

The Reply



We appreciate Matuchansky's interest in our recent *American Journal of Medicine* review on irritable bowel syndrome.¹ We agree completely with his comment that the mixed and alternating subtypes of irritable bowel syndrome, as defined by the Rome criteria, are common in both tertiary referral practices and the community, and may account for as many as 50% of irritable bowel syndrome patients.² We concur with the notion that some presumed "mixed" irritable bowel syndrome patients indeed are constipation-predominant patients who experience looser, or more frequent stools after successful mobilization of the constipated bowel. In these instances a careful history is paramount in establishing this clinical pattern, and should be followed by initiation of an appropriate peripherally acting treatment regimen focused on laxative and secretagogue medications. Still, true cases of mixed-pattern irritable bowel syndrome do exist; although peripherally targeted approaches in such patients admittedly are less satisfactory, alterations in stool frequency and consistency fortunately do have a tendency to trend over days to weeks, thus allowing the patient to implement antidiarrheal or laxative strategies to address the predominant bowel pattern, as indicated.

We again emphasize that the treatment approach presented in this article reflects our clinical practice influenced by our mentor Ray Clouse, and frequently uses centrally acting neuromodulators, such as the tricyclic antidepressants.³ This class of medications to date remains the most effective in modifying the global distress and pain complaints prototypical to irritable bowel syndrome. Further, antidepressants hold the

potential to modulate the neurophysiology (ie, visceral hypersensitivity) underlying the disorder.⁴ Although diarrheal-predominant patients may benefit from the constipating anticholinergic effects of these medications, we frequently invoke similar antidepressant strategies in constipation-predominant and mixed/alternating irritable bowel syndrome patients as well. In these cases the patient may be converted from a mixed pattern to constipation-predominant irritable bowel syndrome, allowing initiation of a secretagogue or laxative in conjunction with the neuromodulator. Infrequently do we find this constipating effect to preclude use of antidepressants in nondiarrheal irritable bowel syndrome patients; rather, the implementation of more aggressive anticonstipation regimens (dietary and/or medications) can successfully address this predictable effect in the majority of cases.

Gregory S. Sayuk, MD, MPH^{a,b,c}

C. Prakash Gyawali, MD, MRCP^a

^aDivision of Gastroenterology
Washington University School of Medicine
St. Louis, Mo

^bDepartment of Psychiatry
Washington University School of Medicine
St. Louis, Mo

^cJohn Cochran Veteran Affairs Medical Center
St. Louis, Mo

<http://dx.doi.org/10.1016/j.amjmed.2015.09.017>

References

1. Sayuk GS, Gyawali CP. Irritable bowel syndrome: modern concepts and management options. *Am J Med.* 2015;128:817-827.
2. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology.* 2006;130:1480-1491.
3. Clouse RE, Lustman PJ. Use of psychopharmacological agents for functional gastrointestinal disorders. *Gut.* 2005;54(9):1332-1341.
4. Hoshino H, Obata H, Saito S. Antihyperalgesic effect of duloxetine and amitriptyline in rats after peripheral nerve injury: influence of descending noradrenergic plasticity. *Neurosci Lett.* 2015;602:62-67.

Funding: None.

Conflict of Interest: None.

Authorship: Both authors had access to the data and a role in writing the manuscript.