

Introduction of the American Pediatric Society's 2010 John Howland Award Recipient, Charles R. Scriver, MDCM

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John Howland, MDCM, was the leader of the first full-time academic Department of Pediatrics at the Johns Hopkins Hospital (1). Howland was a remarkable clinician-scientist, a mentor, and a visionary leader who emphasized patient care in an environment of laboratory research and clinical study. His contemporaries and protégés recognized that he could perceive complex interrelationships (2). The Howland Award was created to recognize and honor outstanding scientists who are also outstanding leaders and teachers.

This year we bestow the honor of the Howland Award on Charles R. Scriver, CC, GOQ MDCM, DSc (Hon), FRS, and FRSC (Fig. 1). Charles Scriver is a legendary biochemical geneticist and student of biology. It is especially appropriate that we honor Charles in Vancouver, Canada, because he is the first Canadian to win this award.

Dr. Scriver is in every way a Canadian. Born in Montreal, he graduated from Lower Canada College in that city and received his BA degree from McGill University in 1951, followed by his MDCM (*Medicinae Doctorem et Chirurgiae Magistrum*) from McGill in 1955. After training in medicine and pediatrics at the Royal Victoria Hospital and the Montreal Children's Hospital, two McGill teaching hospitals, he completed his pediatric residency at the Children's Hospital in Boston. He was then selected as a McLaughlin Traveling Fellow for two years in the Professorial Metabolic Unit of Professor Charles E. Dent at University College Hospital, London. In 1960, Scriver returned to the Montreal Children's Hospital as chief resident in Pediatrics and was hired by Alan Ross, MDCM, Chair of Pediatrics at McGill, to a faculty position. This position, in Biochemical Genetics and Human Genetics, was the first and only position in Scriver's career.

As geneticists know their roots, Scriver came from and knew his distinguished forbears. Although Charles Scriver is a proud Canadian, he has "American" ties. His ancestors were religious refugees from the Rhineland Palatine region of what is now Germany who in 1705 immigrated to Great Britain. The Scriver's then crossed the Atlantic to Rhinebeck-on-Hudson in New York, accompanying other Palatine refugee families who settled along the Hudson. As King

William and Queen Mary had rescued these Palatine refugees, the Scriver's remained loyal to the Crown after July 4, 1776. In 1788, the Scriver's and other refugee families were "invited" to leave for Hemmingford in Lower Canada, now Quebec. Scriver's were prominent in protecting Canada from the American invasion in 1812 and served in Parliament at the time of the Confederation of Canada.

Charles' father, Walter deMouilpied Scriver, MDCM, born of United Empire Loyalist stock, practiced medicine at McGill from 1921 to 1957 and rose to become physician-in-chief at the Royal Victoria Hospital (3). He was interested in metabolism, diabetes, and nephrology. His mother, Jessie Boyd Scriver, MDCM, was one of the first woman graduates of McGill, the first female pediatrician in Montreal, and an early expert in sickle cell disease (4). His mother had prematurely white hair; a trait shared by her son, their only child.

Charles married Esther Pierce in 1956. She is known as Zipper, a name derived from her 3-year-old sister's mispronunciation of "sister." The Scriver's have four children: Dorothy Ellen, a lawyer; Peter Charleton, an academic architect; Julie, a publisher, illustrator, and long-time ballerina; and Paul, a musician and composer.

Charles Scriver established the deBelle Laboratory for Biochemical Genetics at the Montreal Children's Hospital. He brought back to Canada from his training with Dent "a whole new concept of cellular physiology that was just emerging there from biochemical genetics..." (5). Scriver was recruited to this position, and his entire career was spent studying human genetics at the Montreal Children's Hospital and McGill University.

What is the measure of this man, Charles Scriver? He is a Canadian who has immense pride in his country but has been involved with science in the United States, including the National Institutes of Health, the Bar Harbor Genetics Course, the Society of Pediatric Research, the American Pediatric Society, the American Society of Human Genetics and the Society of Inherited Metabolic Disease, and with genetics programs at Johns Hopkins. He served as president of all four of the listed societies. Scriver also has a cabin in Vermont where he writes and relaxes.

It is informative to understand Charles Scriver's heroes: his parents and his family, and the founding fathers of genetics—Gregory Mendel, Sir Archibald Garrod, Francis Galton, and Charles E. Dent. Scriver is a voracious reader and he appreciates authors who write well and capture the plight and glory of man.

Received January 20, 2011; accepted January 21, 2011.

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Presented at the 2010 Annual Meeting of the Pediatric Academic Societies, Vancouver, British Columbia, Canada.

Scriver is also very much a son of Quebec. He is proud to have brought neonatal genetic screening and vitamin D supplementation of milk to the province. He also established programs to improve the quality of science education of secondary school students, placing emphasis on education including human biology and genetics. Charles is a health policy guru who could convince governments to screen for genetic disorders, to improve the quality of science education, and to provide home health care for children with complex conditions. He is also an exceptional mentor whose legacy includes a long list of genetic scholars.

