Training in Inflammation and Enteric Infectious Diseases

Gastrointestinal inflammation, whether infectious, noninfectious, or idiopathic, is a primary mechanism of disease for many patients referred to specialists in digestive diseases. Therefore, it is imperative that trainees be exposed to diagnostic and therapeutic aspects of gastrointestinal inflammatory disorders as components of their fellowship experience. The unique aspects of gastrointestinal infections (related or not related to human immunodeficiency virus [HIV]) and idiopathic inflammatory bowel diseases (IBD) will be discussed separately. The differential diagnoses overlap due to the non-specific presentation of acute or chronic small or large bowel inflammatory disorders.

I. GASTROINTESTINAL INFECTIONS IN NON IMMUNOSUPPRESSED PATIENTS

Importance

The gastrointestinal tract is host to a large and complex microbial flora. In addition, all levels of the gastrointestinal tract (including the liver and biliary tree) are subject to acute and chronic infection by a variety of pathogenic microbial agents (viruses, bacteria, fungi, and protozoa). These infections present, acutely or chronically, as disordered organ function manifested by diarrhea, malabsorption, bleeding, or ulceration, symptoms that are commonly seen by primary care physicians and frequently are the indications for gastroenterological referral. The understanding of gastritis and duodenal ulcer disease has been revolutionized by the recognition of the role of *H. pylori*, whereas the agents responsible for some gastrointestinal diseases known to be infectious (e.g., *Tropheryma whipplei* for Whipple’s disease) have only recently been identified. Many gastrointestinal diseases currently regarded as idiopathic are likely to be the result of infection by currently unrecognized pathogens or idiosyncratic reactions of the host to normal flora. New forms of common pathogens are continually appearing, such as the toxin-producing *Escherichia coli* responsible for hemorrhagic colitis. A gastroenterological specialist, therefore, should be knowledgeable regarding the epidemiology, differential diagnoses, confirmatory diagnostic studies, therapy, and outcomes of treated and untreated gastrointestinal infections in the adult and pediatric populations.

**Goals of Training (GI Infections in Nonimmunosuppressed Patients)**

During fellowship, trainees should gain an understanding of gastrointestinal infections, including the following:

1. The mechanisms of inflammation
2. Elements of the mucosal defense system (including the mucosal immune system and the components of intestinal barrier function)
3. The composition and function of normal enteric flora (including protection against pathogens, colonization resistance, role in metabolism [nitrogen, carbohydrate, fat, vitamins, bile salts], and the effects of antibiotics on the flora)
4. The prevalence, clinical presentation, and virulence factors (including mechanism of toxin action, colonization, translocation, and invasion) of gastrointestinal pathogens (viruses, bacteria, fungi, and protozoa)
5. The pathophysiology of diarrhea due to infection
6. The indications and contraindications for antimicrobial therapy; mechanisms of microbial drug resistance, and risk of infections from altering normal flora (e.g., *Clostridium difficile*)

Clinical skills should include a familiarity with the following diagnostic and histopathologic studies (see Training in Pathology):

1. Microscopic examination of stool: fecal leukocytes and ova and parasites
2. Culture of stool, intestinal fluid, and mucosal biopsy specimens (specimen collection, handling, special stains, and media)
3. Mucosal biopsy interpretation
4. Antigen detection in stool and fluid (enzyme immunoassay, fluorescent antibody) and stool toxin testing
5. Rapid diagnostic tests (DNA probes or polymerase chain reaction)
6. Liver biopsy and interpretation (see Training in Hepatology)

Clinical skills should also encompass the selection and use of antibiotic therapy and methods for preventing infection during endoscopy (disinfection and antibiotic prophylaxis). Clinical exposure to gastrointestinal infections should include the diagnosis and management of patients with common infectious presentations, such as esophagitis (fungal, viral, bacterial); ulcer disease and gastritis (emphasizing the role of *H. pylori* and appropriate antibiotic therapies); acute, chronic, hemorrhagic, and traveler’s diarrhea; bacterial overgrowth; infections in immunocompromised hosts (e.g., transplantation patients); and hepatic inflammation (e.g., liver abscess, hepatitis, cholangitis), including the role of liver biopsy. In addition, concepts of preventive medicine, such as indications for vaccination, routes of infection, dietary and hygienic
practice for travelers, and appropriate recommendations for prophylactic antibiotic therapy, should be included in training.

