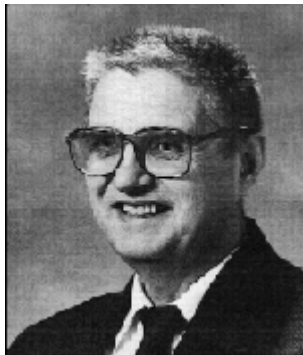


## Obituary

Carl Arthur Goresky - August 25, 1932 to March 21, 1996



Harry L. Goldsmith, PhD

Andreas J. Schwab, PhD

Phil Gold, MD, PhD

*From McGill University and the Montreal General Hospital.*

*Clin Invest Med* 1996; 19 (3): 144-148

---

Reprint requests to: Dr. Harry Goldsmith, University Medical Clinic, Room C10-185, Montreal General Hospital, 1650 Cedar Ave., Montreal QC H3G 1A4; fax 514 937-6961

Copyright 1996, Canadian Medical Association

---

It is with deep regret that we write of the death of Carl Arthur Goresky, professor of medicine at McGill University, Medical Research Council of Canada Career Research Investigator and director of the Division of Gastroenterology at the Montreal General Hospital. Carl died peacefully in the hospital where he practised medicine for 36 years, after a courageous and spirited battle with cancer lasting almost 6 years. He was a consummate physician and scientist, who actively engaged in scholarly research until the very day of his passing.

Carl's greatest achievement in his extensive research was the successful application of rigorous mathematical methods, combined with carefully designed experiments, to explore fundamental physiological phenomena. Biomedical scientists often shun all but the simplest mathematical theories, arguing that they are too difficult and thus not understood by the average physiologist. On the other hand, the sophisticated ideas of theoretical biologists are often far from reality and cannot be verified experimentally. This situation has not improved with the advent of the techniques of molecular genetics. As useful as these techniques are for the assessment of the macromolecular outfit of the cell, the dynamics of rapid, complex physiological processes cannot be

understood without a realistic mathematical description of their principles. Carl's success in this respect was remarkable. His experimental approach was simple but effective, and his mathematical treatments were straightforward in their essence but elaborate in their details.

A brilliant student in high school in Castlegar, British Columbia, Carl entered McGill University at the age of 16 and at 22 had graduated in medicine, having obtained a BSc en route. After a 1-year internship at McGill, he completed his residency training in the United States. His life interest in capillary exchange, cellular entry and metabolic sequestration processes in the microvasculature of liver, lung, heart and brain was sparked during 2 years of his training spent in Dr. Francis Chinard's laboratory at the Johns Hopkins Medical School in Baltimore. Chinard introduced him to the multiple-indicator dilution technique. Carl was immediately fascinated by the elegance of the method. Early indicator dilution measurements designed a century ago by Steward[1] and in the 1930s by Hamilton and associates,[2] could not distinguish the effects of various phenomena, such as fluctuating blood supply and capillary perfusion, cellular uptake, metabolism and secretion, on the retention of indicators within organs. By injecting several tracers simultaneously into the arterial blood stream of an organ and analysing them separately in timed samples of the venous outflow, Chinard sought to unravel the effects of these phenomena.[3] Throughout his career, Carl had a special and fruitful relationship with Chinard; the two scientists were always mutually respectful of each other's knowledge and talents.

Once he was back in Montreal, Carl immediately started experimenting with the multiple-indicator dilution technique in the liver of dogs. By building on what he had learned in Baltimore, and without any further guidance except for the steady encouragement of his doctoral thesis supervisor, Dr. Arnold Burgen, he developed the necessary surgical and experimental procedures to catheterize the portal and the hepatic veins of the animals, taking care to close the abdomen after surgery and before the experiment in order to keep the liver in its natural environment. He soon noticed that when labelled red cells, albumin, sodium, sucrose and water were administered simultaneously, their resulting concentration-time profiles in the venous outflow were linked by a simple mathematical relation: they were superimposable upon a linear expansion of the time scale. He interpreted these results by simple but ingenious hypotheses about two processes: a distribution in the transit times of the hepatic sinusoidal flow paths due to variations in their lengths and in flow velocities of the blood, and a rapid, "flow-limited" equilibration of the tracers among the sinusoidal, interstitial and parenchymal spaces. He introduced these hypotheses at a time when the nature of Disse's space and the existence of fenestrated endothelial cells lining the hepatic sinusoids were unknown. Thus, these ideas constituted a breakthrough. His first paper, published in the *American Journal of Physiology* in 1963,[4] of which he was the sole author, was also the basis of his doctoral thesis, which included two other papers[5,6] (one of which was coauthored by his first student, Dr. Mel Silverman). All three articles were published within 4 years of his arrival in Montreal. The first paper may be considered, with the article on indicator diffusion by Christian Crone published the same year,[7] as the foundation on which the entire area of whole-organ tracer kinetics was later built.

