither would be adequately tested by this method.

Finally, as Barrett and colleagues recognized, the dosage form limits the applicability of their results. The most popular products, and those used in virtually all positive studies, are hydroalcoholic extracts or fresh expressed juice preparations; improved bioavailability, preservation of active compounds, and contact with lymphatic tissue could contribute to their benefits. If Barrett and colleagues

selected capsules solely for their lack of sensory qualities, then placebos and blinding have become no longer means, but ends. They are valuable research tools but are difficult to apply rigorously to therapies that do not come in pill form, whether open-heart surgery or chicken soup. If such therapies are to be evaluated fairly, a more broadly applicable method must evolve.

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2. Turner RB. Echinacea for the common cold: can alternative medicine be evidence-based medicine? [Editorial] *Ann Intern Med.* 2002;137:1001-2. [PMID: 12484717]

TO THE EDITOR: The article on echinacea by Barrett and colleagues (1) has several overt weaknesses. First, alfalfa is not an inactive herb and cannot be used as a placebo. Alfalfa has proven phytoestrogenic actions, is an alterative, detoxifies the blood, is very nutritive, and is antipyretic, any of which may explain why echinacea and alfalfa performed similarly. Were any herbalists on the study team? Just as physicians would not believe an herbalist's claims about cancer research, practitioners of alternative health will not trust this research. It would also have helped to have studied a pharmaceutical drug for a more thorough understanding of cold treatment.

Second, the study was seemingly biased. My daughter looked into participating and was told that the placebo was going to be alfalfa. Why were the researchers telling potential participants this? A person involved in the study also told her that the researchers did not expect positive results for echinacea. By the way, Barrett and colleagues inadvertently identified not 1 but 2 remarkable cold treatments, considering that participants' colds lasted only 6 days after treatment with echinacea and alfalfa and colds normally last 10 days or more.

Third, Barrett and colleagues found that levels of tumor necrosis factor increased with the use of echinacea, but why was this not promoted as a positive result? It is too late to start taking echinacea after one gets a cold. The researchers should have measured the length of time between (or the number of) cold infections in persons taking echinacea or a true placebo for a whole cold season. Immune enhancement was measured to some degree but inadequately. A good study would have measured (in vivo if possible) T-cell activation, macrophage activation, viral receptor blockage, inhibition of hyaluronidase, and release of interferon. Echinacea works best for compromised immune systems, but the study did not evaluate this. In addition, students are a very biased sample.

I am keenly interested in good research, but I do not accept the findings of studies that are not performed by a qualified cross-disciplinary team. This study is just another step backward.

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TO THE EDITOR: Barrett and colleagues did not perform a placebo-controlled trial (1). The study used alfalfa (*Medicago sativa*) for the placebo; however, alfalfa has known biological activity. In 1990, we published a randomized, controlled trial showing the efficacy of *Urtica dioica* compared with placebo lactose in treating symptoms of allergic rhinitis (2). During this study, we also observed that alfalfa is as effective as *U. dioica* in the treatment of allergic rhinitis (Unpublished data).

Alfalfa contains bioactive phytochemicals, including 15% to 22% crude protein, minerals (phosphorus, calcium, potassium, sodium, sulfur, magnesium, copper, manganese, iron, cobalt, boron, molybdenum), vitamins (A, D, E, K, C, B₁, B₂, B₆, B₁₂, niacin, pantothenic acid, inositol, biotin, folic acid), amino acids (immunomodulatory canavanine, arginine, asparagine), phytoestrogenic coumarins (coumestrol) and isoflavones (genistein, daidzein, biochanin A, formononetin), flavones, and antifungal and hypocholesterolemic saponins (3–5). In addition, alfalfa has historically been used to treat upper respiratory tract conditions.

