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The gastroenterology community mourns the loss of Gabriel M. Makhlof, M.D., Ph.D., F.R.C.P. He died peacefully on January 19, 2021 at age 91. He had been Director of Gastrointestinal Research and was an Emeritus Professor of Medicine at the Medical College of Virginia Campus of the Virginia Commonwealth University. He was a world-renown scientist, scholar, and teacher - a pioneer in the field of gastrointestinal peptides. His laboratory made seminal discoveries that significantly advanced our understanding of the function of the gastrointestinal tract in health and disease, in particular the interplay of neural, paracrine, hormonal, and intracellular pathways in the regulation of gastric acid secretion, smooth muscle function, and intestinal motility. Dr. Makhlof enjoyed learning, teaching, and sharing his knowledge. He was an inspirational and generous mentor. Dr. Makhlof was a champion, especially, for young investigators, minorities, women, and those with limited institutional resources and support. He will be missed greatly by family, friends, and colleagues.

Dr. Makhlof was born in 1929 in Haifa during the British Mandate of Palestine. He was married to his beloved wife Avril who preceded him in death in 2007, and is survived by his three children and their families, Eliana Thacher and her husband Hugh; Vivien Barkidjija and her husband John and

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their children John, Gabrielle, Nicholas and George; and Dr. Paul Makhlouf and his wife Stanislava and their daughter Emilia.

Upon graduation from high school in Jerusalem, Dr. Makhlouf, was awarded one of two national scholarships to study medicine at Liverpool University in England. More interested in chemistry than medicine, he accepted the award because he wanted to see the world (and the scholarship paid very well). After being graduated from medical school in 1953, he could not find a job. Consequently, he spent two years with the Jesuits in Lebanon and France before resuming his medical career, working in Palestine with refugees under the aegis of UNRWA (United Nations Relief and Works Agency for Palestine Refugees in the Near East). He then spent two years with the Ministry of Health in Kuwait, where in 1959, he met his wife Avril, a talented artist and scholar. They married and moved to Edinburgh, Scotland. At the University of Edinburgh, he studied classical language and resumed advanced medical research while Avril studied Arabic and began doctoral studies in history and theology. Dr. Makhlouf received advanced accreditation by the Royal College of Physicians of Scotland and England. Both received Ph.D.'s from University of Edinburgh: Gabriel in Physiology and Avril in History.

Again, unable to find a job in Medicine, Dr. Makhlouf took a job in the gastrointestinal research laboratory of Dr. Willard I. Card at University of Edinburgh. Here, he began his life-long studies of the mechanisms governing the control of gastrointestinal secretions. His studies of the mathematical analysis of salivary secretions laid the foundation for his later approach to acid secretion and instilled in him a love of data interpretation. His thesis entitled "The action of Gastrin II on gastric secretion in man" was the first description of the effects of the hormone gastrin in man"- the 'man' being Gabriel himself! Dr. Makhlouf related that he and Dr. McManus flipped a coin to see who would first be injected with gastrin; he lost. So much gastric juice was produced and pouring from the nasogastric juice over both the first and second hours, that both were terrified; eventually, it subsided. The findings were presented by Dr. Makhlouf at the first symposium on gastrin held at UCLA in 1964. There were 10-12 investigators in attendance; Dr. Makhlouf was the youngest. The significance of this was noted by the conference chairman, Dr. Morton I. Grossman, in his published remarks: "Anyone holding that view [that studies of gastric secretion cannot be performed as accurately in man as in dog] should be quickly and permanently disabused of it by studying the data of Makhlouf and Card. These data show a remarkable

reproducibility, rarely achieved in studies in man or dog.” This also established the enduring relationship and exchange of ideas between Drs. Makhlof and Grossman on the role of gastrin and other hormones such as histamine in gastric acid secretion. The two exchanged many letters and data as they worked to disentangle the many and competing hypotheses on control of gastric acid secretion.

