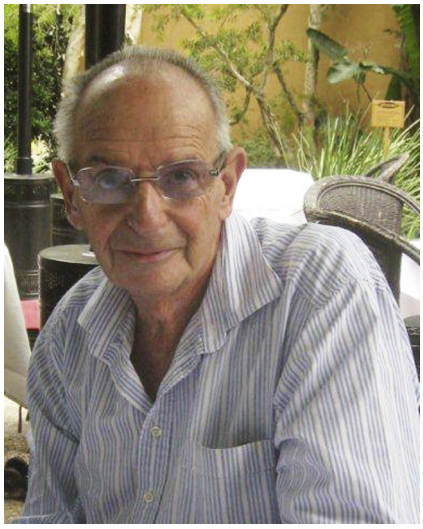
George Sachs, MB, ChB, DSc (August 26, 1935 – November 12, 2019)

George Sachs, Distinguished Professor of Medicine and Physiology at UCLA, passed away peacefully and unexpectedly at home on November 12, 2019. He was a dominant force in gastroenterology for over forty years, and was responsible for the development of PPIs, a therapy that revolutionized management of gastric acid and peptic disorders.[1]

George was born on August 26, 1935 in Vienna, Austria to Arpad and Toni Sachs, both physicians. In those unsettled times, due to the rise of Nazism, his father had the foresight in 1936 to secure a UK visa and a clinical practice in Edinburgh, Scotland. George and his mother joined him in 1939 just prior to the outbreak of the Second World War. George was immediately enrolled in the George Watson College, from which he graduated in 1952 as head of his class (Dux). He read medicine at Edinburgh University, but took time out to obtain a B.Sc. in Biochemistry. An instructor in chemical biology who made a major impact on his subsequent career was Peter Mitchell, Nobel Laureate in 1978 for his far-sighted chemic-osmosis theory to explain ATP synthesis. George completed his medical training in 1960 with honors, and then undertook post-doctoral training at Albert Einstein College and Columbia University, before accepting a faculty position in Physiology and Medicine at the University of Alabama in Birmingham. Under the mentorship of Basil Hirschowitz, Chief of Gastroenterology, George turned his interest to gastric biology. Together they published three dozen papers on the mechanism and regulation of gastric acid secretion. He became increasingly drawn to the involvement of gastric ATPase activity in acid secretion. Using isolated gastric glands, parietal cells and membrane vesicles combined with elegant biochemical and biophysical tools, he determined that a gastric H^+ - K^+ ATPase was responsible for acid secretion. This proton pump carried out an electroneutral exchange of two protons for two potassium ions for each mole of ATP hydrolyzed.



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George recognized the limitations of cimetidine (Tagamet; GlaxoSmithKline, Brentford, London, UK) for treatment of acid-related diseases and hypothesized that the gastric ATPase would be a better target for acid inhibition. A chance encounter with the Swedish pharmaceutical company Hassle AB, later Astra and AstraZeneca, led him to develop the first Proton Pump Inhibitor (PPI). The initial compound, a substituted benzimidazole, was a weak base prodrug that required acid activation to function.[2]

George was recruited to UCLA in 1982 as Director of the Center for Ulcer Research and Education (CURE), and he established the Laboratory of Membrane Biology on the VA Greater Los Angeles Healthcare System campus. He held appointments as Distinguished Professor of Medicine and Physiology, and was a Senior Medical Investigator at the VA. He continued his work on H^+, K^+-ATPase biology, with a shift in focus from molecular mechanisms to secretory physiology.[3] His work on inhibitors led to FDA approval of the first PPI, Omeprazole (Prilosec; AstraZeneca, Cambridge, UK) in 1989. This drug had efficacy in acid inhibition to a degree not seen previously and revolutionized the treatment of gastric ulcers and GERD. He received numerous awards for his work on acid secretion and acid inhibition, including The Janssen Award for Special Achievement in Gastroenterology in 1998 and The Canadian Gairdner International Award in 2004.

George's interest in *Helicobacter pylori* naturally evolved from his background in gastric physiology and acid secretion. He dove into the world of microbiology with the mentality and toolkit of a physiologist, and his laboratory made significant contributions to our understanding of how this bacterium is able to survive in the stomach. He recognized the bacteria as a pathogen and the problems with the complex and multiple antibiotic treatment regimens in an era of rapidly emerging antibiotic resistance. His goal was to better understand the gastric biology of the bacteria, in order to discover gastric colonization mechanisms as potential targets to optimize treatment. His laboratory proved that the bacteria is a neutralophile and he adapted the term "acid acclimation" to explain periplasmic buffering as a means to colonize the acidic gastric surface rather than simply transit the stomach. He was convinced early on that the only membrane protein in the critical urease operon had to be a urea channel, and his laboratory demonstrated the proton gated channel physiology of UreI using oocyte injections, work that was published in *Science*.[4] Following this landmark discovery, his group was able to crystalize the channel and his recent research has been dedicated to unlocking the signaling pathways that work in concert with UreI to facilitate gastric colonization. In parallel, he hoped to develop mechanisms to optimize treatment through use of stronger acid suppression, which would lead to bacterial division and improved antibiotic efficacy. George has been involved in the development of newer acid suppressive medications, including the potassium competitive acid blockers and pro-PPIs, with a persistent desire to both improve treatment of acid-related disease and facilitate eradication of *H pylori*.

Over his long career, he published over 600 papers and reviews, several books, served on editorial boards and review committees at the NIH and VA, and trained numerous students, post-doctoral fellows and visiting faculty, many of whom now hold leadership positions in academia and industry.

His father Arpad played a dominant role in his education and intellectual development by encouraging him as a child to read five books a week, and he remained an avid reader throughout his life. He was particularly drawn to 20th century history, was a staunch devote of Winston Churchill, and was fascinated by his relationship to Franklin Roosevelt.

George has touched the lives of many colleagues, mentees, and friends in a manner that will not be forgotten, and the clinical impact of his work is staggering. Most significantly, George was devoted to his beloved wife, Joyce, who he met in New York in 1963, their four children, Stephen Bennett Sachs (Margo Francis), Andrew Adam Sachs (Elizabeth Evans Sachs), Paula Sachs Grayson (Paul Grayson), Lara Day Sachs-Fishman (David Fishman), and six grandchildren, Oscan Hokin Sachs, Lucas Francis Sachs, Nicholas Arpad Grayson, Natalie Eve Grayson, Oliva Belle Fishman, and Teala Fishman.

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