A placebo is a substance that is pharmacodynamically inert, making it possible to compare an active treatment with one that is inactive. Placebo must have no impact on the responses being studied, and certainly no broad effect on systemic nutrition or immune activity. Since alfalfa is a substance with numerous bioactive phytochemicals and an equally rich herbal medicine tradition, it cannot be considered an appropriate placebo. Alfalfa is a particularly improper placebo for outcome studies in upper respiratory tract conditions, for example, the common cold.

The study by Barrett and colleagues would have been more reliable if a proper placebo were selected and if the authors had also compared the echinacea group with a nontreatment group, which may have demonstrated more clearly the value of echinacea. Barrett and colleagues' study is a comparative study, not a placebo-controlled trial.

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TO THE EDITOR: Barrett and colleagues (1) reported a placebo-controlled trial of echinacea for the common cold. The Food and Drug Administration defines a placebo control as “an identical-appearing treatment that does not contain the test drug . . . the placebo control design, by allowing blinding and randomization and including a group that receives an inert treatment, controls for all potential influences on the actual or apparent course of the disease other than those arising from the pharmacologic action of the test drug” (2). Alfalfa does not meet these requirements because it is a potential influence on the course of the disease and therefore must be considered an active control.

Alfalfa is biochemically complex, containing large amounts of vitamins, minerals, phytoestrogens, and saponins. The saponin constituents alone (molecules with a triterpene or steroid moiety) have shown a wide range of biological activity. Alfalfa saponins are fungicidal, bactericidal, and insecticidal and have cholesterol-lowering properties (3). Alfalfa has also been found to contain an abundance of thyrotropin-releasing hormone–like material (4), which may be the basis of its traditional use in thyroid disease (5). Alfalfa tablets, seeds, and sprouts have also been associated with rare instances of the reactivation of systemic lupus erythematosus and the onset of other autoimmune disorders. As with echinacea, alfalfa is part of the herbal pharmacopoeia and has significant known and no doubt unknown biological effects.

Barrett and colleagues’ study informed us of the equivalent effect of alfalfa and echinacea on the outcomes measured. However, the results cannot be interpreted because neither herb is considered a standard treatment for the common cold.

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IN RESPONSE: Randomized, controlled trials are designed to test specific hypotheses. While bias can be reduced, generalizability and interpretation are limited. In our trial, a specific echinacea preparation was tested against a specific control as a treatment for the common cold. The choice of echinacea was influenced by the literature and by popular practice. Several trials of *Echinacea purpurea* and *E.*

angustifolia preparations had been positively reported (1, 2). Products containing either or both species were in wide use. We chose a capsulized whole plant preparation for its simplicity and ease of manufacture. We avoided a liquid preparation because the taste and tingling sensation of echinacea are notoriously difficult to disguise. We were intent on demonstrating intact blinding, since this had not previously been accomplished. This guided our choice of placebo. Because we used clear gelatin capsules containing the whole plant product, and because some of the herbal taste could leak from the capsules (and was available to participants who opened them), we needed a plant-based product that would be indistinguishable to participants and to research personnel. We settled on whole dried alfalfa because the color and consistency mimicked the echinacea product and no research had reported any effects of alfalfa on the severity or duration of the common cold. However, taste was still distinguishable, so technicians at Shaklee Technica experimented with adding various flavoring agents, eventually finding that a very small amount of thyme and peppermint successfully disguised echinacea’s flavor.

We agree that these choices could affect results. Although a bit far-fetched, it is possible that tiny amounts of peppermint or thyme could block a positive effect of echinacea. It is also possible, although unlikely, that a few grams of alfalfa could be an effective treatment for the common cold. If so, the multimillion-dollar cold remedy industry should shudder, as a few grams of alfalfa costs only a few pennies. Perhaps an alfalfa trial will be carried out, and perhaps some benefit will be found. In the meantime, we stand by the results of our trial: The echinacea preparation we used provided no measurable benefit to college students experiencing cold symptoms. Perhaps it would have worked in an older sample. Perhaps a refined extract or liquid preparation would have worked. Perhaps dosing should occur within 12 hours rather than 36 hours of first symptoms. Our results cannot address these important questions, nor can our trial by itself negate the results of the several positively reported trials. More and better research is warranted.