In the ensuing years, Carl expanded on the same theme, keeping the experimental protocol similar but varying the indicators. Indeed, he continued to use the same equipment -- including the rapid-fraction collector and pumps he brought from Chinard's laboratory in 1960 -- through to his last experiment in September 1995.

When he examined the behaviour of labelled rubidium (as a tracer for potassium) and galactose in the 1970s, the mathematical theory had to be expanded. It became evident to Carl that the input-output relation inherent in an indicator-dilution experiment is analogous to that in an electronic circuit. He therefore contacted Dr. Glen Bach, a mathematician and professor of civil engineering at McGill. Carl quickly learned from him the use of the sophisticated mathematical tools of partial differential equations and Laplace transforms; with Bach, Carl developed the mathematics for the theoretical description of a diffusional barrier across the plasma membrane of the parenchymal cells.[8] This development was based on both Carl's and Christian Crone's 1963 papers and included the independent reformulation of an important equation previously found by Sangren and Sheppard.[9] Later, this model was expanded to include two membrane barriers in series (as found for water in the coronary circulation),[10] and a barrier at the red cell membrane.[11]

Carl's further experimental work involved the uptake and sequestration by the liver of dogs of sulfobromophthalein, bilirubin, copper, glucose, fatty acids, monohydric alcohols, xenon, norepinephrine, lactate and bicarbonate, as well as the assessment of sinusoidal and interstitial spaces under various physiological conditions.[12] With the help of his doctoral students Wilfred Ziegler, Colin Rose and Daniel Cousineau, Carl applied the method to the coronary circulation, particularly with respect to the uptake of oxygen[13] and the uptake and release of norepinephrine by the cardiac sympathetic nerves.[14]

His efforts also led to lengthy and fruitful collaborations with researchers at various other laboratories, foremost among whom was Dr. Jim Bassingthwaite of the University of Washington in Seattle, his coauthor of a chapter in the *Handbook of Physiology*. [15] It was Bassingthwaite who organized the workshop "Whole Organ Approach to Cellular Metabolism: Capillary Permeation, Cellular Transport and Reaction Kinetics," held in Carl's honour at the Montreal General Hospital in July 1995. Among his other collaborators were Drs. Eugenio Rasio of Hôpital Notre-Dame (capillaries of the rete mirabile of the eel), [16] Michel Huet of Hôpital Saint-Luc (cirrhosis of the liver), [17] Sandy Pang of the Faculty of Pharmacy at the University of Toronto (drug disposition and metabolism in the perfused rat liver) [18] and Jim Ryan formerly of the University of Miami and Jean-Lucien Rouleau of Hôpital Sacré-Coeur (angiotensin-converting enzyme). [19] In addition to his remarkable productivity in basic research, Carl actively pursued clinical research in various fields of gastroenterology. Among other achievements, this research led to the discovery of a particular form of trichinosis that affects the Inuit. [20] In relation to this aspect of his research, Carl collaborated with Dr. Ellen Gordon in work on human and rat bilirubin. They isolated nine conjugates of bilirubin with the use of high-pressure liquid chromatography, and used these conjugates to study the rate of excretion in serum and bile. [21] They showed that the formation of a conjugate of bilirubin occurred in the microsomes and

not in the endoplasmic reticulum of the liver cells.[22]

One cannot describe Carl's scientific achievements without mention of the magnificent task he carried out as editor of *Clinical and Investigative Medicine* since 1984. Not only did he significantly raise the scientific standards of the contributed articles through the best peer review, but he also worked hard to put the journal on a sound financial footing. The Canadian biomedical community owes him a great debt of gratitude for his services to the journal.

Throughout his career, Carl's research productivity was prodigious, as evidenced by his authorship of 140 peer-reviewed publications and 28 chapters in books (including 3 in the *Handbook of Physiology*), and his editorial role on two books. Even more remarkable was the fact that, in the last 18 months of his life, suffering considerable discomfort and pain, with several admissions to the hospital, Carl coauthored nine published papers and a further three that are in press.

