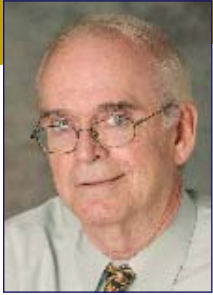


Division of Gastroenterology



J. Thomas Lamont, MD,
Chief

● Overview

The Gastroenterology Division at Beth Israel Deaconess Medical Center is one of the largest academic units in the United States on the basis of clinical activity, number and expertise of faculty, and breadth of research activities. The Division employs 32 physicians and 7 research faculty, 14 clinical and research fellows, and 35 research associates and technicians.

The goals of the Division are: 1) to provide compassionate, timely and cost-effective patient care; 2) to carry out cutting-edge clinical and basic research on gastrointestinal diseases and processes; 3) to teach the science and art of our specialty to students, post-graduate trainees, and to our colleagues; and 4) to provide a nurturing environment for the career development of our faculty. The Division organizes its clinical and academic activities under the leadership of J. Thomas Lamont, Chief of the Division; Myron Falchuk, Director of Clinical Services; Ram Chuttani, Chief of Endoscopy; Nezam Afdhal, Director of the Liver Center; Ciaran Kelly, Director of Fellowship Training, and Eileen Joyce, Administrative Director. By consolidating and improving the efficiency of our merged clinical operations, we have experienced a remarkable growth in patient volume over the past 10 years. In that same interval, we have tripled our research funding and increased our fellowship program from three to four fellows per year.

Michael Curry is the Liver Center Clinical Director. Outpatient GI and Liver consults are provided on both east and west campuses, as well as in our practice satellites in Lexington and Chelsea. The Division is regularly listed in the top twenty in the annual ranking by *US News and World Report*. The Liver Center works in close collaboration with the Liver Transplantation Service in the Department of Surgery to provide support for patients with end-stage liver disease who require transplantation. The GI Division has large referral practices in inflammatory bowel disease, motility disorders, celiac disease and pancreatic diseases. A multidisciplinary approach involving gastroenterologists, surgeons, radiologists and pathologists is provided for patients with complex pancreatic and biliary diseases.

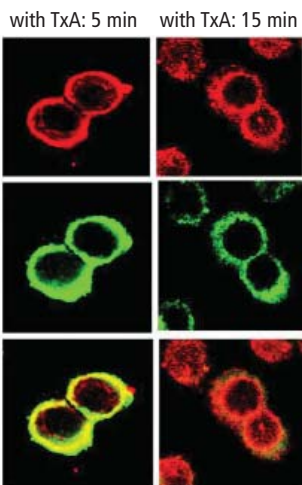
A major clinical activity of the Division is endoscopy and other GI and liver tests, including liver biopsy, breath tests and motility tests. A new state-of-the-art Endoscopy Unit was opened in early 2008 and provides our patients and physicians with a modern and patient-friendly facility that is one of the most advanced and busiest in the New England region. Our Endoscopy Unit has one of the highest procedure volumes nationwide, and is well known for its highly skilled and successful treatment of patients referred for advanced endoscopic procedures. Janet Lewis is nurse manager of GI Endoscopy at BIDMC, and supervises a professional team of 48 nurses, technicians, practice assistants and other staff.

● Clinical Activities

The GI Division has one of the largest referral practices in the United States, seeing 28,000 outpatients and performing 25,000 procedures annually, including more than 2300 ERCP and EUS procedures. Myron Falchuk is Director of Clinical Operations in GI, and

● Quality Improvement

Quality assessment and improvement in the GI Division are overseen by Stanley Rosenberg, Richard Doyle and Dan Leffler, who provide regular feedback to staff regarding quality of our service, and measures to improve our out-



● Confocal microscopy of *Clostridium difficile* toxin A binding to intestinal epithelial cell surface GP96. Na et al. *Infection and Immunity* 2008.

comes. A major GI quality assessment initiative in 2007 was directed at safety and outcomes of colonoscopy. We assessed procedural complications such as perforation and hemorrhage during 2500 colonoscopies. The rates of these complications were markedly lower at BIDMC compared to published national standards. A quality improvement campaign has been initiated to increase safety and accuracy by monitoring and improving withdrawal time during colonoscopy. Another important quality assessment program is directed at improving patient access to our clinicians, and patient satisfaction with their experiences in our office practice and endoscopy suites. Although our patient access is one of the best in the area, Eileen Joyce our GI Division administrative director and her staff are constantly working to improve the "patient friendly" quality of GI services, as well as our ability to respond quickly to referring community and BIDMC physicians.

