

# Gastroenterology

Volume 158 / Number 1

January 2020

[www.gastrojournal.org](http://www.gastrojournal.org)

## Contents

### ON THE COVER



See Hirano et al on page 111 for additional information.

### COVERING THE COVER

1 A. T. Chan and C. S. Williams

### COMMENTARIES

- 4 Screening for Upper Gastrointestinal Malignancies in the United States—Which Immigrant Groups Should Be Considered High-Risk?  
*M. Laszkowska, A. Oh, and C. Hur*
- 9 Developing Quality Metrics For Upper Endoscopy  
*P. Sharma, S. Parasa, and N. Shaheen*
- 14 How Can Individuals and the GI Community Reduce Climate Change?  
*J. A. Williams, J. Y. Kao, and M. B. Omary*

### MEETING SUMMARIES

- 18 FDA Town Hall—New Drug Approvals in Gastrointestinal Disease (2018–2019)  
*M. S. Harris and C. W. Howden, With the contributions of the Division of Gastroenterology and Inborn Errors Products, Office of New Drugs, Center for Drug Evaluation and Research*
- 22 Controversies Around Measuring Drug Toxicity: US Food and Drug Administration and Gastrointestinal Perspectives  
*AGA Clinical Practice Section in Collaboration With the United States Food and Drug Administration*
- 28 2019 Gut Microbiota for Health World Summit  
*G. M. Fuhler and G. A. Hecht, on behalf of the 2019 Gut Microbiota for Health World Summit Meeting Summary Writing Group*



Video



Related article in CGH



Hot Papers From New Investigators



CME quiz



Editorial accompanies this article



Additional online content available



Cover

Publisher: *Gastroenterology* (ISSN 0016-5085) is published monthly (semi monthly in January and May) in two indexed volumes by Elsevier Inc, 230 Park Avenue, New York, NY 10169-0901, USA. Periodicals postage paid at New York, NY and additional mailing offices. POSTMASTER: Send address changes to Elsevier, Journal Returns, 1799 Highway 50 East, Linn, MO 65051, USA. 2020 US subscription rates: individual, \$739.00; student and resident, \$282.00. Outside of the U.S. and possessions: individual, \$968.00; student and resident, \$562.00; surface delivery, no additional charge; air mail delivery, add \$78.00. Prices subject to change without notice.

**MENTORING, EDUCATION, AND TRAINING CORNER**

- 32 How to Approach Burnout Among Gastroenterology Fellows  
*A. J. DeCross*

**EDITORIALS**

- 36 A Minty Breath of Fresh Air for Irritable Bowel Syndrome  
*B. D. Cash*  
See Weerts ZZRM et al on page 123.

- 38 Colonoscopy for Lower Gastrointestinal Bleeding—Time Is Not of the Essence  
*L. Laine*  
See Niikura R et al on page 168.

- 40 Are Noninvasive Scoring Systems for Persons With Chronic Liver Disease Ready for Prime Time?  
*Z. M. Younossi and L. Henry*  
See Hagström H et al on page 200.

- 42 Is Tenofovir Superior to Entecavir in Reducing the Risk of Hepatocellular Carcinoma in Chronic Hepatitis B? The Controversy Continues  
*P. Lampertico and G. V. Papatheodoridis*  
See Yip TC-F et al on page 215.

- 44 Does Pancreatic Cyst Stability Justify Stopping Intraductal Papillary Mucinous Neoplasm Surveillance?  
*J. J. Farrell*  
See Oyama H et al on page 226.

- 46 Know Thy Enemy—Understanding the Role of Inflammation in Severe Acute Pancreatitis  
*S. Iyer, E. P. Bawa, M. Tarique, and V. Dudeja*  
See Sendler M et al on page 253.

- 48 Untangling the 2-Way Relationship Between Red Wine Polyphenols and Gut Microbiota  
*N. Naumovski, D. B. Panagiotakos, and N. M. D'Cunha*  
See Le Roy CI et al on page 270.

- 51 Can We Cross Off Common Kitchen Practices as Causes of Gluten Cross-Contact?  
*B. D. McDonald and S. S. Kupfer*  
See Weisbrod VM et al on page 273.

