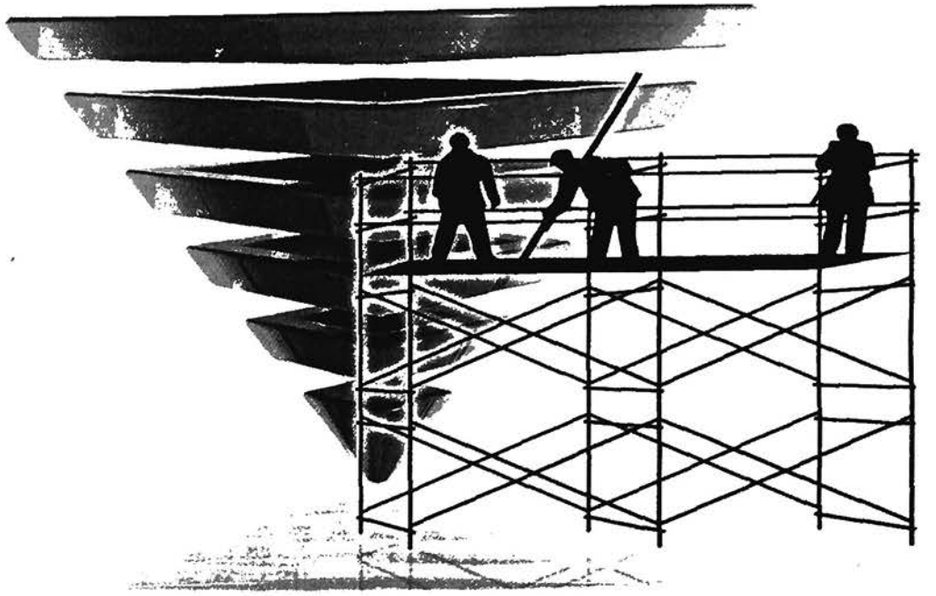
Time To Rebuild Ancient Pyramids



To the Editor:

The classic inflammatory bowel disease (IBD) treatment pyramid presented at every professional meeting that we have attended during the past 35 years has suggested that the foundational layers of IBD management include aminosalicylates, antibiotics, steroids and immunomodulatory therapy, which have historically been the treatment substructure for Crohn's disease and ulcerative colitis. Only after the FDA approval of infliximab in 1998 was this pyramid inverted to suggest a top-down approach, with a precarious balancing act on the tip of an otherwise stable and steady structure.

Newer, targeted biologics preventing trafficking of certain subpopulations of inflammatory T-cells, as well as targeting specific pro-inflammatory cytokines, have been tested in numerous clinical trials. Although biological advances in treating these diseases have transformed the lives of some patients, the limited efficacy, lack of durability, unknown long-term safety issues and enormous cost constraints demand that we question how to redesign this pyramid. Should we turn it upside down, erect a new and solid framework, or simply renovate the pyramid layers to include a customized bedrock?

It is clear in our decades of experience that patients with IBD need a personalized blueprint. Understanding the pathogenesis, genetic factors and environmental interactions in the early stages of this disease is fundamental in designing specific and unique therapies for each and every patient. The idea of a customized plan, although idealistic, in the current fiscal environment may not be tenable.

The specific treat-to-target paradigm involves measurements of drug levels of small molecules and their antibodies, and so far has been cost-prohibitive and not of proven benefit in terms of outcomes for our patients. Most of the IBD community would agree that immunomodulatory therapy is of unproven efficacy in induction and maintenance of remission apart from steroid sparing in IBD; aminosalicylates have minimal or no value in Crohn's induction and maintenance therapy. Steroids have induction benefits in IBD, but long-term therapy has clear safety concerns that outweigh those benefits.

An affordable method for detecting disease with simple serologic and other noninvasive measures is warranted. Controlling environmental factors, including diet, stress, smoking and narcotic dependence, with appropriate collaborative efforts in these areas, is mandatory to achieve better results. An initiative among IBD specialists, in our view, should include allocation of resources and attention—particularly research funding—to provide safer and more effective alternatives for our patients. We have an opportunity to apply unique, novel therapies using agents to repair the mucosal defect and to upregulate natural defenses and other regulators of the deranged cellular immunity. Improving our understanding of the specific role of commensal and other potentially pathogenic microbes should also be a high priority area of exploration.

The bottom line is this: With all of our knowledge and advances in the treatment of patients with inflammatory bowel disease, we still need more research and discovery on causation and a cure for these patients. We need to replace the crumbling pyramid with a new edifice built with integrity, good science and novel therapies.

Ira Shafran, MD
Patricia Burgunder, ARNP
The authors are with the University of Central Florida College of Medicine, in Orlando.