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Alcohol, Postmenopausal Hormones, and Breast Cancer

TO THE EDITOR: In the Nurses’ Health Study cohort, Chen and colleagues (1) found an approximately 2-fold excess risk for breast cancer in women who currently used postmenopausal hormones and drank alcohol. However, the researchers were unable to consider high alcohol consumption. To address this issue, we analyzed data from 2 Italian case–control studies. The first was conducted between 1983 and 1991 in greater Milan (2), and the second was conducted between 1991 and 1994 in 6 centers in various regions of Italy (3). The studies involved 3573 postmenopausal women (median age, 61 years [range, 31 to 74 years]) with a histologically confirmed diag-

Table. Odds Ratios for Breast Cancer in Postmenopausal Women, by Alcohol Intake and Postmenopausal Hormone Use

Alcohol Intake	Postmenopausal Hormone Use	All Postmenopausal Women			Women Who Reported Natural Menopause
		Women with Breast Cancer	Controls	Odds Ratio (95% CI)*	Odds Ratio (95% CI)*
None (abstainers)	Never	970	1152	1†	1†
	Ever	97	82	1.48 (1.08–2.04)	1.39 (0.95–2.05)
1 drink per day	Never	1140	1133	1.19 (1.05–1.35)	1.21 (1.05–1.39)
	Ever	148	129	1.41 (1.08–1.83)	1.35 (0.99–1.85)
2 drinks per day	Never	792	759	1.23 (1.07–1.41)	1.30 (1.11–1.51)
	Ever	63	45	1.60 (1.07–2.40)	2.32 (1.40–3.82)
≥3 drinks per day	Never	327	252	1.62 (1.33–1.96)	1.56 (1.26–1.93)
	Ever	36	20	2.25 (1.27–3.99)	2.95 (1.43–6.11)

* Derived from multiple logistic regression models including terms for age, study center, calendar year of interview, education, smoking habit, body mass index, age at menarche, type of menopause, parity age at first birth, oral contraceptive use, history of benign breast diseases, and family history of breast cancer in first-degree relatives. † Reference category.

nosis of incident breast cancer. Controls were 3572 postmenopausal women (median age, 61 years [range, 34 to 74 years]) admitted to the same network of hospitals for acute, non-neoplastic, non-hormone-related conditions. The participation rate exceeded 95% for both case-patients and controls. Information collected on alcohol drinking included the number of days per week that each type of alcoholic beverage (wine, beer, and spirits) was consumed, the average numbers of drinks per day, and the duration of the habit in years. Each drink included approximately 12 g of ethanol.

In comparison with women who did not drink, the multivariate odds ratio (OR) was 1.62 for women who had never used postmenopausal hormones who consumed at least 3 drinks per day. Compared with never-users of postmenopausal hormones, the OR was 1.48 for ever-users who abstained from alcohol. Women exposed to both factors had an OR of 2.25. Among the 2879 case-patients and 2752 controls who reported natural menopause, the OR for women who were exposed to both factors was 2.95 (Table).

Moderate alcohol drinking is socially acceptable among Italian women (4), and the information on alcohol consumption was satisfactorily valid and reproducible (5). Our findings, based on a uniquely large data set and comparatively high levels of alcohol drinking, provide further evidence of a substantial excess risk for breast cancer in women who drink alcohol and have ever used postmenopausal hormones.

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Update in Hospital Medicine

TO THE EDITOR: Regarding the section on avoiding femoral line placement in Flansbaum and Huddleston's Update in hospital medicine (1), am I the only one who sees the folly of leaving a femoral line in place for more than 4 days? In the study reviewed (2), femoral lines were used for an average of 9.3 days!