**CLINICAL CHALLENGES AND IMAGES IN GI**

- 54 An Unusual Web Stricture in the Cervical Esophagus  
*Y. Umeda, K. Tanaka, and R. Yamada*

- 56 Septic Shock After Travel to Rural Africa  
*B. Quach, S. Han, and A. Attwell*

- 58 Crohn's Disease With Progressive Renal Impairment  
*J. B. Seidelin, L. B. Riis, and R. A. Butt*

- 60 Endoscopic Finding of a Double Lumen in the Esophagus  
*A. V. Patel and I. Dalal*

**ELECTRONIC CLINICAL CHALLENGES AND IMAGES IN GI**For a full list, please see the table of contents online at [www.gastrojournal.org](http://www.gastrojournal.org).**PRACTICAL TEACHING CASES**

- 62 A Case of Unremitting Diarrhea**  
*A. R. Sondhi, L. J. Nayak, and M. D. Rice*

- 65 Superficially Deceiving Gastric Lesion—What Lies Beneath?**  
*I. Pita, L. P. Afonso, and P. Pimentel-Nunes*

**AGA CLINICAL PRACTICE UPDATE: EXPERT REVIEW**

- 67 American Gastroenterological Association Clinical Practice Update: Management of Pancreatic Necrosis**  
*T. H. Baron, C. J. DiMaio, A. Y. Wang, and K. A. Morgan*

**REVIEWS AND PERSPECTIVES****Reviews in Basic and Clinical Gastroenterology and Hepatology**

- 76 Application of Artificial Intelligence to Gastroenterology and Hepatology**  
*C. Le Berre, W. J. Sandborn, S. Aridhi, M.-D. Devignes, L. Fournier, M. Smail-Tabbone, S. Danese, and L. Peyrin-Biroulet*
- 95 Protein Glycosylation as a Diagnostic and Prognostic Marker of Chronic Inflammatory Gastrointestinal and Liver Diseases**  
*X. Verhelst, A. M. Dias, J.-F. Colombel, S. Vermeire, H. Van Vlierberghe, N. Callewaert, and S. S. Pinho*

**ORIGINAL RESEARCH****Full Reports****Clinical—Alimentary Tract**

- 111 Efficacy of Dupilumab in a Phase 2 Randomized Trial of Adults With Active Eosinophilic Esophagitis**  
*I. Hirano, E. S. Dellon, J. D. Hamilton, M. H. Collins, K. Peterson, M. Chehade, A. M. Schoepfer, E. Safroneeva, M. E. Rothenberg, G. W. Falk, Y. Assouline-Dayan, Q. Zhao, Z. Chen, B. N. Swanson, G. Pirozzi, L. Mannent, N. M. H. Graham, B. Akinlade, N. Stahl, G. D. Yancopoulos, and A. Radin*

Dupilumab is safe and effective for treatment of EoE, reducing symptoms and also correcting clinical and structural abnormalities associated with this disease.

- 123 Efficacy and Safety of Peppermint Oil in a Randomized, Double-Blind Trial of Patients With Irritable Bowel Syndrome**  
*Z. Z. R. M. Weerts, A. A. M. Masclee, B. J. M. Witteman, C. H. M. Clemens, B. Winkens, J. R. B. J. Brouwers, H. W. Frijlink, J. W. M. Muris, N. J. De Wit, B. A. B. Essers, J. Tack, J. T. W. Snijkers, A. M. H. Bours, A. S. de Ruiter-van der Ploeg, D. M. A. E. Jonkers, and D. Keszthelyi*

**See editorial on page 36.**

Peppermint oil does not significantly reduce abdominal pain or overall symptoms of relief in patients with IBS, according to the strict endpoints recommended by regulatory authorities. Small-intestinal release peppermint oil does, however, reduce abdominal pain, discomfort, and IBS symptom severity.

- 137 Histopathology Scoring Systems of Stenosis Associated With Small Bowel Crohn's Disease: A Systematic Review**  
*I. O. Gordan, D. Bettenworth, A. Bokemeyer, A. Srivastava, C. Rosty, G. de Hertogh, M. E. Robert, M. A. Valasek, R. Mao, S. Kurada, N. Harpaz, P. Borralho, R. K. Pai, R. K. Pai, R. Odze, R. Feakins, C. E. Parker, T. Nguyen, V. Jairath, M. E. Baker, D. H. Bruining, J. G. Fletcher, B. G. Feagan, and F. Rieder, on behalf of the Stenosis Therapy and Anti-Fibrotic Research (STAR) Consortium*

There are no good histopathologic scoring systems to determine the degree of fibromuscular stenosis and/or inflammation in patients with Crohn's disease.

151

- Community-Based Study of Celiac Disease Autoimmunity Progression in Adults**  
*R. S. Choung, S. Khaleghi, A. K. Cartee, E. V. Marietta, J. J. Larson, K. S. King, O. Savolainen, A. B. Ross, S. V. Rajkumar, M. J. Camilleri, A. Rubio-Tapia, and J. A. Murray*

The risk of celiac disease development is very low – even among adults with positive results from blood tests.

160

- Validation of a Machine Learning Model That Outperforms Clinical Risk Scoring Systems for Upper Gastrointestinal Bleeding**

*D. L. Shung, B. Au, R. A. Taylor, J. K. Tay, S. B. Laursen, A. J. Stanley, H. R. Dalton, J. Ngu, M. Schultz, and L. Laine*

We used machine learning to analyze data from patients with upper gastrointestinal bleeding and identify those at risk for hospital-based intervention or death within 30 days.

