ISSUE BRIEF

State of the State in Gastroenterology

Andrew J. Muir

Gastrointestinal disorders range from life-threatening conditions to benign disorders, but all can impact the daily life of millions of Americans. For colorectal cancer, liver disease, and other conditions, early identification is important to avoid late-stage presentations that carry the greatest mortality risk. The past decade has seen major advances in the development of biologic agents for treatment of inflammatory bowel disease and especially in the development of antivirals for treatment of hepatitis C infection. There is also better understanding of the role of diet in gastrointestinal disorders. New initiatives from research of benign disorders are expected in the next decade.

Gastrointestinal disorders are common and can present a variety of clinical challenges to frontline clinicians. In 2010 in the United States, abdominal pain accounted for more than 15 million office visits and more than 10 million emergency department visits. Diarrhea, nausea, vomiting, and bleeding rounded out the top 5 diagnoses for ambulatory gastrointestinal encounters [1]. The initial evaluation is often appropriately focused on ruling out life-threatening disorders, but many of the more benign gastrointestinal disorders lead to high health care utilization rates and have tremendous impacts on patients' quality of life. As gastroenterologists, our practices are also heavily focused on prevention. Whether for colorectal cancer or hepatitis C virus (HCV) infection, the early identification of disease allows us the greatest opportunity to alter its course. Effective partnerships with primary care clinicians are necessary to initiate screening programs and to identify patients at risk for morbidity and mortality from these disorders. In this issue of the *North Carolina Medical Journal*, we highlight clinicians and researchers from around our state. We are fortunate to have high-quality academic and community practices throughout North Carolina, and the authors of this issue offer updates and provide critiques on the current care of patients with gastrointestinal disorders.

Although colorectal cancer remains the 3rd most common cause of cancer in the United States, an important message to patients is that screening is effective. In this issue, Glenn Harvin reviews the benefits of screening and covers a number of screening options, including colonoscopy, CT colonography, fecal occult blood testing, fecal immunochemical testing, and fecal DNA testing [2]. A report from the National Cancer Institute found that rates of colorectal cancer screening rose from 34.8% to 66.1% over the past 3 decades, and the report estimated that approximately 550,000 cases of colorectal cancer were prevented during this time. Importantly for a screening program, the incidence of late-stage colorectal cancer decreased from 118 cases per 100,000 population to 74 cases per 100,000 population ($P < .001$) [3].

These results are encouraging, but substantial opportunities still exist. While colorectal cancer screening rates have improved, they fall short of desired levels. An analysis from the 2010 National Health Interview Survey revealed that only 58.3% of Americans received colorectal cancer screening at recommended intervals [4]. In order to further reduce morbidity and mortality from this disease, the National Colorectal Cancer Roundtable has established the goal of increasing the colorectal screening rate in the United States to 80% by 2018 [5]. This effort will require reaching out to broad segments of the population. As pointed out in the sidebar by Julius Wilder and Joanne Wilson in this issue, rates of screening are lower among under-represented minorities, those who have lower levels of education, and particularly among those who speak Spanish as their primary language. The Patient Protection and Affordable Care Act of 2010 includes coverage for colorectal cancer screening, but Wilder and Wilson also call for a public health strategy to improve access among diverse groups of North Carolina residents [6].

The advance in treatment of HCV infection is one of the most remarkable medical achievements of our time. In this issue of the NCMJ, Mitchell Mah'moud reviews the current state of HCV therapies [7]. For the past 2 decades, antiviral treatment required interferon-α and was marginally successful with myriad side effects. Many patients were ineligible for treatment or could not complete treatment, and the available regimens were less effective in a number of populations, including African Americans and persons with HIV-HCV co-infection. In contrast, HCV regimens are now all-oral, interferon-free regimens that are extremely well tolerated with cure rates over 90% in all populations. The

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Address correspondence to Dr. Andrew J. Muir, Duke University School of Medicine, DUMC Box 3913, Durham, NC 27710 (andrew.muir@duke.edu).