I argue that in the short run a femoral line is far safer than a subclavian line. The complications associated with femoral lines all occur after 72 hours. Line infections are rare in this time window. If short-term access is needed, it makes more sense to use the femoral vein. If access may be needed for more than 72 hours, a subclavian line should be used. I use femoral lines for all of my patients with diabetic ketoacidosis. They don't need the line longer than 72 hours, and they don't get pneumothorax.

I would love to see a study that compares complication rates between subclavian lines left in longer than 5 days and femoral lines pulled in less than 72 hours. We all know that the infection rate and thrombotic rate will both be lower with the femoral line. If central access will be needed for less than 72 hours, I argue that the femoral vein is better.

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of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *JAMA*. 2001;286:700-7. [PMID: 11495620]

IN RESPONSE: Reducing problems related to central venous catheter placement is a high priority, and we agree with Dr. Painton that appropriate patient screening is prudent and may help avoid needless line-related complications. Typically, patients with significant comorbid conditions who are seen in the intensive care unit have longer hospital stays, in addition to continued needs for intravenous access. The patients in the study by Merrer and colleagues (1) reflect this and, as a result, required longer placement of both subclavian and femoral lines. The investigators stated that “catheters were removed at the discretion of the ICU [intensive care unit] team when they were no longer needed or if an adverse event occurred.” Whether greater reductions in catheter duration were possible is unclear.

In critically ill patients without peripheral access in whom brief needs for central line placement can be predicted (probably a limited subset), a strategy favoring anatomic sites with lower complication rates would be appropriate. While infectious and thrombotic complications are always a risk, it is unlikely that these problems “all occur after 72 hours,” and good judgment should direct the location of any intravascular device. If avoiding pneumothorax is the sole concern, subclavian access should be attempted at the discretion of the physician. Ultrasound guidance also reduces the potential for complications (2).

In patients with diabetic ketoacidosis, such as those Dr. Painton describes, large-bore peripheral lines should be the optimal choice for access. They will both minimize complications and maximize fluid resuscitation rates if the patients are very ill.

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Acute Migraine Treatment Guideline

TO THE EDITOR: I have had migraines for 30 years and therefore read Snow and colleagues' article on migraine management and prevention (1) with interest. I have used almost all of the medications mentioned in the article and continue to get migraines at least once per week, sometimes twice. My migraines are characterized by nausea, occasional vomiting, photophobia, and intense right-side frontal pain, along with a sense of unease. There is no aura. The triptans I have taken—sumatriptan, naratriptan, and rizatriptan—do work with varying onset of action and sometimes rebound pain. I have also

used acetaminophen, butalbital, and caffeine (Fioricet, Novartis, Basel, Switzerland); nonsteroidal anti-inflammatory drugs; acetaminophen; and even zolpidem to allow me to get to sleep when I have a headache that is not responding. β -Blockers do not lessen the severity or frequency of my attacks. I have even tried cold showers, usually to no avail. Menopause did not affect my attacks, nor did hormone replacement therapy.

After reading several articles on use of botulinum toxin type A (Botox, Allergan, Inc., Irvine, California) for the treatment of migraine and other chronic headaches, I asked my husband, a dermatologist, to inject my frontalis area bilaterally. I received 16 U of botulinum toxin type A and was headache-free for 6 weeks. I then developed a severe migraine that lasted for several days. Another set of injections was given during an attack, and although the attack was not aborted, I subsequently enjoyed another 6 weeks of freedom. I had not gone for such a long period without a headache since I was 25 years of age.

Binder and associates (2) examined the effectiveness of botulinum toxin type A in 106 women and noted a complete response rate of 51% (mean response duration, 4.1 months) among the 77 women who had true migraine, according to American Headache Society criteria. Ten women also had an acute response to therapy during attacks. In another study of botulinum toxin therapy in 134 patients who had migraine, tension, or chronic daily headaches more than 15 days per month, 88% improved and 92% of those who had a series of 4 treatments at 3-month intervals responded (3).