Scriver is a writer. His vivid language makes sentences sing and what he writes is provocative. He has published a remarkable number of books, chapters, and original articles including the incomparable *The Metabolic and Molecular Bases of Inherited Disease* (6). One of the editions of this text won the AMA Medical Writing Award as the best publication of the year in 1995.

The essence of Charles Scriver mainly lies in his extraordinary imagination. Academic medicine has numerous highly

intelligent clinicians and scientists who are storehouses of information and have the capacity to intuit connections. Charles' imagination, however, allows him to see connections we cannot grasp. He also perceives downstream consequences and events that will result in large-scale change. Two quotations from Albert Einstein are pertinent. First, "To raise new questions, new possibilities, to regard old problems from a new angle, requires creative imaginations and marks real advance in science." He also said "Logic will get you from A to B. Imagination will take you everywhere."

Examples of Scriver's mind at work are the concept of inborn errors of transport disorders, the integration of human genetics with the human genome project, and the recognition that information could be updated in real time with an online edition of his remarkable text. He also challenged us to understand the biologic processes that underlie the physiology, cellular biochemistry, and pathophysiology of man and his variant conditions. Scriver could design figures that not only explained data effectively but also did so in an encompassing and contextual fashion. He had the capacity to envision new diseases or disorders. Charles' name appears on the initial reports of more than 30 disorders. This ability to place these entities into context helped to define the phenotypic spectrum. For instance, adolescent cystinosis was a component of the heterogeneous nature of cystine storage disease. The vitamin-sensitive aminoacidopathies are a further example of this contextual thinking. He also recognized that the accident of nature, the PHEX Hyp mouse, discovered at the Jackson Laboratory in Bar Harbor, ME, would not only represent a murine model for X-linked hypophosphatemic rickets but could be used to study heredity, pathophysiology, treatment, and prognosis of this inherited form of rickets.

Scriver became a serious student of phenylketonuria. His studies over his career examined the hereditary pattern, genetic screening, for dietary avoidance of the amino acid, the organization of home health for patients, and, more recently, the myriad of pathways that can be mutated within the phenylalanine hydroxylase complex in liver. There can be point mutations, gene deletions, cofactor binding abnormalities, and immaturity of the enzyme system.

Scriver was and is highly efficient. He followed the dictum of Sir William Osler, another Canadian McGill graduate who was a founder of the American Pediatric Society. A great writer and teacher, Osler stated, "Live life in day-tight compartments" (7). Scriver lived that admonition.

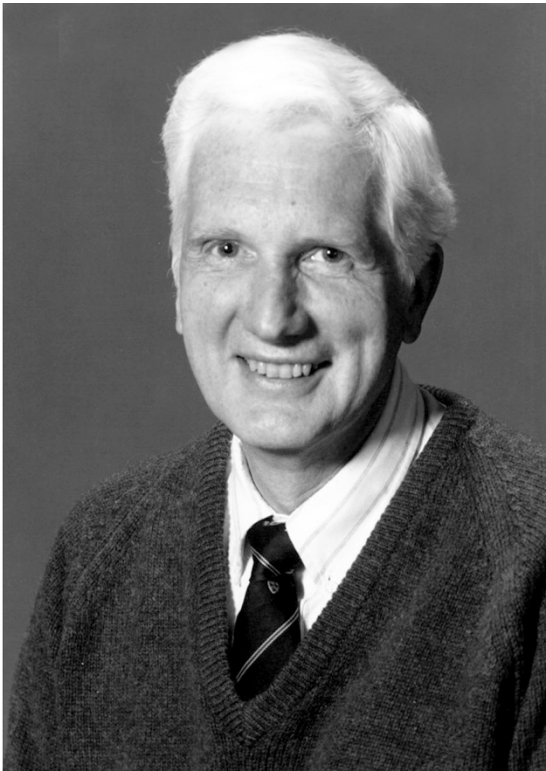


Figure 1. Charles R. Scriver, MDCM

Table 1. A comparison of John Howland and Charles Scriver

	Howland	Scriver
Favorite winter haunt	New Hampshire	Vermont
Favorite summer haunt	Chatham, Cape Cod (Howland's home)	Bar Harbor, Maine (Genetics course)
Favorite form of water	Ice and snow	Ice and snow
Patient evaluation	Careful, illuminating	Careful, illuminating
Mentor of future pediatric leaders	Two generations	Two generations
Rickets	Discovered vitamin D with Park and McCollum, described animal models of rickets (beagles), added vitamin D to dairy products in USA	Described hereditary forms of rickets, described Mendelian forms of rickets (mice), added vitamin D to dairy products in Quebec
Legacy	His concepts and his mentees	His concepts and his mentees

In many ways Charles Scriver is similar to John Howland (Table 1). Both had large concepts that they put into action. Both had enormous influence on the development of pediatric research and on concepts that altered the lives of children both locally and around the world. The 2010 John Howland Award recipient is a renowned biochemical geneticist and human biologist. It is an honor to present this award to Dr. Charles Robert Scriver.

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