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• EDITORIAL •

Blossoming of gastroenterology during the twentieth century

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INTRODUCTION

Awareness of the digestive system began with the dawn of civilization, when man observing the feeding habits of animals in the surrounding environment, experimented with foods, edible and inedible. Identity came with discoveries of the digestive organs during the 16th and 17th centuries. Function was revealed by physiologic studies of digestion, absorption and secretion, metabolism, and motility during the 18th and 19th centuries. Diagnostic access improved with the technological advances of the 20th century. Understanding of gastrointestinal (GI) disease followed growth of the basic sciences and gastroenterology's increased involvement in scientific research during the 20th century.

The scientification of medicine and gastroenterology began during the latter part of the 19th century when the discovery of bacterial causes of disease revealed the potential of research in the discovery of new knowledge, and when the dogma of the past began to yield to clinical and basic investigation. Additional impetus came from A. Flexner's 1910 report on medical education, documenting the importance of a scientific foundation in medicine. Funds for gastroenterologic investigation were small, but research was in progress in the physiology laboratories of academic medical centers. Early in the 20th century, gastroenterology was yet an incompletely defined activity; but during the 1920s, outstanding clinicians established gastroenterology programs at university academic centers and major clinics. The entry of scientifically trained young physiccians into gastroenterology during the 1930s and 1940s increased research interest.

Specialization in medicine was underway and, in the United States in 1940, gastroenterology was certified as an academic specialty, important to the attraction of students and support for education and research. Similar recognition occurred elsewhere, but further progress was interrupted by World War II (1939-1945).

Post-World War II was a highly productive period for the basic and biomedical sciences. Wartime discoveries had documented the remarkable success of research and had motivated public and governmental support of basic investigation. This trend accelerated in the United States, when the office of Scientific Research and Development (U.S. War Department) transferred 44 research contracts with universities and with industry to the then fledging National Institutes of Health (NIH) at the end of World War II. The General Medicine Study Section of the National Institute of Arthritis and Metabolic Diseases (NIH) became a major support of GI research and training. During the 1960s, 1970s and 1980s, academic medical center faculties enlarged and research training programs increased, creating new technologies and new disciplines. Important advances occasionally developed from insightful clinical observations. A classic example concerns the "epidemic" of pellagra, considered an infection early in the 20th century and accounting annually for 250 000 cases and 7 000 deaths in 15 Southern cotton-growing U.S. states. In 1914, at age 40, Dr. Joseph G. Goldberger of the Public Health Service, through shrewd clinical observations of patients, hospital staff, and patient diets, implicated a dietary deficiency (confirmed later as a nicotinic acid deficiency) as the cause of pellagra. However, scientific activity was associated with much prestige, and gastroenterology sought to become more "scientific".

Gastroenterology essentially incorporates basic concepts and technology, from multiple scientific disciplines, into its own investigation. The early 1900s' view of swallowing, as the forceful "bolting" of food from the throat directly into the stomach, was replaced by the recognition of pharyngeal and esophageal neuromuscular function, facilitating the physiological management of swallowing disorders. Histologic and microbiologic examination of endoscopically obtained gastric biopsies replaced the subjective diagnosis of "chronic gastritis". Not until the 1980s, however, was the role of *Helicobacter pylori* in gastritis and peptic ulcer identified. Multidisciplinary research clarified the process of gastric secretion and led to the development of H_2 blockers and proton pump inhibitors. Metabolic studies identified the specific L-glutamine requirement for the intestinal epithelium and the short-chain fatty acid, n-butyrate, for the colonic epithelium. Research into the nature of inflammation led to more effective strategies for the treatment of inflammatory bowel disease. Cellular biology identified the intracellular heat shock proteins, trefoil peptides, and stem cell growth factors, with therapeutic potential. The important role of genetic influence, in the development of colorectal cancer, celiac disease, and inflammatory bowel disease, was extended to other GI diseases.