The mechanism of action of botulinum toxin type A for migraine relief is unknown but is thought to be related to acetylcholine inhibition and a blocking action on the parasympathetic nervous system (2). Side effects are rare and mild (4). However, according to the dermatology literature, blocking antibodies can develop; I do not know whether this would negate the effects for headache. Neither Snow and colleagues (1) nor a recent review by Goadsby and coworkers (5) mentioned botulinum toxin type A as a potential preventive medication for migraines. I believe that its use should be carefully studied, since it appears to be an effective treatment.

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IN RESPONSE: Dr. Marino provides a very interesting account of her journey toward achieving relief from her migraines. Happily, she has found a preventive therapy that is effective for her. Dr. Marino cites

several reports on the use of botulinum toxin therapy in migraine headache and asks why it was not included in the evidence review for the American College of Physicians guidelines. First, I must point out that the College's guideline is based on an exhaustive systematic review of the evidence, performed under the auspices of U.S. Headache Consortium (1, 2). These evidence reviews covered published studies up until the year 1998. In addition, only trials that were judged to be well-designed randomized, controlled trials could be included (3). In order for a recommendation to be made, many such trials directly relevant to the recommendation had to yield a consistent pattern of findings. Thus, the study by Binder and associates (4) that Dr. Marino cites would necessarily be excluded from the review because of its design (nonrandomized, uncontrolled, open-label).

Since completion of our review, a single randomized, double-blind, controlled trial of the use of botulinum toxin type A in migraine prevention has been published (5). Silberstein and associates studied 123 patients with a history of 2 to 8 moderate to severe migraine attacks per month. Participants were randomly assigned to receive 25 U or 75 U of botulinum toxin type A injection or injection of vehicle control. The authors concluded that pericranial injection of 25 U safely and substantially reduced migraine frequency (at 3 months) and severity (at 2 and 3 months). Of interest, those treated with 75 U showed no significant effects. Even if this trial had been available at the time of our review, however, we could not make a recommendation on the basis of a single small study. Further large-scale randomized, controlled studies are needed to confirm these results, identify the most efficacious doses, and demonstrate long-term efficacy and safety.

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CLINICAL OBSERVATION

Editor's Note: The lead author of the following Clinical Observation was 1 of a dozen Associates of the American College of Physicians selected to present a clinical vignette at the 2002 Annual Session in Philadelphia. We are proud to present this case report through a special arrangement with the Council of Associates of the College.

An Unusual Case of Ischemic Bowel

TO THE EDITOR: *Case Report:* A 67-year-old woman presented with acute abdominal pain that had persisted for 12 hours. The pain was sharp and generalized throughout the abdomen with associated nausea and vomiting. The patient's medical history included myocardial infarction and hypercholesterolemia, and she was taking metoprolol, lisinopril, atorvastatin, and estrogen-progesterone. The patient was in mild distress; her blood pressure was 149/63 mm Hg, her pulse was 74 beats/min, and her respiratory rate was 22 breaths/min. She had a slightly distended abdomen, hypoactive bowel sounds, diffusely tender epigastrium, rebound, and guarding. Rectal examination revealed no masses, and stool was guaiac positive. The physical examination was otherwise unremarkable.

Initial laboratory tests showed a leukocyte count of 19×10^9 cells/L, 85% of which were neutrophils. Results of Sequential Multiple Analysis-7, lactic acid, amylase, and liver function tests were all within normal limits. Abdominal computed tomography demonstrated dilated proximal small bowel with thickened and edematous

Figure. Small bowel on computed tomography and an inflamed vein on pathologic section.