Training Process
The training and experience for the diagnosis and treatment of gastrointestinal infection should include participation in the evaluation and management of outpatients and inpatients with the presentations and diagnoses listed above and should include the appropriate use of diagnostic tests, indications, complications, and application of therapy in these disorders. Additional exposure to related sciences (immunology, microbiology, and molecular biology) and related fields of medicine (infectious diseases and laboratory, anatomic, and surgical pathology) can be obtained through conferences, seminars, and literature reviews as well as practical demonstration of techniques.

II. GASTROINTESTINAL DISORDERS IN IMMUNOSUPPRESSED PATIENTS

Importance
According to a 2004 report of the World Health Organization, 40 million people worldwide are infected with HIV. AIDS is the leading cause of death of persons aged 15–59. In 2005, the National Institutes of Health reported that 40,000 new HIV infections occur annually in the United States and the infection rate in African American males has doubled over the past 10 years. Most, if not all, patients with AIDS will manifest at least one AIDS-related disorder of the gastrointestinal tract, hepatobiliary system, or pancreas. Many other patients are immunosuppressed due to congenital or acquired conditions or due to the effects of immunosuppressive drugs given to treat other ailments or to prevent rejection of transplanted organs. Many of these patients also suffer from opportunistic infections. Therefore, it is important for gastroenterological specialists to recognize and know how to evaluate and treat infections in immunosuppressed patients.

Goals of Training (GI Disorders in Immunosuppressed Patients)
During fellowship, trainees should be able to assess the broad range of gastrointestinal symptoms and signs of illness in immunosuppressed patients and be able to differentiate AIDS-related from AIDS-unrelated conditions. Esophageal disorders include infectious esophagitis (fungal, viral, HIV, and neoplasms). Trainees should be able to assess AIDS gastropathy and other infectious and neoplastic gastric disorders. They should be able to assess disorders of the small intestine, including causes of diarrhea in immunosuppressed patients; interpret endoscopic, barium, and computed tomographic and ultrasound examinations; and treat bacterial, fungal, viral, and protozoal infections of the small bowel in patients with AIDS. Trainees should also recognize causes of colorectal disorders, including proctitis, proctocolitis, and AIDS-related malignancies (e.g., Kaposi's sarcoma) and should be familiar with the indications for and interpretation of flexible sigmoidoscopic, colonoscopic, and radiographic studies of the colon.

Within the biliary system, trainees should be capable of evaluating causes of hepatomegaly, abnormal liver test results (infections, neoplasia, drugs), and the interaction of hepatitis viruses and HIV; distinguish AIDS cholangiopathy and cholecystitis; and assess indications for liver biopsy. AIDS-associated pancreatic disorders, including causes of pancreatitis (infected, neoplastic, toxic), the implications of hyperamylasemia, and the nutritional evaluation of pancreatic disorders in patients with AIDS (assessment of nutritional status and development and implementation of nutritional therapies, including enteral and parenteral) should be incorporated (see Training in Nutrition).

Trainees should be able to determine the cause of and prescribe a rational treatment plan for common opportunistic and neoplastic conditions in a cost-effective and humanitarian fashion.

Training Process
Training and experience within the 18-month core clinical experience should include inpatient and outpatient consultative evaluations of patients with AIDS who have dysphagia/odynophagia, diarrhea, rectal bleeding, abnormal liver enzymes/hepatomegaly, abdominal pain, and hyperamylasemia. In addition, extensive interactions between trainees and specialists in laboratory medicine, diagnostic and interventional radiology, and infectious disease and immunology should be available through formal conferences and in the evaluation and management of individual patients.

III. IDIOPATHIC INFLAMMATORY BOWEL DISEASE

Importance
IBD is a unique disorder for which gastroenterologists provide both primary care and consultative services. Because these diseases are uncommon in the general community, general internists and family physicians typically have little experience in the spectrum of clinical presentation and therapeutic options. Expertise in diagnosis, including the interpretation of diagnostic studies and ability to implement a therapeutic plan and assume longitudinal follow-up for patients with these chronic disorders, differentiates gastroenterological specialists from primary care physicians.

Goals of Training (Idiopathic Inflammatory Bowel Disease)
During fellowship, trainees should become proficient in the following:
1. Recognition of clinical and laboratory features (including serum antibody testing) of intestinal inflammation that may aid in differentiating between Crohn’s disease and ulcerative colitis.

2. Distinction between the signs of intestinal inflammation from those of secretory and osmotic diarrhea and from symptoms of irritable bowel syndrome.