Because of Carl's extraordinary contributions to research in his areas of interest, his equally remarkable contributions to patient care, teaching and administration in the Canadian academic milieu, particularly at McGill University and the Montreal General Hospital, may sometimes be overlooked.

Carl was an outstanding gastroenterologist. Up to a week before his final admission to hospital, he took an active role in patient care in the Division of Gastroenterology at the Montreal General Hospital. His obvious compassion and concern for the patients who came under his care was often commented upon by those privileged to have him as their physician. Indeed, the Montreal General Hospital often received substantial philanthropic donations from Carl's very grateful patients and their families.

As a teacher, Carl always used the opportunity of talking to undergraduate students, graduate students, medical students and medical residents to illustrate the manner in which the clinician-scientist brings knowledge from the bedside to the bench and back to the bedside. The same was true if he was "rounding" on General Internal Medicine Services on the hospital wards or with the specialty residents in gastroenterology. Each such contact was an occasion for him to point out that basic research in medical science is not an ivory-tower pursuit but has real and rapid applications to the improvement of patient care. There were occasions when Carl would become so involved in a topic that his erudite delivery would leave the resident staff agape. However, he seldom failed to send reprints of the material that he had discussed on the wards, and, very soon, the physician-in-chief would be astonished to hear the residents discussing the topic in a fashion that clearly indicated that they had been impressed and their knowledge base improved by this most remarkable individual. Moreover, many residents who had not considered becoming clinician-scientists were "turned on" to this possibility by having been exposed to Carl Goresky.

The question often arose as to whether Carl, with all of his other interests and activities, would have the patience to administer the Division of Gastroenterology. Suffice it to say that when he took the position of director of gastroenterology at the Montreal General Hospital, he performed the task with the same excellence he brought to all of his other initiatives. He built on the strengths of the division, formerly headed

by Dr. Douglas Kinnear, and opened new areas of activity. Concomitantly, he recruited young clinician-scientists and ensured that they were protected so that they could continue successfully with their research endeavours and their clinical and teaching responsibilities would not be short-changed.

Because of the manner in which he carried out his activities in the hospital, it was soon recognized that Carl would be a superb candidate to lead the merger of the divisions of gastroenterology of the Montreal General Hospital and the Royal Victoria Hospital, both teaching hospitals of McGill University. Indeed, it was the Division of Gastroenterology that was the first to become fully integrated within the new McGill University system.

Carl was honoured many times by his peers not only for his contributions to biomedical science but also for the impact he has had on Canadian and North American medicine. In 1982 he received the prestigious Eugene Landis Award from the Microcirculatory Society. More recently, he was awarded the Gold Medal of the Canadian Liver Foundation and the Distinguished Achievement Award of the American Association for the Study of Liver Diseases. He also received the G. Malcolm Brown Award and the Distinguished Service Award of the Canadian Society for Clinical Investigation as well as the Distinguished Service Award of the Canadian Liver Foundation. The Medical Research Council of Canada gave him an award for 35 years of excellence in research. Most wonderful was the recognition of a lifetime of devoted service to medical science, for which he was inducted into the Order of Canada as Officer, last November. The very last award, which he received 2 weeks before his death, was the Ivan T. Beck Lectureship Award from the Canadian Association of Gastroenterology and the Canadian Association for the Study of the Liver.

Throughout his life, science and medicine competed with, nay, were fulfilled by a love of the mountains of his home province of British Columbia, as well as by a love of hunting and fishing, activities in which he could engage and still be thinking about his research. His talents as an amateur photographer were amply rewarded by the beauty of the alpine lakes and meadows, [reproduced here](#) as a small tribute to his memory. Many were the beautiful fall afternoons that he left the hospital behind, collected his dog and gear, and met a long-time friend, physician David Gorman, to hunt woodcock in the rolling hill country of New York state close to the Quebec border. As late as last November, barely out of his hospital bed, with strict instructions to rest, he went hunting one last time, and to the astonishment of his companions, bagged two grouse, one after the other, as they rose rapidly from the bushes. Few of his colleagues knew that Carl was also an accomplished pianist, who could have competed with the best, had he not decided to pursue a career in medicine.