● *Educational Programs*

The Gastroenterology Division sponsors one of the most competitive fellowship training programs in the country, under the direction of Ciaran Kelly and Douglas Horst. Supported by an NIH T32 Training Grant, the program has twelve fellows, four in each of the three years. The program offers three distinct pathways for fellows who wish to pursue academic careers as: 1) basic researchers, 2) clinical or translational researchers, or 3) clinician/teachers. The division also offers advanced one-year fellowships in liver disease, therapeutic endoscopy, motility or IBD. One of the major criteria used to select fellows for our program is academic potential as evidenced by commitment to research and teaching. Approximately three fourths of our graduates enter academic full-time careers after graduation at top academic centers across the country and abroad.

After the completion of basic clinical training in the first year, fellows begin two to three years of mentored basic or clinical research training with intense hands-on experience. Trainees are supervised by experienced faculty mentors with a wide range of interests and expertise from basic cellular and molecular biology to

clinical and translational research. A training committee consisting of Ciaran Kelly, Thomas Lamont, Cox Terhorst and Simon Robson supervises trainee selection and monitors each trainee's research progress. A rich menu of didactic courses, seminars, and conferences is also provided for trainees. Research training for GI fellow is supported by an NIH T32 Training Grant (Program Director Ciaran Kelly) which provides salary support for 4 MD or PhD post-doctoral researchers each year. Clinical research training is supported by the "Clinical Investigator Training Program" at BIDMC, and by the "Scholars in Clinical Science" program at Harvard School of Public Health. Both of these programs provide a structured, two year curriculum for GI fellows after completion of clinical training with a combination of didactic



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● Drs. Myron Falchuk and Thomas Lamont review an endoscopy report.

instruction and a mentored clinical research project. GI Fellows in these two pathways are required to write a thesis for a master's degree from Harvard School of Public Health.

Medical student education in gastroenterology and liver diseases is supervised by Helen Shields, one of the leading teachers at Harvard Medical School and course director of the second year medical school course "Gastrointestinal Pathophysiology". This course is annually cited as one of the highest rated

courses by our medical students. GI Fellows interested in the teacher/clinician pathway are offered teaching opportunities in years 2 and 3 of training. Fellows serve as discussion group leaders or as seminar discussants for medical students, and are regular participants in introductory clinical examination courses, and also participate in teaching medical students and residents on GI and Liver electives.

Sanjiv Chopra, a faculty member in the Liver Center, is Faculty Dean for Continuing Medical Education at Harvard. He has a leadership position in organizing post-graduate courses, including the annual "Advances in Gastroenterology" course, one of the longest standing and most popular courses of its kind in the country. The Liver Center annually hosts several scientific courses in liver disease focused on research in fibrosis and treatment of viral hepatitis. Ram Chuttani and Douglas Pleskow offer several unique live endoscopy courses yearly that draw participants and faculty from all over the world.

● *Research Activities*

The GI Division has active basic science, translational and clinical research programs, supported by extramural funding of \$6.5 million in 2007. A total of 13 faculty members engaged in basic research are supported by 21 grants from NIH, with additional grant support from disease-related foundations and industry. The GI Division Basic Research Program occupies 14,000 square feet of laboratory space and is responsible for research training of 20 post-doctoral fellows in gastroenterology and basic research in GI-related areas. GI Division researchers are recognized nationally and internationally for their clinical and research contributions and are invited frequently to participate in international symposia and courses, and to serve on NIH, FDA and foundation-based grant review committees.

