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lated to changes in gut function, psychoactive medications for central analgesia [antidepressant agents] are indicated."

I agree that antidepressant agents can be used in the presence of gut dysfunction; conversely, motility-acting agents are not suited for severe, continuous pain with or without gut dysfunction. In addition to the study by Greenbaum and colleagues (1) (which showed reduction of diarrheal symptoms and the number of slow contractions in the rectosigmoid in patients with diarrhea-predominant irritable bowel syndrome), two recent studies have shown positive effects of antidepressant agents on small-bowel motility (2, 3). Imipramine, a tricyclic antidepressant agent with substantial anticholinergic effects, was shown to slow jejunal phase III propagation velocity and to prolong orocecal transit time in normal persons and in patients with diarrhea-predominant irritable bowel syndrome (2). In another study by the same research group (3), administration of paroxetine—a selective serotonin reuptake inhibitor—reduced orocecal transit time in controls and patients with diarrhea-predominant irritable bowel syndrome. No data were available on possible effects on symptoms.

To expand on my previous recommendations, I emphasize three points: First, antidepressant agents may improve symptoms of the irritable bowel syndrome by affecting motility, independent of mood-altering or analgesic effects, but confirmatory studies correlating symptoms with changes in motility and adjusting for depressive mood are needed. A practical approach would be to choose a tricyclic agent with anticholinergic properties for diarrhea-predominant irritable bowel syndrome and a selective serotonin reuptake inhibitor for constipation-predominant irritable bowel syndrome.

Second, motility-altering agents are better suited for treating such symptoms as postprandial pain and diarrhea on an as-needed basis. Conversely, because antidepressant agents require several weeks to become effective and have a long duration of action, they are best prescribed when symptoms are frequent or continuous.

Finally, the role for motility-altering agents in other functional gastrointestinal disorders (for example, functional dyspepsia, esophageal motility disorders, and anorectal disorders) is not well established, requires further study, and must be determined on an individual basis. Because of their central analgesic effects, however, antidepressant agents may help when symptoms are severe and refractory.

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Recognition of IgD and Periodic Fever

To the Editor: The hyperimmunoglobulinemia D and periodic fever syndrome (HIDS) is characterized by recurrent febrile attacks with abdominal symptoms, joint involvement, skin lesions, and lymphadenopathy. The syndrome has been diagnosed in 66 patients, most from Europe (1). The clinical picture and the elevated serum IgD levels (>100 U/mL) complete the diagnosis. Although no treatment is available, a correct diagnosis removes uncertainty and allows the patient to be informed on the benign prognosis of the syndrome.

To our knowledge, HIDS has been diagnosed in only two patients in the United States (2). Although population variation may explain the lack of cases, we believe that under-reporting of cases plays a substantial role. Possible reasons for such under-reporting include lack of awareness and limited availability of reliable IgD determinations. For example, on the basis of a case history and examination of a serum sample, only 6 of 85 Dutch laboratories could diagnose HIDS correctly. Few specialized laboratories in the United States routinely measure IgD levels. In one study (3), laboratories were asked about measurement of IgD levels. All laboratories used one radial immunodiffusion method to assess IgD and measured only a few (<20) samples weekly (3). Although this method has a limited sensitivity, the range of serum IgD levels in HIDS is such that the diagnosis should be made. However, most samples in the United States are shipped, and IgD is susceptible to spontaneous fragmentation during storage due to proteolytic enzymes that are present in serum and may influence the results (4). This problem is avoided in a recently developed enzyme-linked immunosorbent assay (ELISA) used to determine IgD levels in human serum. We use a commercial monoclonal antibody that binds to Fc regions of IgD (Dako, Copenhagen, Denmark) and human serum with known IgD concentration (Behring, Marburg, Germany) as a reference. The lower limit of detection with our ELISA is 3 U/mL.

We found that storing IgD for as long as 5 months or repeated freeze-thawing cycles had no influence on the detection of IgD. This suggests that fragmentation does not influence the results of our assay. The use of an accurate ELISA for measuring IgD levels could enhance recognition of cases of HIDS in the United States.

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Meta-Analysis and Bouillabaisse

To the Editor: In his thoughtful editorial on the recent controversy over calcium channel blockers (1), Dr. Messerli correctly points out that the research methods used in two recent studies on this topic (2, 3) are prone to various biases. Although we agree with the general comments made in the editorial, we make three points about the case–control study by Psaty and colleagues (2).

Dr. Messerli states that this study may have been subject to selection bias and that hypertensive patients with coronary artery disease may have been more likely to be treated with calcium antagonists than with diuretics. Psaty and colleagues, however, present results that address this concern: Among persons with cardiovascular disease, 52.5% were receiving diuretics and only 37.4% were receiving calcium channel blockers. Furthermore, all persons with known cardiovascular disease were excluded from the study's principal analysis.

A second form of bias that can arise in case–control studies is recall bias, in which differential recollection of previous exposures can lead to spurious associations between disease and exposure variables. Although recall bias may have affected the recording of potential confounding variables, the exposure variable of medication use was determined from computerized pharmacy data, not from patient recall.

Finally, Psaty and colleagues did their study on a well-defined patient sample—enrollees in the Group Health Cooperative of