Top. Abdominal computed tomography scan showing small-bowel dilatation and thickening (arrow) with mucosal enhancement. **Bottom.** Medium-sized vein with exuberant inflammation surrounding the vessel wall and a thrombus in lumen (right). A muscular artery is unaffected (left). (Hematoxylin-eosin; original magnification, $\times 100$.)

walls (Figure, top). At emergency exploratory laparotomy, 60 cm of necrotic proximal small bowel was resected. Histopathologic examination revealed acute vasculitis with thrombosis of the mesenteric veins. Surrounding the veins was an inflammatory cell infiltrate composed of numerous neutrophils, eosinophils, and histiocytes with a partial hemorrhagic infarct. Arteries were not involved (Figure, bottom). Results of tests for antineutrophil cytoplasmic antibodies and antinuclear antibodies were negative. Erythrocyte sedimentation rate was 16 mm/h. There was no evidence of systemic vasculitis. The patient received no further treatment and remained well 6 months after surgery.

Discussion: Most cases of mesenteric ischemia are due to superior mesenteric embolism, arterial thrombosis, nonocclusive ischemia, or mesenteric venous thrombosis. Less commonly, the cause may be classified in 1 of 5 broad categories: mechanical injury, drugs, hematologic disease, vasculitides, and other (for example, post-coronary artery bypass or peritoneal dialysis) (1). Most vasculitides of the gastrointestinal tract are secondary to systemic vasculitis (2). Patients in whom vasculitis is suspected should be tested for systemic vasculitis.

While localized gastrointestinal vasculitis is unusual, venulitis is decidedly rare. In the largest review of localized gastrointestinal vasculitis, localized polyarteritis nodosa was the most common cause, accounting for more than 50% of all cases (3). Vasculitis affecting only the veins accounted for 19% of cases. Isolated mesenteric venulitis is also a rare disorder; fewer than 50 cases have been reported in the literature (4). The typical patient is older than 40 years of age and has acute or subacute onset of abdominal pain and diarrhea followed by peritonitis. Surgical resection is required in all cases. Histopathologic characteristics consist of lymphocytic infiltration and thrombosis of the inflamed veins. The arteries are not involved, and eosinophils are seen in up to 70% of cases. The cause of the disease is unclear (5).

Localized mesenteric venulitis is found in the literature under several different names, including idiopathic enterocolic lymphocytic phlebitis, mesenteric inflammatory veno-occlusive disease, intramural mesenteric venulitis, idiopathic colonic phlebitis, enterocolic lymphocytic phlebitis, and giant-cell granulomatous phlebitis (6). Although histologic differences exist among cases, the common feature is localized vasculitis affecting the veins and sparing the arteries. The individual variations in histologic characteristics raise the possibility of an unusual type of venulitis with several different causes or, alternatively, a single disorder characterized by a spectrum of histologic change (7).

Conclusion: This case illustrates several important points. Vasculitis may occur in a localized segment of the gastrointestinal tract, and removal of the affected bowel is the only treatment required. In addition, vasculitis may be confined to the veins. A venous source of intestinal ischemia is rarely suspected and may be overlooked on angiography (8).

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CORRECTIONS

Correction: Treatment of Chronic Hepatitis C in a State Correctional Facility

In an article on treatment outcomes for incarcerated persons with hepatitis C virus infection (1), the response rate for all patients who completed treatment and had data available 6 months after treatment should have been reported as 40% (26 of 65 patients) rather than 46% (26 of 57 patients).

Reference

- Allen SA, Spaulding AC, Osei AM, Taylor LE, Cabral AM, Rich JD. Treatment of chronic hepatitis C in a state correctional facility. Ann Intern Med. 2003;138:187-90. [PMID: 12558357]

Correction: National Kidney Foundation Practice Guidelines for Chronic Kidney Disease

In the National Kidney Foundation practice guidelines for chronic kidney disease (1), the Cockcroft–Gault equation is printed incorrectly on page 143. It should be $C_{Cr}(\text{mL}/\text{min}) = [(140 - \text{age}) \times \text{weight}] / 72 \times S_{Cr} \times (0.85 \text{ if female})$, where C_{Cr} is creatinine clearance, S_{Cr} is serum creatinine concentration in mg/dL, age is in years, and weight is in kg.

