In memoriam: Gerald (Gerry) Salen, MD (1935–2020)

Shailendra B. Patel1,2, G. Stephen Tint3,4, Akira Honda5, and Scott M. Grundy6,7,8

1Division of Endocrinology, Diabetes and Metabolism, University of Cincinnati, Cincinnati, OH, USA; 2Cincinnati Veterans Affairs Medical Center, Cincinnati, OH, USA; 3(Retired) Research Service, Department of Veterans Affairs Medical Center, East Orange, NJ, USA; 4Department of Medicine, UMDNJ-New Jersey Medical School, Newark, NJ, USA; 5Joint Research Center and Department of Gastroenterology, Tokyo Medical University Ibaraki Medical Center, Ibaraki, Japan; 6Center for Human Nutrition, Dallas, TX, USA; 7North Texas Health Care System Veterans Affairs Medical Center, Dallas, TX, USA; and 8Department of Internal Medicine, Dallas, TX, USA

The fields of bile acid metabolism and rare diseases lost a giant on November 19, 2020. Gerald (Gerry) Salen was born in Philadelphia, PA, on February 13, 1935, to Henry and Belle Salen, both of whom were from families that had emigrated to the United States from Bialystock and Odessa in Eastern Poland/Ukraine in the 1880s, fleeing the pogroms. He received a bachelor of science degree in Pharmacy from Temple University in Philadelphia and subsequently received his MD from the Thomas Jefferson School of Medicine in Philadelphia. Following his residency in Gastroenterology at Jefferson, and a research fellowship for 1 year at Jefferson, he secured a position as a Guest Investigator and Associate Physician in the lab of Dr Edward “Pete” Ahrens at the Rockefeller University in 1966. The University at that time was at its scientific peak, and it was a unique opportunity for young investigators to initiate their careers. The Ahrens’ laboratory was in a particularly productive period of research on the metabolism of cholesterol, bile acids, and related sterols. Several research fellows or junior faculty members were beginning their distinguished careers in medicine at that time in the Ahrens’ lab: Alan Hofmann, Norton Spritz, Jan Davignon, Eder Quintao, Robert Lees, and one of us (Scott Grundy). Dr Ahrens was reportedly a tough task master; this was a rich opportunity for Gerry Salen to begin his scientific career in clinical research. Although his early focus was on the metabolism of non-cholesterol sterols, specifically sitosterol and cholestanol (1), Dr Ahrens insisted that research be carried out primarily in humans. It was during this time that Gerry became interested in patients with a rare disease called Cerebrotendinous Xanthomatosis (CTX) and thus began a more than 5-decade plus life-long passion to uncover the pathophysiology of this rare bile acid disorder in humans (2). This rare disorder is caused by loss of sterol 27-hydroxylase (CYP27A1), which causes a lack of chenodeoxycholic acid production and an accumulation of cholestanol and toxic bile alcohols. He also carried out investigations on the metabolism of sitosterol, which led to a long-standing interest in another rare human disorder, Sitosterolemia (3).

By 1969, he was affiliated with the section of Gastroenterology at the New York Veterans Hospital and the Department of Medicine at New York University Medical Center. He started his own laboratory
focused on patient-oriented research and invited one of us (Steve Tint) to join him. Four years later, they moved to UMDNJ when he became the Director of Gastroenterology and, together with Sarah Shefer, formed a long collaborative effort that lasted until each retired from active research. In the early 1970s, he started a clinical practice at Cabrini Medical Center in NYC at the invitation of Dr Ervin Mosbach. With Mosbach and Shefer, he developed new sensitive methods for measuring the activities of HMG-CoA reductase and cholesterol 7α-hydroxylase in human tissue samples (4) and demonstrated increased HMG-CoA reductase and decreased cholesterol 7α-hydroxylase activities in the liver from patients with gallstone. He was a pioneer in the assay of these rate-limiting enzyme activities using clinical samples (5).

The fundamental and careful clinical studies of patients with CTX and Sitosterolemia laid the foundation for the advances in the discovery of their pathophysiological changes; for CTX, appreciating that the key loss of chenodeoxycholic acid (CDCA) and the accumulation of bile alcohols led to a chronic persistent damage of the blood-brain barrier, together with improvement of this with replacement CDCA, which remains the mainstay treatment of this disease (6–8). For Sitosterolemia, his clinical studies in affected patients and controls showed that the affected subjects had an inability to excrete cholesterol and sitosterol into bile and thus localized the defect to the hepatobiliary system (9). The subsequent molecular elucidation of the defective genes for these diseases confirmed the validity of these findings.

Gerry remained a champion for CTX advocacy; he supplied CDCA free to all of the patients with CTX he was affiliated with (courtesy of the Falk family and their chemical company in Germany, who shipped this to him on a regular basis). Unfortunately, with newer US Food and Drug Administration (FDA) regulations enacted in the late 2000s, no such drugs could be imported and he helped guide bringing CDCA (previously approved only for gallstone dissolution) as an FDA-sanctioned medication that could be prescribed, although to this day it is not officially approved for CTX management.

And the most remarkable aspect of Gerry’s life was how devoted he was to all of his patients and the care and access he afforded them; 3 days before he passed away, he accepted a phone call about one of his patients with CTX and discussed the CDCA dosing and management, despite his deteriorating condition. His devotion was matched by his scientific and clinical creativity, when he crafted the ileal bypass treatment for his patients with Sitosterolemia, persuading a very skilled surgeon to perform this surgery (10). This was the most effective therapy for the control of this disease and a very bold step, until he and one of us (Shailendra Patel) worked with Merck-Schering Plough to show ezetimibe is also very efficacious as a long-term therapy (11). His lifetime of work will continue to help patients for many generations to come.

**Author ORCIDs**
Shailendra B. Patel  https://orcid.org/0000-0003-0046-5513
Akira Honda  https://orcid.org/0000-0003-0902-8272
Scott M. Grundy  https://orcid.org/0000-0003-2956-7900

**REFERENCES**