The review focused on mechanisms of ethionine carcinogenesis. Effects of this methionine analog in prokaroytes and eukaryotes, similarities in the carcinogenic process between the steps with ethionine and other hepatocarcinogens, and possible cellular metabolic bases for some steps were included. (The SCP® indicates this manuscript has been cited in over 405 publications.)

During medical school in Toronto, and subsequently in graduate school in Berkeley, I became increasingly interested in studying the biochemical basis for the development of cellular and tissue changes in disease, so I placed special emphasis on acute cell injury. The development of the concept of metabolic antagonism late in the 1930s and the availability of a few analogs, including ethionine, led naturally to the study of the metabolic disturbance induced in animals by ethionine. These studies gave us new insights into the quantitative modulations of some biochemical networks relating to methionine, such as the imbalance between the synthesis of S-adenosylmethionine and its utilization as a methyl donor.1 This orientation became useful in later studies on liver carcinogenesis with ethionine, since it highlighted the concept that quantitative variations in normal metabolic pathways may play an essential role in the development of disease.