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challenges now are identifying patients and helping them access treatment. HCV infection is extremely subtle during the first few decades of disease, and patients may not report signs or symptoms until the late stages of cirrhosis or liver cancer. Given that 75% of Americans with HCV infection are baby boomers, the US Preventive Services Task Force recommends HCV screening for all Americans born between 1945 and 1965. Screening and linkage to care is imperative to attack HCV infection at the population level.

In a stirring sidebar, Sarah Rhea and colleagues at the North Carolina Department of Health and Human Services highlight the recent 3-fold increase in cases of HCV infection among young, rural-dwelling persons who inject drugs [8]. These findings are linked to the increase in opioid injection in the United States in the past decade and the corresponding increased rates of opioid- and heroin-related hospitalizations and fatalities in North Carolina. The North Carolina Department of Health and Human Services is aggressively addressing HCV in our state through the establishment of new partnerships with health care providers and other stakeholders and through efforts that include HCV screening, prevention education, and linkage to care and treatment.

New HCV medications will lessen the burden of liver disease from HCV infection in the next decade, but recent data have emerged showing that nonalcoholic fatty liver disease (NAFLD) is the next epidemic of cirrhosis. This disorder is more common among patients who are obese and/or have diabetes mellitus, and NAFLD is on a trajectory to surpass HCV infection as the most common reason for liver transplantation in the United States [9]. In this issue, Tyler Thrasher and Manal Abdelmalek review this disorder and discuss the spectrum of disease ranging from simple steatosis (fatty liver), through the inflammation of nonalcoholic steatohepatitis (NASH), to cirrhosis and hepatocellular carcinoma [10]. As with many liver disorders, patients may have minimal or no symptoms until very advanced stages of the disease, and mild elevations in liver enzyme levels might be the only clue to the problem. Initial treatment approaches for NAFLD have focused on gradual and sustained weight loss, and dietary change, exercise, and bariatric surgery have all demonstrated efficacy through improvements in liver enzyme levels and histology. NAFLD is an area of intense research right now, particularly in terms of understanding mechanisms of injury and guiding pharmacologic interventions. Many clinical trials are examining a diverse array of targets aimed at either inflammation or fibrosis.

Despite the progress in therapeutics, many patients with chronic liver disease will develop end-stage liver disease or hepatocellular carcinoma. In this issue, Carl Berg discusses the advances in liver transplantation for these conditions. One-year graft survival is now 89%, and 5-year graft survival is 78%. Limited access to transplantation and particularly long waiting times are major concerns for patients, but a series of changes in the allocation system during the past 2 decades have reduced death on the waiting list and improved access to organs for patients with more advanced liver disease. The adoption of the model for end-stage liver disease (MELD) score for allocation of organs was a landmark moment, and the system evolved again in 2016 with adoption of the MELD-Na score, which gives priority to patients with low serum sodium levels. A persistent critical issue for the field is that the number of available organs is inadequate for the approximately 15,000 Americans and more than 200 North Carolinians awaiting liver transplantation. Living donor liver transplantation is an alternative option for some patients, but concerted efforts are needed to improve organ donation [11].

Inflammatory bowel disease also has seen great progress in therapeutics in the past decade, which is fortunate since the burden of Crohn's disease and ulcerative colitis continues to increase. In one of the largest epidemiologic studies in the United States, prevalence of these conditions among adults was 201 per 100,000 persons for Crohn's disease and 238 per 100,000 persons for ulcerative colitis. The prevalence of both conditions was lower in the South compared with other regions [12]. In this issue of the NCMJ, Will Harlan and colleagues review the diagnosis of these conditions and various therapeutic approaches, including the expanded use of biologic agents [13]. The major goals of therapy are to induce clinical and endoscopic remission and to minimize the need for corticosteroids and surgery. With an expanded array of agents, clinicians can now optimize therapy by measuring drug levels and antibodies prior to initiation of treatment or in the setting of treatment failure.