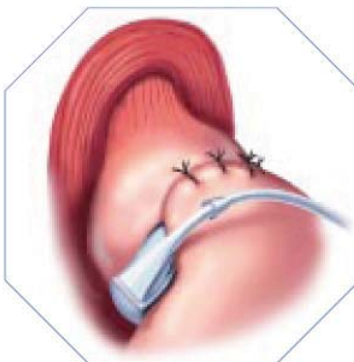
Basic science research in GI is led by eleven senior faculty principal investigators, all of whom receive substantial extramural research support. Nezam Afdhal's laboratory is exploring the contribution of mucin glycoproteins

<i>Research Funding • AY'07</i>	
Federal Direct	2,927,769
Federal Indirect	1,492,353
Other Direct	2,772,893
Other Indirect	454,443

to cholesterol gallstone nucleation, and the biophysics of mucin polymerization and gelation. Steven Freedman studies basic secretory mechanisms of pancreatic ductular secretion and the role of fatty acids and eicosanoids in cystic fibrosis. Alphonso Brown specializes in pancreatic diseases and is exploring the role of endothelial cell molecules in the pathophysiology of acute pancreatitis and also as an early marker of severe acute pancreatitis. Ciaran Kelly's group, including Andrew and Sarah Keates, studies various aspects of intestinal immune responses to *Clostridium difficile* infections and bacterial pathogenesis of *Helicobacter pylori*. Daryl Lau's laboratory collaborates with investigators in the Infectious Diseases Division on immunopathogenesis of hepatitis B virus. Efi Kokkotou studies how the brain-gut neuropeptides interact with adipocyte, neuronal and epithelial receptors to cause or amplify intestinal inflammation. Dezheng Zhou and colleagues are investigating the role of a novel orphan receptor Nurr-1 in cancer angiogenesis. Simon Robson and Keiichi Enyoji explore basic themes in xenotransplantation and vascular biology, particularly the role of endothelial cell ectonucleotidases in thromboses, inflammation and liver disease. Detlef Schuppan's research group, including faculty member Yuri Popov, explores the immunopathogenesis of celiac disease and mechanisms of liver injury related to fibrosis and cirrhosis. David Wang studies basic mechanisms of cholesterol gallstone disease including hormonal and genetic contributions to lithogenesis in mice and humans. Thomas Lamont's laboratory is investigating the pathophysiology of *Clostridium difficile* infections, and the role of toxin receptors in causing colitis. The newly formed Skip Ackerman Center for Molecular Therapeutics in the GI Division has as its major goal the development and testing of new drugs to treat GI cancer, inflam-



● Combined biliary and duodenal metal stenting to palliate pancreatic cancer



● Laparoscopic Treatment for Obesity

mation and infection. The Center is directed by Chiang Li and Andrew Keates and is currently preparing to initiate a trial of a novel RNA inhibitor to treat familial intestinal polyposis.

The GI Division also has a well-funded and productive clinical research group of ten faculty investigators. Nezam Afdhal and his faculty co-investigators Michael Curry, Diarmuid Manning and Gerond Lake-Bakaar in the Liver Center conduct clinical trials in viral hepatitis and cirrhosis. The Pancreas Center, under the direction of Steven Freedman, and with Alphonso Brown carry out studies of genetic profiles in pancreatitis, and new forms of therapy for chronic pancreatitis and cystic fibrosis. Ram Chuttani, Douglas Pleskow and Mandeep Sawhney in the Center for Interventional Endoscopy and the Swallowing Center are conducting trials of state-of-the-art technologies to treat reflux esophagitis and pancreatobiliary diseases and developing new tools for therapeutic endoscopy. The Celiac Disease Center, directed by Ciaran Kelly and Detlef Schuppan, and in collaboration with Dan Leffler, is one of the largest of its kind in the US and is testing new diagnostic tests and treatment regimens for patients with gluten-sensitive enteropathy. The Motility Center, led by Tony Lembo, is studying new drugs for gastric retention and irritable bowel syndrome (IBS), and is the clinical arm of a large NIH-funded study of the placebo effect

in IBS patients. The IBD Center, which includes Adam Cheifetz, Mark Peppercorn, Alan Moss and Ken Falchuk, is exploring new therapies for Crohn's disease and ulcerative colitis.

The GI Division plans to develop a GI Clinical Research Center to increase patient recruitment and to facilitate our multidisciplinary approach for patient management. We plan to recruit additional faculty in IBD, Motility and Liver Diseases, and to expand our large scale patient-oriented databases on patients with major GI and liver diseases.