3. Differentiation of chronic idiopathic IBD from other specific entities, such as acute self-limited (infectious) ileitis and colitis, drug- or radiation-induced colitis, ischemic bowel disease and diverticulitis.

4. Understanding the indications for and interpretation of serologic, endoscopic, radiological, historical, and microbiological studies used in the diagnosis and evaluation of patients with IBD.

5. Understanding the cost-benefit and risk-benefit ratios for endoscopic and radiological procedures used to diagnose, define disease extent and severity, and to assess complications of ulcerative colitis and Crohn’s disease.

6. Recognition of different presentations of IBD, including the pediatric manifestations, anorectal complications, and inflammatory versus fistulizing versus fibrostenotic patterns of Crohn’s disease, and be able to recognize these various presentations on history-taking and physical examination.

7. Recognition and management of the intestinal (hemorrhage, obstruction), extraintestinal (ocular, dermatologic, musculoskeletal, hepatobiliary, urinary tract), and nutritional complications of ulcerative colitis and Crohn’s disease.

8. Understanding the influence of IBD on pregnancy and of pregnancy on IBD and acquire knowledge on the safe use of IBD medications during pregnancy.

9. Recognition and management of the adverse effects of medicines used in the treatment of IBD, including the role of measuring serum enzyme (thiopurine methyltransferase) and 6-mercaptopurine metabolite levels in conjunction with the use of immunomodulators.

10. Addressing issues pertaining to family history and genetic counseling, including knowledge about the implications of gene mutations relevant to IBD.

11. Awareness of the long-term cancer risks in ulcerative colitis and Crohn’s disease and be able to implement appropriate cost-effective surveillance programs.

12. Understanding the histopathologic criteria for diagnosis of dysplasia in ulcerative colitis.


14. Diagnosing postoperative complications of surgery in ulcerative colitis (including pouchitis after ileo-anal anastomoses) and Crohn’s disease (including the differentiation and management of postoperative diarrhea).

15. Sensitivity to psychosocial influences as well as the consequences of IBD on patients and on family dynamics.


17. Understanding the indications, contraindications, and pharmacology of nonspecific therapies, including new biologic therapies such as infliximab, anticholinergic agents, antidiarrheals, and bile salt sequestrants; oral and topical aminosalicylates; parenteral, enteral, and rectal corticosteroids; and immunosuppressants (purine analogues and methotrexate) antibiotics and probiotics used in relevant clinical situations.

18. Understanding the impact of antibodies to biologic agents and how to prevent, diagnose, and manage immunogenicity to biologic agents.

19. Understanding the indications for enteral and parenteral alimentation and be able to implement nutritional therapies (see Training in Nutrition).

In addition, trainees should be capable of diagnosing and differentiating other inflammatory disorders, including collagenous and microscopic colitis, NSAID enterocolopathies, diverticulitis (including medical and surgical complications), radiation enteritis and colitis, Whipple’s disease, celiac sprue, diversion colitis, graft-versus-host disease involving the gastrointestinal tract, and the solitary rectal ulcer.

**Training Process**

Unlike many other purely consultative aspects of gastroenterology, trainees should be able to assume responsibility for the care of both inpatients and outpatients with IBD, encompassing diagnosis, acute and chronic treatment, long-term follow-up, and counseling of the families and/or significant others. Adequate experience should include exposure to hospitalized as well as ambulatory patients, including the initial assessment and longitudinal management of patients with IBD, particularly in the ambulatory setting, under the supervision of skilled attending physicians.

**Assessment of Competence**

Knowledge of inflammation and enteric infectious diseases should be assessed as part of the overall evaluation of trainees in gastroenterology during and after the fellowship, as outlined in Overview of Training in Gastroenterology. Questions relating to inflammation and enteric infectious diseases should be included on the board examination and should reflect a general knowledge of this content.
Training in Malignancy

Importance
The digestive tract has the highest incidence of cancer of any organ system of the body. Approximately 24% of cancer deaths in the United States are due to gastrointestinal cancers; 230,000 gastrointestinal cancers occur each year in the United States, with 110,000 deaths (American Cancer Society statistics, 2003). Importantly, appropriate intervention can dramatically alter the natural history and mortality of certain malignant and premalignant diseases. Patients who are treated in a timely manner can usually return to normal lives and will not be burdened by crippling chronic disease. For example, in theory, colon cancer is almost entirely preventable.

