



IN MEMORIAM

Jon Irwin Isenberg
Professor of Medicine
UC San Diego
1937-2003

The Department of Medicine and the Division of Gastroenterology lost a multifaceted and beloved physician-scientist when Jon Isenberg died at home on October 10, 2003 after a long and valiant struggle against cancer. Jon Isenberg was a talented, thoughtful, and conscientious clinician who was very much loved by his patients, a consummate clinical investigator, and a nationally recognized leader in Gastroenterology. He was Chief of the Division of Gastroenterology, Department of Medicine from 1978 until 1992, and he served as President of the American Gastroenterological Association from 2000 to 2002.

Jon was born in Chicago. After high school, he attended the University of Illinois in Champaign- Urbana, graduating with honors in chemistry, a discipline that he later drew upon to great effect in his physiological and clinical studies. He attended medical school at the University of Illinois in Chicago, graduating in 1963. He showed an early talent for research, as a medical student co- authoring a paper on an immunological micromethod. This presaged his calling to academic medicine. After an internship in Miami, he returned to the “windy city” where he received additional postgraduate training.

In 1966, he was accepted for a fellowship providing clinical and research training in Gastroenterology at the UCLA- affiliated Wadsworth Veterans Administration Hospital in Los Angeles, then the venue of Morton Grossman, director of the Center for Ulcer Research and Education (CURE), one of the nation’s leading gastric physiology laboratories. Morton Grossman became Jon’s mentor. After a brief stint in the army, Jon was made a member of CURE and was appointed to the faculty of UCLA. Impressively, only five years later, in 1971, he became chief of the Division of Gastroenterology at the Wadsworth Hospital and director of its Gastroenterology training program. Jon rapidly rose to the rank of professor. In 1979, he was recruited to UCSD to lead the Division of Gastroenterology, a post that he held for the next 13 years. After relinquishing that position, he continued to make major contributions on the national level through his leadership role in the American Gastroenterological Association.

Jon will long be remembered by his patients who had deep affection and respect for his clinical abilities. He was a warm and caring physician with a charisma that enhanced his natural teaching talents.

Jon’s initial research was concerned with the pathogenesis of peptic ulcer disease, which for decades was considered to result from excessive gastric acid secretion. Jon used animal models to characterize the effect of insulin and other hormones on gastric acid secretion. He also studied patients with excessive gastric secretion caused by gastrin- secreting tumors and showed that such patients have inappropriate responses to high doses of the hormone, secretin, providing a clinical diagnostic tool that was widely used. Soon thereafter, the first H₂ blockers – potent inhibitors of gastric acid secretion – were developed, and duodenal ulcer research entered an entirely new era. Jon characterized the effects of these new agents on gastric secretion in well- designed clinical studies, which he continued following his move to San Diego. He directed studies examining the gastric secretory response to alcoholic beverages, including beer and wine. Later in his career, Jon changed his research direction to focus on the effect of agents such as prostaglandins and hormones on duodenal bicarbonate secretion, a major defense against duodenal ulcer disease. He developed a

method for studying bicarbonate secretion using occluding balloons to isolate the duodenum in humans and extended this work to animal studies in order to identify the channels and transporters involved. By studying mice in whom the CFTR chloride channel had been ablated by genetic knockout, Jon showed that this chloride channel was intimately involved in duodenal bicarbonate secretion. After the unexpected discovery that peptic ulcer is often caused by a bacterium, named *Helicobacter pylori*, Jon and his colleagues showed that infection with these bacteria decreased duodenal bicarbonate secretion, and that, with ablation of the bacteria, duodenal bicarbonate secretion once again returned towards normal. All of this work was done by an unending stream of research fellows from throughout the world, who were guided from project design to completion of the paper.

Jon also had the ability to identify excellent basic scientists whose work could be applied to his physiological approaches and this led to effective and lasting collaborations. While these physiological and pharmacological studies were being pursued, Jon skillfully and tirelessly served his university, his subspecialty, and government granting agencies including the National Institutes of Health and the Veterans Administration. He served on the editorial boards of 11 journals and reviewed submitted manuscripts for many other journals. His most notable contributions outside the university centered on his main professional society, the American Gastroenterological Association (AGA). Jon's loyalty and service to the AGA were eventually recognized in his selection as the organization's president. It is a mark of his tenacity that he completed his term to acclaim even at a time when his health was beginning to fail.

Jon was elected to the most prestigious associations for clinical investigators, including the American Society of Clinical Investigation and the American Association of Physicians. He was frequently named as one of "America's Best Doctors". He was a widely sought after speaker and consulted extensively with pharmaceutical companies during the decades when potent antisecretory agents were developed. Two pharmaceutical companies (Janssen, Johnson & Johnson) have endowed a Jon Isenberg lecture in his honor.

Jon married Laurie Lipman in 1962 and their three children (Noah, Nancy, and Rebecca) survive him. In 1997, he married Birgitta Mårtensson from Stockholm, who collaborated with Jon both during sabbaticals in Sweden and in his laboratory at UCSD over the past several years.

Jon was a gracious host, a charismatic teacher, a caring physician, and a valued mentor. He epitomized the "triple threat" – a physician and teacher who was also capable of making pivotal research advances. While he could be brusque at times, this exterior belied his true nature, which encompassed an abiding and sincere interest in the lives and careers of those he taught in both the clinic and the laboratory. As a result, he inspired great loyalty in his many trainees. He also had friends throughout the world, especially in Sweden where he spent several extended periods in the laboratory of his great friend and collaborator, Gunner Flemstrom. He was deeply appreciative of the value of rigorous clinical investigation. It is because of the work of Jon Isenberg and that of his colleagues in peptic ulcer research that this common and distressing disease is slowly disappearing from the western world. We shall miss him greatly.

Alan F. Hofmann
Martin F. Kagnoff
Kim E. Barrett, Chair