

Philip Hench, a Nobel Link in the Evolution of The Canada Gairdner International Awards

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In the past 50 years the Gairdner Foundation has established itself in medical science as a leading philanthropy like the American Lasker Award and The Swedish Nobel Prize¹. To celebrate its 50th anniversary the Foundation has been honored with a 20 million dollar endowment from the 2008 Canadian federal budget. In recognition of Canadian contributions as a world leader in health research the awards have been renamed The Canada Gairdner International Awards².

James A. Gairdner (1893–1973), financier and philanthropist, created his Foundation in 1957 to recognize scientific achievement in a tangible way. Since then The Gairdner Foundation has become Canada's foremost international award, with many winners later becoming Nobel laureates. Moreover, under the leadership of President and Scientific Director Dr. John Dirks and the support of the Gairdner Family it has become a national program with awardees making presentations at many academic centers across Canada².

Gairdner was both a scholar and a distinguished track and field athlete. He served overseas in the First War, retiring with the rank of major. In the early 1920s he began his investment career as a leading stockbroker and industrialist. In keeping with a family tradition he was interested in the clinical and research aspect of medicine. Through his relationship as a patient with leading Toronto Rheumatologist the late Dr. Wallace Graham (1905–1962), Gairdner took a particular interest in arthritis. His involvement culminated in his appointment in 1950 as the first Lay President of what we know today as The Arthritis Society of Canada³.

Born in Sudbury, Ontario in 1905, Dr. Graham, like Gairdner, was a man of many talents⁴ (Figure 1). He graduated from dentistry and medicine in Toronto and was a varsity track record holder for the 3 mile run, unbroken until Bruce Kidd's performance 34 years later. Before the war, Graham did postgraduate work in London, England and later was elected a Fellow of the Royal College of Physicians of London. Postwar he specialized in the rheumatic diseases and became Chief of the Arthritis Service at Toronto's Sunnybrook Veterans Hospital. He was instrumental in the establishment of the Canadian Rheumatism Association and in 1948–1949, with dedicated volunteers led by Mary Pack of Vancouver, he became the first president of the Canadian Arthritis and Rheumatism Society known today as The Arthritis Society. His first board of directors included Mr.



Figure 1. Dr. Wallace Graham, MD, MRCP, FRCPC, FRCP, 1906–1962.

Gairdner, the first lay president, Mr. Norman Urquhart, Mr. Lou M. Wood, and Mr. Edward Dunlop as founding Executive Director. His leadership in rheumatology extended from the national to the international arena as President of the Pan American League Against Rheumatism and Vice-President of the International League Against Rheumatism, where his dynamic personality energized the battle against arthritis. It is not surprising, then, to learn that The Gairdner Foundation was established “with the encouragement” of Wallace Graham, who also served as Chairman of the Medical Advisory Board of the Foundation from its inception until his untimely death in 1962³. Graham had also been the chief organizer of the 9th International Congress on the Rheumatic Diseases held in Toronto in June 1957, at which

the announcement of the establishment of the Gairdner Foundation and Awards was the major event (Figure 2).

A second event of the Congress was the presence of Dr. Philip Hench (1896–1965), recipient of the Nobel Prize in 1950 for his part in the discovery of cortisone and adrenocorticotrophic hormone⁵ (Figure 3). The announcement of the Gairdner Award and Nobel Laureate Hench's participation was no coincidence⁶. He had been the friend and inspiration for Wallace Graham since wartime days. Their connection had started when Wallace as a naval officer was flying home from England in a cargo plane after North Atlantic convoy duty; on board was only one other passenger, Dr. Paul Holbrook of Tucson, Arizona, then President of the American Rheumatism Association. After the two men talked, Holbrook invited Wallace to meet with Dr. Hench in Hot Springs, Arkansas in 1944. There Hench was the Chief of Medicine at the Army and Navy Hospital and director of the US Army Rheumatism Center (Figure 4). Hench of course was well known in American medicine because of his research productivity: any meeting was stimulated by his questions aimed at clarifying the difference between facts and opinion⁵. After their meeting Graham and Hench maintained contact and until Wallace's death consulted each other regularly.