Gastroenterologists are responsible for the management of several patient groups who are at particularly high risk for gastrointestinal and associated extraintestinal cancers. These include groups of patients with FAP, HNPCC, Peutz-Jeghers syndrome, and the juvenile polyposis syndromes; patients with nonsyndromic family histories of cancer (particularly colorectal cancer); patients with a prior history of gastrointestinal neoplasia, IBD, gastroesophageal reflux disease, Barrett’s esophagus, chronic atrophic gastritis, chronic pancreatitis, and celiac disease; patients who previously have had a gastrectomy; and patients infected with H. pylori. In addition, gastroenterologists manage patients with chronic viral hepatitis B and C, which predisposes them to the development of hepatocellular carcinoma (HCC), as do the iron storage diseases, for which diagnostic testing is now available. Furthermore, patients with primary sclerosing cholangitis and certain other related conditions are at risk for developing biliary tract cancers. Each of these high-risk conditions has a unique natural history and lends itself to diagnostic surveillance or therapeutic intervention.

Gastrointestinal cancer has been an area in which there has been a rapid emergence of new concepts. There has been an explosion of information in the area of tumor genetics. A model of multistep carcinogenesis for colorectal cancer has been developed, which represents the first coherent formulation of cancer pathogenesis. Two important concepts are the role of nutrition in the genesis of gastrointestinal cancers and the emerging role of cancer chemoprevention for high-risk groups. It has recently been appreciated that aspirin and related compounds may play an important role in preventing cancer. New classes of pharmacological agents (including aspirin and certain nonsteroidal anti-inflammatory agents) may be indicated in the primary prevention of colon and other gastrointestinal cancers. The application of these modalities is likely to become commonplace, making it essential for the gastroenterologist to understand the indications for and uses of chemopreventive agents. In view of the major advances in the prevention, diagnosis, staging, and treatment of gastrointestinal malignancy and the impact these advances will have on the practice of gastroenterology, this field deserves particular emphasis in the education of gastroenterology trainees.

Goals of Training
During fellowship, trainees should:
1. Develop a sound knowledge of tumor biology to a level similar to that traditionally achieved for acid-base or smooth muscle physiology. Balanced training now should reflect the state-of-the-art and the relative importance of cancer to this field.
2. Develop a thorough familiarity with the literature on cancer epidemiology, primary prevention, and screening for colorectal cancer with fecal occult blood tests as well as endoscopic and radiological approaches.
3. Become knowledgeable about the recommended guidelines for screening for gastrointestinal neoplasia and the literature supporting these recommendations.
4. Be able to read and interpret literature about the emerging technologies and know how to evaluate novel technologies and approaches.
5. Have a working knowledge of clinical genetics and understand the approaches to the genetic diagnosis of FAP, HNPCC, and other rarer polyposis syndromes. They should recognize the clinical characteristics of these diseases, the distinctions among the familial forms of cancer, the specific diagnostic and screening tests for each, and the rational approaches to their treatment.
6. Learn the principles of neoplastic growth as they relate to therapy, including endoscopic treatment as well as traditional surgical approaches. A complete understanding of the management of premalignant conditions is necessary.
7. Become familiar with the pathological interpretation of tissue biopsies (endoscopic and percutaneous) and have a thorough working knowledge of the management of dysplastic lesions. They must understand the distinctions among the varieties of colorectal polyps and their management.
8. Learn the principles of chemotherapy for gastrointestinal cancer and radiation treatment for early and advanced tumors. They must understand the initial management of those patients in whom the diagnosis of gastrointestinal cancer has just been made.
9. Understand how to counsel patients who have had gastrointestinal neoplasia and how to manage patients who inquire about the man-
management of positive family histories of gastrointestinal cancer. Trainees should understand the principles and importance of genetic counseling as it pertains to genetic testing and the management of the inherited gastrointestinal diseases. They should be familiar with the prognoses associated with different types of gastrointestinal cancer.

10. Become familiar with the technical considerations in the therapy of colorectal adenomas and carcinomas. They should be thoroughly experienced in colonoscopic polypectomy of pedunculated and sessile polyps and ablative therapies for sessile lesions. Trainees must understand the capabilities and limitations of endoscopic mucosectomy for early gastrointestinal cancers.

11. Understand the appropriate surveillance and surveillance intervals for patients at high risk for developing cancer and those in whom premalignant epithelium has already been detected.

