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Biosketch

John Senior, a native of Philadelphia (17 July 1927), attended the Central High School of Philadelphia (B.A., 1945), studied chemical engineering at Drexel University (1948), physics at the Pennsylvania State University (B.S., 1950), and medicine at the University of Pennsylvania (M.D., 1954). After internship and medical residency (1954-7), he was a clinical fellow in gastroenterology (1957-9), all at the Hospital of the University of Pennsylvania. He then was a National Institutes of Health Special Research Fellow at Harvard University and Massachusetts General Hospital (1959-62), where he worked out mechanisms of intestinal absorption of fats across the small intestinal epithelial cells into lymph and blood in the rat and man.

Returning to Penn, he established a Gastrointestinal Research Laboratory at the Philadelphia General Hospital (PGH), and worked on detection of viral hepatitis after transfusion of blood ("serum hepatitis"). PGH was the first hospital in the world to screen donor blood for a marker ("Australia antigen") of hepatitis B and to exclude positive units from use, leading to the reduction of post-transfusion hepatitis incidence there by 65%. He worked closely with the discoverer of that antigen, Baruch Blumberg, who was awarded the Nobel Prize in Medicine or Physiology in 1976 for discovery of the hepatitis B virus.

Senior was elected to the Council of the American Association for Study of Liver Diseases in 1969, was its 25th President in 1973-4, and served on its Governing Board until 1979. He investigated use of computer simulation of patients for testing candidates for certification of medical competence by the American Board of Internal Medicine and National Board of Medical Examiners (part-time at the Presbyterian Hospital). He returned to Penn at Graduate Hospital, in 1974 to direct its Clinical Research Center, then opened a special treatment unit for serious medical complications of alcoholism in 1975 for over 3500 patients referred from Philadelphia and six surrounding counties in Pennsylvania and New Jersey from 1974-9.

He worked in pharmaceutical research and development, at Squibb as Director of Regulatory Projects (1979-81), then at Sterling-Winthrop Research Institute as Vice President for Worldwide Clinical Affairs (1981-4). He was an independent consultant (1984-95) to pharmaceutical companies in Europe, Japan, and North America for design and optimization for approvability of clinical trial data and new drug applications.

In June 1995 he joined the Center for Drug Evaluation and Research, Food and Drug Administration (FDA) as a medical reviewer for gastrointestinal drugs. In January 2000 became Senior Scientific Advisor to the Office of Drug Safety, consulting on drug-related liver problems to reviewing divisions and conducting research on detecting and attributing causality for idiosyncratic drug-induced liver injury. In July 2003 he was named Associate Director for Science, Office of Surveillance and Epidemiology in 2005, and serves as principal consultant in hepatology at the Agency, focusing on preventing serious drug-induced liver injury.

He has been married to the former Sara Elizabeth Spedden (CW'52) of East Falls, Philadelphia PA since 27 December 1952; they have three grown children, six grandchildren, and two great-grandchildren. He is a retired Rear Admiral, Medical Corps, United States Naval Reserve, after serving 39 years (1945-84).

Abstract: Is the eDISH Program the Long-Sought and Best Current Biomarker of DILI ?

Many papers are being published that attest to a present unmet need for a new and better biomarker for DILI, which has been a diagnosis of exclusion. The eDISH (evaluation of Drug-Induced Serious Hepatotoxicity) program was developed about 12 years ago to assist in the identification and diagnosis of serious liver injury caused by drugs in subjects under study in controlled clinical trials. It was not originally intended to be a biomarker, but in retrospect it really is a sequential, compound series of biomarkers that performs better than any single biomarker found to date. It first looks at a series of serum aminotransferase measures to detect elevations indicative of acute hepatocyte injury, then looks at whether the injury is extensive enough to show diminution in liver overall function using clearance of bilirubin, then gathers additional biomarkers to exclude or diagnose various viral infections or medical conditions that might cause abnormal findings, and finally a clinical narrative that allows understanding of how the investigator or medical person in charge reached a conclusion that the cause was probably drug-induced, initially hepatocellular, and serious enough to cause either jaundice or significant retention of bilirubin. The overall eDISH program performs like a series of biomarkers and it has been found to be the best diagnostic tool so far. Addition of another biomarker that would allow prediction of life-threatening severity and need to consider transplant, would make the program even better. Perhaps it is too much to ask of any single biomarker to do all that.