Reference

- Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med. 2003;139:137-47. [PMID: 12859163]

Finding Ping

TO THE EDITOR: This letter is written as a follow-up to an earlier essay (1). The encounter with Jiajia occurred in May 2001. When I returned to the United States in June, I initiated a search for her. In July, the U.S. Consulate General in Chengdu responded, providing the name of Jiajia's father and his address in a village near Chongqing. I sent him a letter, in English, with no real expectation of a reply. In November, a letter came from him, in Chinese, that included a photograph of Jiajia.

A Chinese graduate student translated the letter, which stated that Jiajia was doing well but that she had been born with only 1 lung and had therefore been prone to many colds and to pneumonia. The graduate student introduced me to several of his Chinese friends. One, Xuexian Yan, a physician from Chongqing, had both graduated from and worked in the medical school there. He offered to contact physicians there to facilitate Jiajia's care. Although it seemed there was little curative potential, we thought that preventive and acute care requirements could be bolstered. Jiajia's father had written, "Jiajia is better compared with when we met at the airplane. We are worried whether she would face more difficulty and bitterness in the future. By all means, we promise to bring Jiajia a healthy and normal life, no matter how hard it would be. This is the biggest wish of us as her parents."

The now deeply involved Xuexian made telephone contact with a professor at the Children's Hospital in Chongqing who said he was willing to see Jiajia. After making many other telephone calls, Xuexian finally reached Jiajia's parents on the last day of February 2002. He learned that Jiajia had died in October after contracting an infectious disease and developing a high fever. She had been in the county People's Hospital, and her mother had been with her.

We have continued to communicate by telephone and by mail with Jiajia's parents. They do have a son, now 12. Her father is 39, and her mother is 30. Whether they will have another child is unknown. They have sent us additional pictures of Jiajia, and memories of her remain very much alive both with her family and with her friends. Although she lived only 18 months, she left her mark and deeply affected the lives of those around her.

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Priapism Induced by Proton-Pump Inhibitors and Misoprostol

TO THE EDITOR: To my knowledge, sexual side effects from antiulcer medications have been reported only once in the medical litera-

ture, in the case of a 77-year-old man taking omeprazole and isordil who developed painful nocturnal erections lasting up to 36 hours (1). I describe what may be the second documented case of proton-pump inhibitor-induced priapism and the first case of priapism related to misoprostol.

A 61-year-old man taking etodolac, atenolol, pravastatin, and aspirin was prescribed esomeprazole, 40 mg/d, to treat gastritis so that he could continue taking etodolac for severe noncardiac chest pain. An uncomfortable nocturnal erection lasting 2 to 6 hours developed after each of the 6 times that he took a dose of esomeprazole. On further questioning, the patient reported that he had had the same experience with rabeprazole 2 years earlier, but his physician at the time had not believed him. Misoprostol was substituted for esomeprazole at an initial dosage of 100 μ g twice per day; the dose was slowly titrated upward. When the dose had reached 400 μ g twice per day, the patient had nocturnal erections lasting 2 to 6 hours each time he took misoprostol (3 times in all). By this time, the noncardiac chest pain had resolved, and therapy with etodolac and misoprostol was discontinued. At 6-month follow-up, the patient had had no further episodes of priapism, and he confirmed that the disorder had developed only while he was taking proton-pump inhibitors and misoprostol.

This patient's sustained erections probably reflect 2 different physiologic pathways. Omeprazole causes calcium-channel-dependent relaxation of isolated corpus cavernosum, while misoprostol causes comparable relaxation that is prostaglandin mediated (2, 3). Similar mechanisms may be at work in rare persons who are unusually susceptible to substituted benzimidazole adenosine triphosphate inhibitors and prostaglandin E₁ analogues. Priapism can be a medical emergency, resulting in penile infarction. Therefore, clinicians need to take seriously any reports of priapism during therapy with proton-pump inhibitors or misoprostol, especially since relaxation of corpus cavernosum can be demonstrated in vitro for both classes of medications.

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