As discussed in this issue by David Olson and Martin Scobey [14], *Clostridium difficile* infection is the most frequently reported nosocomial pathogen in the United States. A surveillance study in 2011 identified 453,000 cases of *C. difficile* infection and 29,000 associated deaths [15]. Metronidazole and oral vancomycin remain first-line treatments for this infection, but high rates of recurrent disease and treatment failure have emerged in the past decade [16]. The hypervirulent BI/NAP1/027 strain has been identified in a number of high-profile outbreaks. In 2011, the US Food and Drug Administration approved fidaxomicin for the treatment of *C. difficile* infection, and phase III studies demonstrated lower recurrence rates with fidaxomicin compared to vancomycin. However, use of fidaxomicin has been limited by its high cost and by the lack of improved efficacy over vancomycin when treating the BI/NAP1/027 strain. Recurrence of infection therefore remains a treatment challenge. A recent development in the treatment of *C. difficile* infection has been fecal microbiota transplantation. Although only observational studies are available at this point, a recent systematic review of 18 observational studies with 611 patients reported a primary cure rate of 91.2% [17]. Fecal microbiota transplantation is available at a number of centers in North Carolina.

Symptoms affecting the digestive tract are common, accounting for millions of office and emergency department

visits in the United States each year. Although many of these encounters are for benign disorders such as irritable bowel syndrome or gastroesophageal reflux disease (GERD), these conditions can have tremendous negative impact on patients' quality of life. As an example, 18.1%–27.8% of the American population report weekly symptoms of GERD [18]. In this issue, Lane Wilson and Kellner Pruett discuss medical therapies for GERD, including some of the risks of these agents and concerns regarding overtreatment of this condition [19].

As patients become more educated about their health, they are seeking a variety of options to improve how they feel. In this issue, Leslie Gaillard reviews the growing trend of gluten-free diets among many people without celiac disease. Similarly, the FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diet involves a food elimination approach that removes sources of highly fermentable carbohydrates, including fructans. This diet has been effective in improving gastrointestinal symptoms in functional bowel disorders [20].

Another disorder receiving more attention is fecal incontinence, or accidental bowel leakage, which affects more than one-third of patients attending primary care clinics. In this issue of the NCMJ, William Whitehead and colleagues discuss some of the basic diagnostic and management strategies for this condition [21]. One of their key points is that primary care providers can significantly impact the care of patients with this disorder. Conservative management is within the community physician's scope of practice and can lead to improvement for 60% of those affected, with 20% of affected patients achieving continence. There is great need for clinicians to initiate discussions about fecal incontinence to help patients overcome embarrassment and seek appropriate evaluation and treatment.

Diverticular disease is another common disorder that receives a thoughtful critique by Anne Peery in this issue. In the United States, diverticular disease results in more than 2,500,000 clinic visits, 330,000 emergency department visits, and 200,000 hospital admissions annually [22]. In this issue, Peery questions some long-standing tenets of diverticular disease, including the role of fiber in the development of diverticulosis and the use of antibiotics in the management of acute diverticulitis [23]. Recently, there has been a resurgence in research about diverticular disease, which should help to guide clinicians on appropriate management.

The field of gastroenterology has seen considerable advances in the past decade. Efforts to improve screening rates have led to significant reductions in colorectal cancer. HCV treatment has gone from marginally effective toxic therapies to all-oral antivirals that offer a cure to almost all patients. Liver transplantation offers long-term survival, and the allocation system is now more fair and balanced. At the same time, this issue of the NCMJ highlights ongoing clinical challenges. *C. difficile* infection is more common than in the past, and there are particular challenges in cases of treatment failure and recurrence. Our ongoing obesity epidemic means that we are likely to see more cases of NAFLD, and we anticipate the results from a number of clinical trials that should help us to understand new therapeutic approaches. At the same time, we see many opportunities for research to improve the health of our patients through better management of benign disorders that impact many patients' daily quality of life. NCMJ

Andrew J. Muir, MD, MHS chief, Division of Gastroenterology, Duke University School of Medicine; director, Gastroenterology and Hepatology Research, Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina.

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