Hench became a member of the staff of the Mayo Clinic in 1923 where he established the first American Training Center for rheumatic diseases in 1926. It was notable that Hench in the 1930s observed that women with rheumatoid arthritis who were either pregnant or jaundiced saw their disease disappear⁷. These observations led Dr. Hench and



Figure 2. Dr. Wallace Graham, Mr. James A. Gairdner, and his son J.S. (Jock) Gairdner at the announcement of the Gairdner Foundation Awards at the Ninth International Congress on Rheumatic Diseases, Toronto, Canada, 1957.



Figure 3. Dr. Philip Hench and Dr. Wallace Graham, at the Ninth International Congress on Rheumatic Diseases, Toronto, Canada, 1957.

his colleagues to consider metabolic causes for rheumatoid arthritis, with a special interest in the cortex of the adrenal gland.

The history of the discovery of cortisone, particularly with respect to other treatments for rheumatoid arthritis, has been reviewed elsewhere⁸. However, from the perspective of the Canada Gairdner International Awards, it is of interest to ask if Hench's observations, which he published in a systematic form in the *British Medical Journal* in 1938⁹, would have logically led to the discovery of cortisone. In the 1938 publication, Hench reviews his own experience with the association of the onset of jaundice and improvement of arthritis and touches on the history of that observation, including that it was "causally noted by Still in 1897." Hench goes on to speculate that "The responsible factor may be a chemical agent. This agent substance-X may be a normal constituent of the bile (bilirubin..)." Of significant interest is that in the same issue of the *British Medical Journal* we find a letter to the Editor by Stanley Hartfall and colleagues¹⁰. These authors complain that Hench fails to "mention [that] the toxic jaundice which is often seen in gold treatment" is associated with a worsening of rheumatoid arthritis, and to provide statistical evidence that this is so. They refer to their extensive experience with gold treatment



Figure 4. Dr. Wallace Graham and Dr. Philip Hench, Hot Springs, Arkansas, 1944.

(1500 cases) and toxic jaundice (in 119), and to their 2 publications in *The Lancet* in 1937^{11,12} Hartfall, *et al* conclude that their evidence does not support Hench's earlier or present claim of the association between jaundice and improvement of rheumatoid arthritis. The case then for bilirubin as the "normal constituent" responsible for the improvement in rheumatoid arthritis becomes much weaker or is refuted.

During the war, work on adrenal physiology was stimulated by rumors that beef adrenal glands were being imported from Argentina to Germany so Luftwaffe pilots could have hormone injections to enable them to reach higher altitudes. A National American Conference held in May 1941 also led to big investment in adrenal physiology by the American National Research Council and the pharmaceutical firm Merck and Company¹³. However, after the war, interest in this research plummeted because there would be no market for a hormone that was thought to be useful only to persons with adrenal insufficiency called Addison's disease. When the late President John F. Kennedy, who suffered from Addison's, had his health restored by cortisone¹⁴, the use of compound E was restricted to persons with suspected Addison's disease, which excluded the Mayo Clinic team. Despite this setback Hench and his biochemist colleague Ed Kendall, who had previously isolated thyroxine, persisted in their exploration of the possibility that rheumatoid arthritis could be controlled by adrenal cortical extracts. In describing the treatment proposal for their first patient with rheumatoid arthritis they emphasized Addisonian features to entice permission from Merck¹³. Their patient received compound E September 21, 1948 and made an amazing recovery. The same results would be confirmed in many other patients thanks to compound E, later called cortisone. The team's scientific treatment protocol remains a milestone in medical history because cortisone controlled inflammation and adverse immune responses unlike any-

thing seen before. In the 1985 *History of Rheumatology in the United States*, authors Smyth, Freyberg and McEwen wrote: "The events of 1948 through 1950 elevated the study of arthritis and rheumatism to a higher level...physicians engaged in the field (like Graham and Hench) were called "rheumatologists," a name not commonly used before 1950"¹⁵.