Gastroenterology's 20th-century technological progress was equally impressive. The study of esophageal motility progressed from balloon kymography to intraluminal catheter manometry, transducers, and neuropharmacologic methodology. Fiberoptic endoscopy expanded diagnostic access to virtually all areas of the gastrointestinal tract. Safer polyethylene tubing eased transintestinal intubation and perfusion studies, and with small bowel biopsy and radioimmuno-assays, clarified intestinal absorption mechanisms. Microbiological and chromatographic tech-nologies, including hydrogen and carbon-14 breath tests, increased knowledge of the enteric flora, enabling the diagnosis of bacterial overgrowth responsive to antibacterial therapy. Needle biopsy of the liver established the morphological basis of hepatic disease and provided guidelines for the treatment of hepatitis and the monitoring of

liver transplantation. Discovery of the Australia antigen stimulated research, identifying seven types of hepatitis viruses (A, B, C, D, E, F, G), a major impetus in the growth of knowledge of liver disease. Biochemical and chromatographic technology determined the composition of bile and the process of formation, as well as the chemical dissolution of cholesterol gallstones. Enzyme and protein chemistry established the synthesis and trafficking of intracellular proteins and intracellular enzyme activation as the cause of acute pancreatitis. Transmission, electron microscopy and laser-scanning confocal micros-copy facilitated the study of intestinal epithelial cells, intracellular protein processing, and epi-thelial barrier function. Molecular biological techniques made possible the cloning of genes for cystic fibrosis, sodium, calcium, glucose, and amino acid transport. Advances in radiologic image intensification, ultrasonography, computed x-ray tomography of the abdomen, and magnetic resonance imaging among other achievements, increased access to the gastrointestinal tract.

Neuro-humoral and neuro-immune interactions of the GI tract, mediating colonic motility and visceral sensitivity, replaced psychogenic hypotheses of the irritable bowel. Studies of gastrointestinal immunology, including the gut mucosal immune system and the molecular mechanisms of inflammation, generated new pathogenic concepts and therapeutic resources in inflammatory bowel disease (IBD). Measurements of gastrointestinal blood flow, including laser Doppler velocimetry, facili-tated recognition of abdominal vascular impairment. Neurogastroenterology introduced methods of electrophysiology and cellular neurophysiology, identified the enteric nervous system as a "minibrain with intelligent circuits", and provided new understanding of "physiologic" GI disorders. Transgenic methodology created innovative animal models, enabling multidisciplinary studies of intestinal inflammation.

Expanded access to the gastrointestinal tract, including fiberoptic endoscopy, biopsies of the esophagus, stomach, small intestine, and colon, X-ray (CT scan)-guided biopsy of the liver and the pancreas, tests of hepatic and pancreatic functions, breath tests, quality X-rays, ultrasonography, computerized abdominal tomography, magnetic resonance imaging, and assessment of gastrointestinal motility improved the diagnosis of digestive disorders. Gastrointestinal therapy advanced with the discovery of sulfonamides, antibiotics, adrenocortical steroids, immune modifiers, H_2 receptor blockers, proton pump inhibitors, anti-inflammatory compounds, nutritional supports, vaccines, cancer chemotherapy, organ transplantation, and increasingly skilled abdominal surgery.

Many favorable circumstances converged to bring gastroenterology into the mainstream of advancing scientific thought, including an enlarging body of scientific knowledge, technological innovations permitting safer, more precise human studies, increased support of research and training, controlled clinical studies, establishment of research and scientific training programs, by the NIH and private philanthropy, and the enlarging global scientific communication network (journals, databases, electronic and computer systems).

The major accomplishment of gastroenterology during the 20th century has been the successful application of new scientific knowledge and technology to the investigation of gastrointestinal disorders. Digestive diseases involving multiple disciplines and innovative technology today are recognized as exciting and challenging problems. Now that gastroenterologic research frontiers are at the cutting edge of modern science, including such "new" sciences as biotechnology, structural biology, and pharmacogenetics, together with the ongoing molecular disciplines (microbiology, immunology, genetics). They will establish the 21st century as the gastroenterologic century.

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