● *Awards and Honors*

Efi Kokkotou was awarded an AGA Foundation Bridging Grant in 2007 and her first NIH-NIDDK R-01 grant in 2008. In 2007, Helen Shields was recognized by the graduating class at HMS as the Best Preclinical Instructor. Alan Moss was awarded the Excellence in Tutoring Award at Harvard Medical School in 2008. Nezam Afdhal was awarded a Fulbright Fellowship for a research program on hepatitis in Egypt. Alphonso Brown received the Robert Wood Johnson Medical Faculty Development Award and the American College of Gastroenterology Governor's Award for Excellence in Clinical Research. Andrew Keates received a FIRST Award for basic research from the Crohns and Colitis Foundation of America. Sarah Keates

● *Faculty*

Nezam Afdhal, MD	Keiichi Enyoji, PhD	Efi Kokkotou, MD, PhD, ScD	Yuri Popov, MD
Harry Anastopoulos, MD	Kenneth R. Falchuk, MD	Gerond Lake-Bakaar, MD	James Rabb, MD
Michael Apstein, MD	Myron Falchuk, MD	J. Thomas Lamont, MD	Simon Robson, MD, PhD
Alphonso Brown, MD	Steven D. Freedman, MD, PhD	Darryl Lau, MD	Stanley Rosenberg, MD
Adam Cheifetz, MD	Douglas Horst, MD	Daniel Leffler, MD	Mandeep Sawhney, MD
Catherine Cheney, MD	Gail Kaufman, MD	Tony Lembo, MD	Detlef Schuppan, MD, PhD
Sanjiv Chopra, MD	Andrew Keates, PhD	Diarmuid Manning, MD	Sunil Sheth, MD
Ram Chuttani, MD	Sarah Keates, PhD	Seema Maroo, MD	Helen Shields, MD
Michael Curry, MD	Ciaran Kelly, MD	Alan Moss, MD	Jacqueline Wolf, MD
Glen Doherty, MD	Susan Kelly, MD	Mark Peppercorn, MD	Dezheng Zhao, PhD
Richard Doyle, MD		Douglas Pleskow, MD	

received the REGAL Award from the University of Kansas and an Endowed Research Scholar Award from the AGA. Thomas Lamont was a recipient of the AGA Distinguished Mentor Award and was named an Honorary Fellow of the Royal College of Physicians of Ireland. Mark Peppercorn received the Janssen Award for outstanding achievement in Gastroenterology and the AGA Distinguished Clinician Award.

Our faculty are frequently named to "Best Doctor" lists published by *Boston Magazine* and several national publications. These GI staff have been named as "Best Gastroenterologists" in the past five years (often more than once): Nezam Afdhal, Adam Cheifetz, Sanjiv Chopra, Ram Chuttani, Kenneth Falchuk, Myron Falchuk, Douglas Horst, J. Thomas Lamont, Mark Peppercorn, Stanley Rosenberg and Jacqueline Wolf. This year Drs. Helen Shields and Jacqueline Wolf received the 2008 Outstanding AGA Women In Science award.

● *Selected Publications*

- Kokkotou E, Moss A, Torres D, Savidge T, O'Brien M, Kirkland J, Flier J, Maratos-Flier E, Pothoulakis C. Melanin-Concentrating Hormone (MCH), a neuropeptide regulating energy balance, is a major mediator of intestinal inflammation. *Proc Natl Acad Sci U S A* 2008; 105(30):10613-8.
- Keates S, Han X, Kelly CP, Keates AC. Macrophage inflammatory protein-3 α mediates epidermal growth factor receptor transactivation and ERK1/2 MAPK signaling in Caco-2 colonic epithelial cells via metalloproteinase-dependent release of amphiregulin. *J Immunol* 2007; 178:8013-8021.
- Kim H, Rhee SH, Pothoulakis C, Lamont JT. Inflammation and apoptosis in *Clostridium difficile* enteritis is mediated by PGE2 up-regulation of Fas ligand. *Gastroenterology* 2007; 133:875-86.
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- Schuppan D, Afdhal NH. Lancet Seminars: Liver cirrhosis. *Lancet* 2008; 371:838-51.
- Künzli BM, Nuhn P, Enyoji K, Banz Y, Smith RN, Csizmadia E, Schuppan D, Berberat PO, Friess H, Robson SC. Disordered Pancreatic Inflammatory Responses and Inhibition of Fibrosis in CD39-Null Mice. *Gastroenterology* 2008; 134:292-305.
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