168

- Efficacy and Safety of Early vs Elective Colonoscopy for Acute Lower Gastrointestinal Bleeding**

*R. Niikura, N. Nagata, A. Yamada, T. Honda, K. Hasatani, N. Ishii, Y. Shiratori, H. Doyama, T. Nishida, T. Sumiyoshi, T. Fujita, S. Kiyotoki, T. Yada, K. Yamamoto, T. Shinozaki, M. Takata, T. Mikami, K. Mabe, K. Hara, M. Fujishiro, and K. Koike*

**See editorial on page 38.**

We found that early colonoscopy which was performed within 24 h of admission did not improve identification of stigmata of recent hemorrhage or rebleeding risk compared with elective colonoscopy in acute lower gastrointestinal bleeding patients.

176

- Effects of Low FODMAP Diet on Symptoms, Fecal Microbiome, and Markers of Inflammation in Patients With Quiescent Inflammatory Bowel Disease in a Randomized Trial**

*S. R. Cox, J. O. Lindsay, S. Fromentin, A. J. Stagg, N. E. McCarthy, N. Galleron, S. B. Ibraim, H. Roume, F. Levenez, N. Pons, N. Maziers, M. C. Lomer, S. D. Ehrlich, P. M. Irving, and K. Whelan*

The low FODMAP diet improved certain non-inflammatory gut symptoms in quiescent IBD. Although the diet impacted the gut microbiome, it did not affect markers of gut inflammation.

189

- HLA-DQA1\*05 Carriage Associated With Development of Anti-Drug Antibodies to Infliximab and Adalimumab in Patients With Crohn's Disease**

*A. Sazonovs, N. A. Kennedy, L. Moutsianas, G. A. Heap, D. L. Rice, M. Reppell, C. M. Bewshea, N. Chanchlani, G. J. Walker, M. H. Perry, T. J. McDonald, C. W. Lees, J. R. F. Cummings, M. Parkes, J. C. Mansfield, P. M. Irving, J. C. Barrett, D. McGovern, J. R. Goodhand, C. A. Anderson, T. Ahmad, and PANTS Consortium*

We identified a genetic variant that increases risk of development of antibodies against anti-TNF agents, which reduces their effectiveness in treatment of Crohn's disease.

## Clinical—Liver

- 200 Ability of Noninvasive Scoring Systems to Identify Individuals in the Population at Risk for Severe Liver Disease**

*H. Hagström, M. Talbäck, A. Andreasson, G. Walldius, and N. Hammar*

**See editorial on page 40.**

New scoring systems are needed to evaluate risk of fibrosis in the general population and in primary care, but current scores can be useful in predicting events in a subsample of persons with risk factors for NAFLD.

215

- Tenofovir Is Associated With Lower Risk of Hepatocellular Carcinoma Than Entecavir in Patients With Chronic HBV Infection in China**

*T. C.-F. Yip, V. W.-S. Wong, H. L.-Y. Chan, Y.-K. Tse, G. C.-Y. Lui, and G. L.-H. Wong*

**See editorial on page 42.**

Tenofovir disoproxil fumarate treatment is associated with a lower risk of hepatocellular carcinoma than entecavir treatment in a territory-wide cohort of Chinese patients with chronic hepatitis B.

**Clinical—Pancreas****226 Long-term Risk of Malignancy in Branch-Duct Intraductal Papillary Mucinous Neoplasms**

  *H. Oyama, M. Tada, K. Takagi, K. Tateishi, T. Hamada, Y. Nakai, R. Hakuta, H. Ijichi, K. Ishigaki, S. Kanai, H. Kogure, S. Mizuno, K. Saito, T. Saito, T. Sato, T. Suzuki, N. Takahara, Y. Morishita, J. Arita, K. Hasegawa, M. Tanaka, M. Fukayama, and K. Koike*

**See editorial on page 44.**

Branch-duct intraductal papillary mucinous neoplasms have a high risk of developing into different types of pancreatic cancer and should be followed for long periods of time.

**Basic and Translational—Alimentary Tract****238 Mutated CEACAMs Disrupt Transforming Growth Factor Beta Signaling and Alter the Intestinal Microbiome to Promote Colorectal Carcinogenesis**

  *S. Gu, S. Zaidi, M. I. Hassan, T. Mohammad, T. M. Malta, H. Noushmehr, B. Nguyen, K. A. Crandall, J. Srivastav, V. Obias, P. Lin, B.-N. Nguyen, M. Yao, R. Yao, C. H. King, R. Mazumder, B. Mishra, S. Rao, and L. Mishra*

We identified a mutant protein in colorectal adenocarcinoma cells that blocks a pathway that regulates proliferation and expansion of the cells, and increases amounts of bacterial species that have been associated with development of colon tumors.