A whole generation of clinical investigators was inspired by these discoveries and contributed to a new era that involved learning how to best use cortisone and minimize its side effects in the treatment of rheumatic diseases, rheumatoid arthritis, lupus and rheumatic fever, as well as inflammatory diseases in every branch of medicine. This was why the Nobel Prize in physiology and medicine was awarded to Hench, Kendall, and Reichstein: "for the discovery in the hormones of the adrenal cortex, their structure and biologic effect"⁵. Hench and Kendall also received the 1949 Lasker Award of the American Public Health Association. Like the Banting and Best discovery of insulin the introduction of cortisone to medicine was a great practical breakthrough in clinical and research medicine and the type of achievement that improved the quality of human life envisioned by James A. Gairdner.

Since Hench's appearance at the International Congress and the announcement of the Gairdner Awards in June 1957, many Gairdner winners have made contributions to a better understanding of rheumatic diseases and later became recipients of the Nobel Prize, for example, rheumatologist Barry Blumberg 1976 and gastroenterologist Barry Marshall 2005 for contributions to new insight in infectious aspects of disease; to Rodney Porter 1972, Jean Dausset 1980, Niels Jerne 1984 for elucidation of immunologic structures and mechanisms; to Sir James Black and George Hitchings 1988 for their discoveries of important principles of drug treatment such as gastroprotection, disease modifying agents, and the control of gouty arthritis¹.

Knowledge of these events, and of the circumstances connecting Hench, Graham, and Gairdner, make it easy to understand how the discovery of cortisone and the Nobel Prize to Graham's good friend Philip Hench inspired Graham's pivotal "encouragement" of James Gairdner to establish his Foundation.

REFERENCES

1. Hulse E, Dirks J. The Gairdner Foundation: a celebration. Toronto: Gairdner Foundation;1999:4.
2. The Gairdner Foundation. [Internet home page. Accessed October 24, 2009.] Available from: <http://www.gairdner.org>.
3. Walters A. Obituary, J. Wallace Graham. *Can Med Assoc J* 1963;88:104-6.
4. Obituary. Dr J Wallace Graham. *Ann Rheum Dis* 1963;22:116.
5. Philip Showalter Hench 1896-1965, in memorium. *Arthritis Rheum* 1965;8:573-6.
6. Graham KM. Origins and early beginnings of the Canadian Arthritis Society and the first rheumatic disease units in Canada. *J Rheumatol* 2000;27:1592-8.

7. Hench PS. Recent investigations on rheumatism and arthritis in the United States. *Ann Rheum Dis* 1940;ii:19-40.
8. Karsh J, Hetenyi G Jr. An historical review of rheumatoid arthritis treatment: 1948 to 1952. *Semin Arthritis Rheum* 1997;27:57-65.
9. Hench PS. Effect of jaundice on rheumatoid arthritis. *Br Med J* 1938;2:394-8.
10. Hartfall SJ, Garland HG, Goldie W. Rheumatoid arthritis and jaundice [letter]. *Br Med J* 1938;2:592-3.
11. Hartfall SJ, Garland HG, Goldie W. Gold treatment of arthritis. A review of 900 cases. *Lancet* 1937;2:784-88.
12. Hartfall SJ, Garland HG, Goldie W. Gold treatment of arthritis. Toxic reactions. *Lancet* 1937;2:838-42.
13. Polley HF, Slocumb CH. Behind the scenes with cortisone and ACTH. *Proc Staff Meet Mayo Clin* 1976;51:471-7.
14. Mandel LP. Endocrine and autoimmune aspects of the health history of John F. Kennedy. *Ann Intern Med* 2009;151:350-4.
15. Smyth CJ, Freyberg RH, McEwen C. History of rheumatology in the United States. Ch. 1 and 2. Atlanta: The Arthritis Foundation;1985.