J. J. R. Macleod

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Twenty years ago, on March 16, 1935, the death of John James Rickard Macleod brought to a close the career of one of the most distinguished physiologists of his time. He was noted for original research in the physiology of respiration and metabolism, for his success as a teacher of undergraduate and graduate students, for the clarity of his scientific writing and for his leadership in teaching the clinical application of physiology and biochemistry. To physicians with a special interest in diabetes he became well known for his own researches in carbohydrate metabolism and particularly for the opportunity which he gave to Banting and Best to carry on in his laboratory the work which led to the discovery of insulin.

Macleod was born in Scotland on Sept. 6, 1876, the son of a minister of Aberdeen. He graduated from the medical school of Aberdeen University with honors in 1889. He received the Anderson Travelling Fellowship which gave him an opportunity to study in Leipzig and Berlin. Later he studied at Cambridge, receiving the D.P.H. He became a demonstrator in physiology and later lecturer in biochemistry at the London Hospital Medical School. In 1901, he was the McKinnon Research Scholar of the Royal Society. In 1903, at the age of twenty-seven, he became Professor of Physiology at Western Reserve University in Cleveland. In 1918, he became Professor of Physiology at the University of Toronto and Assistant Dean of the Faculty of Medicine. He left Toronto in 1928 to become the Regius Professor of Physiology at his alma mater in Scotland.

Macleod's first physiological researches were concerned with the intracranial circulation, a subject which he investigated in cooperation with Leonard Hill, the outstanding English physiologist at the turn of the century. His attention was next directed to the control of respiration, a study which he continued from 1902 to 1922. In 1908, he became interested in experimental glycosuria and in 1913 he published a book on diabetes and its pathological physiology. In 1921 his studies were concerned with the control of the blood sugar level in normal and depancreatized animals and the role played by the liver and also the pancreas in the metabolism of sugar.

Physiology and Biochemistry in Modern Medicine was the title of the textbook first published in 1918, which extended widely Macleod's reputation as a medical teacher. This textbook, which was welcomed by students in Toronto and in medical schools in other parts of the world as well as by practicing physicians, went through seven editions in less than two decades.

In speaking of Macleod's appointment to the Chair of Physiology at the University of Toronto, Sir Henry Dale[1] said: "Macleod's tenure was of course to be one of historic importance for the world reputation of the Department and of the Medical School to which it belonged and, less directly, for the advancement everywhere of physiology and experimental medicine. He succeeded to a Department unusually well equipped by the standards of those days for research in the general field of physiology including that of his own special interest

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in the problems of carbohydrate metabolism.'

'In this special field Macleod had himself already made some sound experimental contributions to the then generally accepted canon of knowledge; and there could have been few, if any, who had a better command than his of the numerous literature of the researches and theories which dealt with it. When young Frederick Banting, therefore, with a recent surgical experience from war service and little more than a student's knowledge of physiology, came asking, with a burning eagerness and a sense of a mission for an opportunity to make a new attempt to obtain from the islets of the pancreas, the hormone insulin, the production of which speculation had long credited them, Macleod was well qualified to give him a discouraging account of the failure of many earlier attempts, most of them by workers of a much riper experience. It was a fair and proper warning; and it is to be counted to Macleod's lasting credit that having given it, he agreed nevertheless, to give Banting also the desired opportunity. Possibly he had seen that methods then newly available for measuring the minute quantities of glucose present in small samples of blood, might have produced a significant improvement in the chances of success for a further attack on such a problem. And it should be further remembered in any case that Macleod had produced a class of students well trained in these new methods of microanalysis and in determinations of the respiratory balance of oxygen consumed and carbonic acid exhaled.'

'It was Macleod also, who saw that if Banting's attempt was to give any intelligible result, he must have the cooperation of somebody with this recent biochemical training; and this recommendation was responsible for bringing Charles Best, recently graduated in Science, trained in the necessary biochemical methods, and himself rendered eager by a family contact with diabetes, to do something for those whom it afflicted, into the historic collaboration. Frederick Banting supplied on his part the determined unquenchable initiative and an equipment with the necessary surgical technic. The collaboration was to be one of intimate understanding, with no question between the two participants of any but an equal sharing of its success . . .'

Professor Velyien E. Henderson,[2] one of Macleod's colleagues in the Faculty of Medicine at Toronto, also wrote of Macleod's prestige in research on carbohydrate metabolism when he joined the University of Toronto: "Soon his laboratory attracted a group of young workers in physiology. It was due to Professor Macleod's established reputation as an authority on carbohydrate metabolism that Dr. Banting, now Sir Frederick, came to Toronto to consult him and to pursue his investigations on the pancreas with the assistance of C. H. Best, then a young assistant who eventually succeeded Professor Macleod as Professor of Physiology at the University of Toronto. These investigations led to the brilliant and important discovery of insulin by Dr. Banting and Dr. Best.'

'With the aid of Dr. J. B. Collip, the first stages of purification of insulin were undertaken and arrangements made for its commercial production. . . .'

'In recognition of this very important discovery, Dr. Banting and Professor Macleod were awarded jointly the Nobel Prize, the former sharing the award with Dr. Best and the latter with Dr. Collip."

The discovery of insulin was followed by intensive research in the Department of Physiology as efforts were made to investigate the physiologic functions of insulin, and to use it as a tool to uncover and disentangle some of the secrets of metabolism. As a senior medical student at the University of Toronto, I had witnessed the first use of insulin in the treatment of human diabetes. I had seen the emaciated almost moribund 14-year-old boy selected for the initial trial respond as by a miracle to the treatment started on Jan. 11, 1922, and I was aware of the exciting activities under way in Macleod's laboratories. I therefore accepted eagerly a Fellowship in Physiology which was offered me on graduation and which led to an opportunity to serve for a period of three years as a member of Macleod's team. Thus I became well acquainted with the man who wore the Professor's gown. My personal memories of Macleod recall a man who sought to give his assistants a free opportunity to develop their own ideas and to work out their experiments independently, who offered guidance, without dominance, and who was generous in providing opportunities for participation in scientific meetings (and on one occasion at least in providing personal financial assistance for travel to a distant meeting).

Macleod received many honors. He became President of the American Physiological Society in 1922 and of the Royal Canadian Institute in 1925. He was a Fellow of the Royal Society of Canada, a Fellow of the Royal Society in England, and a Fellow of the Royal College of Physicians. He received the honorary degree of Doctor of Science from the University of Toronto and of Doctor of Laws from the University of Aberdeen. His greatest honor was the esteem of his students, assistants and colleagues.

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[1] Dale, H. H.: Address at Special Convocation, University of Toronto. Diabetes 3:30-35, January-February 1954.

[2] Henderson, V. E.: Obituary. J. J. R. Macleod. Science 81: 355, April 12, 1935.

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