**Basic and Translational—Pancreas****253 NLRP3 Inflammasome Regulates Development of Systemic Inflammatory Response and Compensatory Anti-Inflammatory Response Syndromes in Mice With Acute Pancreatitis**

  *M. Sendler, C. van den Brandt, J. Glaubitz, A. Wilden, J. Golchert, F. U. Weiss, G. Homuth, L. L. De Freitas Chama, N. Mishra, U. M. Mahajan, L. Bossaller, U. Völker, B. M. Bröker, J. Mayerle, and M. M. Lerch*

**See editorial on page 46.**

We identified immune mechanisms that contribute to the development of inflammation in patients with severe pancreatitis and found therapeutic agents that can reduce this response.

**CONTINUING MEDICAL EDUCATION (CME)/MOC ACTIVITIES****e14 CME Exam 1: A Case of Unremitting Diarrhea****e16 CME Exam 2: Superficially Deceiving Gastric Lesion—What Lies Beneath?****e17 CME Exam 3: Histopathology Scoring Systems of Stenosis Associated With Small Bowel Crohn's Disease: A Systematic Review****e18 CME Exam 4: Ability of Noninvasive Scoring Systems to Identify Individuals in the Population at Risk for Severe Liver Disease****BRIEF COMMUNICATIONS****270 Red Wine Consumption Associated With Increased Gut Microbiota  $\alpha$ -Diversity in 3 Independent Cohorts**

  *C. I. Le Roy, P. M. Wells, J. Si, J. Raes, J. T. Bell, and T. D. Spector*

**See editorial on page 48.**

**273 Preparation of Gluten-Free Foods Alongside Gluten-Containing Food May Not Always Be as Risky for Celiac Patients as Diet Guides Suggest**

  *V. M. Weisbrod, J. A. Silvester, C. Raber, J. McMahon, S. S. Coburn, and B. Kerzner*

**See editorial on page 51.**

**SELECTED SUMMARIES**

- 276 **Peroral Endoscopic Myotomy versus Pneumatic Dilation in Achalasia: Dissecting the Randomized Controlled Trial**  
*R. Yadlapati and S. Gupta*
- 278 **Prediction of Inflammatory Bowel Disease: A Step Closer?**  
*J. Torres*

**CORRESPONDENCE**

- 280 **Organ Preservation in Early Esophageal Cancer**  
*M. Barret, J.-E. Bibault, and R. Coriat*
- 280 **Reply**  
*M. Muto and K. Minashi*
- 281 **Simplified Magnetic Resonance Index of Activity for Crohn's Disease—Let's Try to Kick It Up a Notch**  
*S. H. Park and S. H. Park*
- 282 **The Simplified Magnetic Resonance Index of Activity (MARIA) for Crohn's Disease Is Strongly Correlated With the MARIA and Clermont Score: An External Validation**  
*N. Williet, S. Jardin, and X. Roblin*
- 283 **Pantoprazole in Prevention of Gastroduodenal Events in Patients Receiving Rivaroxaban and/or Aspirin—A Short Word of Caution**  
*M. Bronswijk*
- 284 **Pantoprazole in COMPASS—No Prevention of Gastroduodenal Events or Other Useful Net Results**  
*A. Donzelli and G. Giudicatti*
- 285 **Reply**  
*P. Moayyedi, J. W. Eikelboom, and S. Yusuf*
- 286 **Corrections**

**Access to the full content of *Gastroenterology Online* is available to all subscribers!**

AGA members have seamless access to full *Gastroenterology* content from the AGA Web site. Simply sign in to <http://www.gastro.org>, visit the Publications section of the Web site, and click on *Gastroenterology*. You will be directed to the Journal Web site and will have full access to all content without having to supply a different username and password. Members can also visit <http://www.gastrojournal.org> directly and click on "Activate Online Access." Nonmember subscribers must create an online user account and activate their subscription to access the full text of articles on *Gastroenterology Online*. To activate your individual online subscription, please visit <http://www.gastrojournal.org> and click on "Activate Online Access." To activate your account, you

will need your subscriber account or member number, which you can find on your mailing label (AGA members must use their 10-digit member number, including leading zeros). If you have any questions regarding your online subscription please call Elsevier Customer Service at (800) 654-2452.

Institutional access to *Gastroenterology Online* will be allowed only by limited site licensing. Further instructions will be available online. Personal subscriptions to *Gastroenterology Online* are for individual use only and may not be transferred. Use of *Gastroenterology Online* is subject to agreement to the terms and conditions of use as indicated online.

**AGA Member Number**

**Sample  
mailing  
label**

GAST0000101864

JANE DOE  
531 MAIN ST  
CENTER CITY, NY 10001-001

**Your Account Number**

1GAST V91-4 1234567-8  
JANE DOE  
531 MAIN ST  
CENTER CITY, NY 10001-001