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Obituary Serge C.Renaud

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Close to his 85th birthday, Professor Serge Renaud passed away on Sunday October 28th 2012, walking along the lake in his village in the Medoc wine region of south west France. He kept until the end the desire to be aware of the latest development of his ideas, always on the lookout for novel research.

Half-French, half-Canadian, he was born on November 21st 1927 in Cartelègue, Blayais, a small town which named the town square in his honor in 2006. He grew up in the Bordeaux region, where his grandfather had a vineyard, and learned early about healthy eating habits: fruits, vegetables and some wine with water.

After beginning his medical training in France, he moved to Canada in 1951 where he was lumberjack to pay for university costs. "When I left France at the age of 24, I couldn't imagine there was a population in the world that didn't drink wine with meals" he said. He noted immediately dietary issues with especially low fruits and vegetables, possibly associated with frequent episodes of myocardial infarction (MI), even among young hockey players, despite their French gene pool.

After finishing his training and being awarded the VMD degree in 1957, where he was first in his class at Saint-Hyacinthe, Montreal, he chose to devote himself entirely to research. His first scientific paper was published in 1957 with Hans Selyé, the discoverer of the "stress" reaction, with whom he made a brilliant start to his career. Selyé wanted him to become his principal assistant. However, Serge Renaud preferred instead to focus his research on diet as a key factor in the development of coronary heart disease (CHD). He was awarded a PhD degree in Experimental Medicine and Surgery in 1960, and began to realize that thrombosis was the main event in MI, based especially on his observations of autopsy material. He observed that such thrombosis was independent on cholesterol levels, 30 years ahead of his time.

Serge was Head of the Laboratory of Experimental Pathology, Montreal Heart Institute, for 13 years. In 1971, he became Visiting Professor at Boston University, in the Department of Pathology. He then returned to Montreal and became Professor of Pathology at the University of Montreal. He became Professor and Director, Department of Nutrition, Faculty of Medicine, at the University of Montreal in 1975. He returned part-time to France in 1973 to take care of his parents, and entered into INSERM as Director of Research in Lyon, within the Cardiology Hospital. He regretted the move to France in some ways, as research conditions in France were not those offered by Canada. He completed his academic career as Research Director INSERM in Bordeaux, where he remained until retirement; even later he received an emeritus position there and went to his office every day for the next 10 years, launching a follow-up cohort study on 100,000 subjects in the center for preventive medicine of Nancy and an intervention trial about atrial fibrillation recurrences with Dr. Dominique Lanzmann-Petithory.

Thus, as early as 1960, Serge decided to investigate extensively the relationship between nutrition, especially saturated fats (SFA), and thrombosis. He said himself that most of the success he had in research on CHD resulted from that decision. He developed an original method to investigate platelet reactivity in humans: the "caravan", a mobile laboratory to reach rural populations of different countries and measure immediately platelet functions in relation to SFA, alpha-linolenic

acid (ALA), calcium, alcohol, polyphenols and smoking. It was only a Cretan type of diet with a high intake of ALA that was able to normalize all platelet tests, thus reducing the risk of coronary thrombosis.

The Seven Country Study revealed that subjects in Crete were doing, or eating, something right, as Crete had by far the lowest CHD mortality rates of the 7 countries and regions studied, despite having higher serum cholesterol. "Something protects the Cretans which does not reduce their cholesterol", proposed Serge Renaud. He guessed that it was ALA. He designed then a randomized secondary prevention trial on coronary patients, with an ALA enriched diet with canola oil and margarine, in comparison with the typical low-SFA diet being proposed at the time. After 6 months, the cardiologist who followed the patients wanted to change the diet because the cholesterol did not decrease among the subjects on the ALA diet! But Serge Renaud knew that thrombosis was the important factor. Then the trial was stopped because of striking differences between the groups, compared to the prudent diet, the "Cretan" diet reduced cardiac death by 76%, non-fatal MI by 73%, and total death by 70%. The protection observed was found to begin as early as two months after diet modification began. The main article issued from that study was published in *The Lancet* in 1994, and is still referred by the experts in the field as the "Lyon intervention study".

In 1991, Morley Safer from "60 min," the popular CBS television program in the United States, came with Dr. Curtis Ellison to his laboratory in Lyon, to ask Serge his opinion on the cardiovascular protection of the French. Serge Renaud suggested, taking great precautions, that alcohol could be one of the key protective factors. Morley Safer, holding a glass of red wine, concluded the television segment saying: "The explanation of the French Paradox may lie in this inviting glass". Scientists and medical doctors will usefully read the tribute published by Bruno Simini in *The Lancet* on January 1st, 2000: "Serge Renaud, from French Paradox to Cretan miracle".

Serge Renaud allowed Michel Lagarde (ML) to apply for an INSERM Research Scientist position through his research unit when ML was a Research Assistant at Pasteur Institute. Ten years later, ML left the research unit for a position in Dijon before coming back to Lyon to take over another INSERM research unit. During this ten year period, ML benefited from Pr Renaud's open minded way of seeing experimental research. ML still remembers active discussions about studying molecular mechanisms of disease. Serge Renaud believed that mechanisms are useful, but are secondary to the observation of facts, that he considered as the primary targets of INSERM. Serge Renaud's way of managing people was always impregnated of humanist philosophy, ML says. When conflicts arose between people, he always advised them to go back to humanities: "Go back to reading Victor Hugo, this will help you by taking some distance." Whenever problems arose, Serge Renaud's leitmotiv was, "Never give up!"

Serge also published books for the public, such as "The Healthy Diet," in 1995, and "The Cretan Diet, Incredible Protector of our Health," in 2004. For his overall contribution to scientific research, Serge Renaud received numerous prizes such as the Award of the "Fondation Française de Nutrition" in 1983, and the Nestlé award of Nutrition in 1997. In 2005, he received the highest distinction in France for his general contribution to society: the "Légion d'Honneur".

As Professor Fulvio Ursini from the University of Padova in Italy said in a tribute provided by members of the International Scientific Forum on Alcohol Research (www.bu.edu/alcohol-forum) on 1 November 2012: "We are all in debt to Serge for the lesson he gave to our scientific community: curiosity as the sole reason to investigate, diligence in observing the facts, unbiased stringency in interpreting results, and definitely not least, the modesty that only a great man can have. We shall keep him in our memory as an example and a mentor of the meaning of being a scientist." Of further interest to the ISSFAL members, Serge Renaud was a "founding father" of the Society.