After short faculty positions at the Medical Schools of Tufts University and the University of Alabama-Birmingham, Dr. Makhlof moved to Richmond, Virginia in 1970 as Professor of Medicine, Director of Gastroenterology Research, and Co-Director of the Gastroenterology Fellowship Training Program at the Medical College of Virginia. He continued his studies of gastric acid secretion and with his colleagues established a holistic model of acid secretion demonstrating the roles of histamine, somatostatin and other hormones/peptides from gastric fundus and antrum. In the 1980s, his interests in neuropeptides and hormones led him, additionally, into the field of smooth muscle biochemistry and physiology, and ultimately to gut motility. His studies were equally as foundational in understanding smooth muscle and how it is regulated. He and his collaborators were the first to isolate single smooth muscle cells from the mammalian stomach. This approach was transformative of motility at the time and allowed him to delve into the biophysics of peptide-receptor interaction, the intracellular signaling pathways which initiated responses, and the mechanisms of contraction and relaxation during peristalsis. These studies too led to models of smooth muscle function and to the role of the enteric nervous system in the regulation of peristalsis that have stood the test of time.

Dr. Makhlof was the recipient of many awards for his scientific accomplishments and served many leadership positions in the American Physiological Society (APS), the American Gastroenterological Association (AGA), and the National Institutes of Health (NIH). He was funded continuously for over 40 years by the NIH, including a MERIT award, and published over 225 peer-reviewed papers and chapters. He was Associate Editor of the *American Journal of Physiology: GI & Liver Section* and served on the editorial boards of major gastrointestinal publications including the *American Journal of Physiology*, *Gastroenterology* and *Journal of Gastrointestinal Motility (Neurogastroenterology & Motility)*. He was editor of the comprehensive Handbook of Physiology: Section 6 Volume II: Neural and Endocrinology of the Gut. Dr. Makhlof was a member of the VA Merit Review Board and several cycles of NIH Study Sections, serving as

Chairman of the General Medicine A2 (Gastroenterology) NIH Study Section from 1981-1983. He was Chairman of the AGA Council on Hormones and Receptors, the AGA Gastroenterology Research Group, and Steering Committee of the American Motility Society. Considered by the AGA as "one of the most outstanding gastrointestinal physiologists of the modern era", he was awarded numerous national and international awards. Most notable include the American Physiology Society Gastrointestinal and Liver Section Horace Davenport Distinguished Lectureship Award, the Janssen Award for Lifetime Achievement in GI Motility, the AGA Distinguished Lifetime Achievement Award, the AGA Mentor Research Scholar Award, the Mort Grossman Distinguished Lectureship Award from the International Hormone Symposium on GI Hormones, the Wiley Dodds Research Lecture Award from Medical College of Wisconsin, and the John Walsh Distinguished Lectureship from CURE. He received many other awards and honorary lectureships too numerous to mention. Most recently, on the occasion of his 80th birthday, VCU Health established the Gabriel Makhoul Education Fund to support the education of current trainees by funding an annual lecture by a distinguished visiting speaker (Priscilla.wiggin@vcuhealth.org).

In addition to his professional accomplishments, Gabriel had many areas of interest and accomplishment. He and his wife Avril spent many hours appreciating and enjoying artistic expression. He was particularly adept at primitive sculpture in stone and in expression through combined natural wood and metal art while his wife tackled the same subject in paint. He also loved history and politics, his knowledge of which often surprised and amazed visitors to the lab. Conversations of current events and political history often went far into the evening, rivaling scientific topics. Most of all, Gabriel was deeply spiritual, "Be grateful for all God places before you." Under a stern exterior was a gentle, gracious, and compassionate man. He spent much of his time talking to and teaching students and fellows, making sure they understood the bigger picture. He cared for the families of all who passed through his lab, making sure that they understood that family came first. He cared strongly about ways to bring people of different beliefs and faiths together. In his latter years, he spent much of his time reaching out to the sick and needy in the Richmond community. He always erred on the side of objectivity in personal and scientific endeavors, often opting to give a paper or an idea a chance to find its own level of acceptance. He touched many lives for the better and his guidance and sensitivity will be greatly missed. As he ended every conversation, "peace".

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