12. Gain additional experience, for those who desire advance training, in the placement of endoscopic stents, laser ablation, photodynamic therapy, endoscopic ultrasound, fine-needle aspiration of tumors, endoscopic mucosectomy, and endoscopic celiac ganglion block for patients with pancreatic cancer (level 2 training).

Training Process

Cognitive
Throughout the entire fellowship period, trainees should participate in the screening, diagnosis, and management of all types of gastrointestinal malignancies. Lectures in molecular and cellular biology as well as clinical oncology and screening, treatment, and palliation of gastrointestinal cancer should be included in the core curriculum. Lectures should be provided by experts in interventional endoscopy, oncology (medical and surgical aspects), radiation oncology, and medical genetics. It is critical that trainees understand the emerging role of the gastroenterologist in multiple aspects of gastrointestinal cancer. To achieve these goals, many programs will be required to invite outside consultants.

Coverage of the following topics should also be provided:
1. Changes in screening and surveillance recommendations.
2. The evolution of genetic testing and counseling for FAP, HNPCC, and other familial forms of gastrointestinal cancer.
3. Novel approaches to the diagnosis of gastrointestinal cancer, including endoscopic approaches, radiological approaches, nuclear medicine, ultrasound/endoscopic ultrasound, and new genetic techniques.
5. Techniques used in the basic science investigation of gastrointestinal cancer, including flow cytometry, polymerase chain reaction assays, mutation analysis, methylation assays, DNA sequencing, and linkage analysis.

Endoscopic
Endoscopic training in the diagnosis and management of gastrointestinal cancer is required. Recommendations for the duration, frequency of procedures, and other details are covered in Training in Endoscopy. However, areas relevant to gastrointestinal malignancy that require specific attention include the following:
1. Endoscopic management of Barrett's esophagus.
2. Familiarity and at least limited experience with the indications, techniques, and management implications of laser therapy, photodynamic therapy, and stents for palliating esophageal cancers.
3. Management of upper gastrointestinal neoplasia in FAP, including the management of gastric, duodenal, and periampullary lesions.
4. Endoscopic management of the gastric remnant following Billroth I and II surgery
5. Recognition of neoplasia in the pancreaticobiliary tree.
6. Familiarity and at least limited experience with the indications, techniques, and management implications of therapeutic endoscopic retrograde cholangiopancreatography for pancreatic and biliary cancers.
7. Proper technique for polypectomy for pedunculated and sessile polyps, including saline injection.
8. Familiarity with the indications, techniques, and management implications of the emerging endoscopic imaging techniques for surveillance of gastrointestinal malignancies such as confocal laser endoscopy, chromoendoscopy, and optical coherence endoscopy.
10. Surveillance of the colon in IBD, including considerations for normal-appearing mucosa and abnormal-appearing mucosa.

Gastroenterology trainees should become familiar with the appearance of cancer by using the following radiological and pathological techniques:
1. Radiological: gastrointestinal cancer on barium upper gastrointestinal series, barium enema, CT colography, CT scans, and MRI/MRCP
2. Pathological:
   a. Recognition of Barrett's epithelium and dysplastic change in Barrett's mucosa
   b. Recognition of intestinal metaplasia and atrophy in the stomach
   c. Recognition of neuroendocrine and stromal cell tumors of the gastrointestinal tract
   d. Identification of neoplastic and non-neoplastic polyps and malignancies
   e. Recognition of the depth of invasion of cancer in the polyp or into the wall of the colon and its significance
f. Recognition of dysplasia versus reactive changes in IBD

The roles of radiology and pathology are specifically addressed by Training in Radiology and Training in Pathology.

Certain trainees may elect to receive additional training in advanced endoscopic procedures, level 2 training (see Training in Endoscopy). These procedures should not be attempted by all trainees; rather, they should be reserved for those who wish to spend the time to master these techniques and may be reserved for selected centers.

These procedures include the following:
1. Endoscopic ultrasound of the esophagus, stomach, duodenum, and rectum
2. Dilating, stenting, and tissue sampling of the esophagus and biliary and pancreatic tree
3. Ablative therapy of neoplasms using laser
4. Photodynamic treatment of epithelial neoplasia in Barrett’s esophagus
5. Fine-needle aspiration of masses in the liver and pancreas.

Assessment of Competence

Knowledge of malignancy should be assessed as part of the overall evaluation of trainees in gastroenterology during and after the fellowship, as outlined in Overview of Training in Gastroenterology. Questions relating to malignancy should be included on the board examination and should reflect a general knowledge of this content.