

John R. Senior, M.D.
Associate Director for Science (Hepatology)
Office of Pharmacovigilance and Epidemiology,
Center for Drug Evaluation and Research, FDA
john.senior@fda.hhs.gov



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: The Isoniazid Story – One More Time, With Implications

You have heard learned and passionate arguments about the danger of rechallenging a liver that has shown injury from a drug by re-administering the drug, and the strong conclusion that it should never be done. Drs. Papay and Hunt have been the leading advocates of this position since their work together at GSK. We have all heard but perhaps not fully appreciated lessons learned over many decades from the drug, isoniazid (INH). It was found useful in preventing activation of tuberculosis in people exposed, but at some risk of induced hepatocellular injury that could be fatal if ignored. After three decades of dicker about it, the work of Charles Nolan and associates in 1999 finally concluded that it could be used safely, without routine monthly monitoring of all patients with serum aminotransferase measurements, but that early symptoms of anorexia, nausea, fatigue, or jaundice should not be ignored. Symptoms should be immediately reported by the patient and immediately followed up by the treating physician to confirm liver injury, assess liver function, and its short-term course, stopping the drug permanently if serious hepatotoxicity was found. In 11,151 patients observed there were 11 cases, with no deaths. It is now still recommended that INH prophylaxis be given, but not recklessly. Deaths are still occasionally being reported when the lessons were not learned. It is of interest that a very recent paper (January 2016, Epub ahead of print) by one of tomorrow's speakers, Jack Utrecht, will make comments on some recent findings.