Carl was a devoted husband, father and grandfather, and a much treasured friend to many colleagues, among whom we were privileged to count ourselves. For all that has been noted here, and for so much more, we can say with the Bard, "We shall not see his like again."

## References

1. Steward GN: Researches on the circulation time and on the influences which affect it. IV. The output of the heart. *J Physiol* 1897; 22: 159-183
2. Hamilton WF, Moore JM, Kinskam JM et al: Studies on the circulation. IV. Further analysis of the injection method and of changes in hemodynamics under physiological and pathological conditions. *Am J Physiol* 1931; 99: 534-551
3. Chinard FP, Enns T: Transcapillary pulmonary exchange of water in the dog. *Am J Physiol* 1954; 178: 197-202
4. Goresky CA: A linear method for determining liver sinusoidal and extravascular volumes. *Am J Physiol* 1963; 204: 626-640
5. Goresky CA: Initial distribution and uptake of sulfobromophthalein in the liver. *Am J Physiol* 1963; 207: 13-26
6. Goresky CA, Silverman M: Effect of the correction factor of catheter distortion on calculated liver sinusoidal volumes. *Am J Physiol* 1964; 207: 883-892
7. Crone C: Permeability of capillaries in various organs as determined by use of the "indicator diffusion" method. *Acta Physiol Scand* 1963; 58: 292-305
8. Goresky CA, Ziegler WH, Bach GG: Capillary exchange modeling: barrier-limited and flow-limited distribution. *Circ Res* 1970; 27: 739-764
9. Sangren WC, Sheppard CW: Mathematical derivation of the exchange of a labeled substance between a liquid flowing in a vessel and an external compartment. *Bull Math Biophys* 1953; 15: 387-394
10. Rose CP, Goresky CA, Bach GG: The capillary and sarcolemmal barriers in the heart: an exploration of labeled water permeability. *Circ Res* 1977; 41: 515-533
11. Goresky CA, Bach GG, Nadeau BE: Red cell carriage of label: its limiting effect on the exchange of materials in the liver. *Circ Res* 1975; 36: 329-351
12. Cousineau D, Goresky CA, Rose CP: Blood flow and norepinephrine effects on liver vascular and extravascular volumes. *Am J Physiol* 1983; 244: H495-H504
13. Rose CP, Goresky CA: Limitations of tracer oxygen uptake in the canine coronary circulation. *Circ Res* 1985; 56: 57-71
14. Cousineau D, Goresky CA, Bach GG et al: Effect of  $\beta$ -adrenergic blockade on in vivo norepinephrine release in canine heart. *Am J Physiol* 1984; 246: H283-H292
15. Bassingthwaite JB, Goresky CA: Modeling in the analysis of solute and water exchange in the microvasculature. In Renkin EM, Michel CC (eds): *Handbook of Physiology: the Cardiovascular System*, vol IV, American Physiological Society, Washington, 1984: 549-626
16. Rasio EA, Bendayan M, Goresky CA: Diffusion permeability of an isolated rete mirabile. *Circ Res* 1977; 41: 791-798
17. Huet P-M, Goresky CA, Villeneuve JP et al: Assessment of liver microcirculation in human cirrhosis. *J Clin Invest* 1982; 70: 1234-1244
18. Pang KS, Goresky CA, Schwab AJ: Deterministic factors underlying drug and metabolite clearances in rat liver perfusion studies. In Ballet F, Thurman RG (eds): *Research in Perfused Liver: Clinical and Basic Applications*, John Libbey,

London, England, 1991: 259-302

19. Dupuis J, Goresky CA, Ryan JW et al: Pulmonary angiotensin-converting enzyme substrate hydrolysis during exercise. *J Appl Physiol* 1992; 72: 1868-1886

20. Viallet J, MacLean JD, Goresky CA et al: Arctic trichinosis presenting as prolonged diarrhea. *Gastroenterology* 1986; 91: 938-946

21. Gordon ER, Goresky CA: A rapid and quantitative high performance liquid chromatographic method for assaying bilirubin and its conjugates in bile. *Can J Biochem* 1982; 60: 1050-1057

22. Gordon ER, Goresky CA: The formation of bilirubin diglucuronide by rat liver microsomal preparations. *Can J Biochem* 1980; 58: 1302-1310

---

[CIM June 1996 / MCE Juin 1996](#)

---

[CMA Webspinners / Les fileurs du Web de l'AMC](#)