

A SHORT ESSAY ON THE IMPORTANCE OF DOGS IN MEDICAL RESEARCH

CHARLES H. BEST

One could list hundreds or even thousands of researches in many countries of the world in which the advance of science and the art of the physician and surgeon have been founded in large part on the experimental use of dogs. There have been many good articles written in England and they usually start with the work of Harvey, the discoverer of the circulation of the blood. He used dogs as his experimental animals. The circulation of the lymph, the processes of digestion, the work of the neurophysiologists upon the brain and the spinal cord, methods of life-saving, work on the development of safe anesthetics and of thousands of drugs, have been gained by experiments using dogs.

I am familiar with many extensive descriptions (which have come from England and from the United States and, indeed, from many other countries) concerning the contributions of dogs, but in this short article I would like to concentrate on the discovery of insulin, and its application to the treatment of diabetics throughout the world. The earliest reference which I have easily available is the treatise on the experiments on the pancreas and on the flow of lymph by Johann Conrad von Brunner of Switzerland, who published his article in Amsterdam in the year 1683. This book was given to me by Frau Oskar Minkowski and had been in her husband's library in Germany. Brunner was not really interested in diabetes but he attempted to remove the pancreas in order to study the effect upon the digestive processes. He was successful in securing an almost complete removal in at least one case because his dog showed all the signs and symptoms of diabetes. But Brunner was more interested in the glands which now bear his name and the lymph patches in the intestine were named after his friend Payer.

The experiments of von Mering and Minkowski in 1889 which showed conclusively that complete removal of the pancreas always resulted in fatal diabetes, are milestones in the history of this disorder. Dogs were the experimental animals. The same can be said of the work of Starling, Paulesco, Kliner, Zuelzer, E.L. Scott, Prof. J.J.R. Macleod, Prof. Murlin of Rochester, New York, and hundreds of others. It was therefore inevitable that Fred Banting and I would choose the dog as our experimental animal. Banting was an expert surgeon and I was familiar with the then modern methods of estimating blood and urinary sugar, ketone bodies, nitrogen, and other constituents of tissue fluids. I had spent part of my final year in the physiology and biochemistry course studying the respiratory quotients.

Both Fred Banting and I had personal interest in diabetes. He had watched a child in Alliston, Ontario, lose weight and eventually develop diabetic coma and die. My aunt, a trained nurse, developed diabetes in 1912. She was a patient of Dr. Elliott P. Joslin who placed her on the Allen under-nutrition regimen. She followed this diet faithfully but died in diabetic coma in 1918.

When Prof. Macleod gave us facilities in the Department of Physiology he stated that ten dogs would be available to us. The cost of these animals in those days (1921) was about one dollar each. I do not remember exactly how many animals we used before the discovery phase of insulin was complete - it may have been 20. Those not provided by the laboratory we purchased from our personal funds. We had no stipends and indeed no appointment in the laboratory.

This is not the place to describe the experiments in detail. We had our difficulties initially but in August and September we performed scores of experiments which were dramatically successful in providing convincing evidence of the presence of the internal secretion of the pancreas.

We looked after our dogs ourselves; fed them and cleaned the cages. We trained them to put out their paws for withdrawal of blood and we made them as comfortable as we could under the circumstances. I do not think that in these or subsequent experiments we ever inflicted pain and discomfort on dogs which we would not have been willing to accept ourselves. The animals which were depancreatized before insulin was available and which lived for ten days to two weeks, were necessary as controls for the animals which were to receive insulin.

When Prof. Macleod returned to Toronto in the middle of September (he had left early in June) he stated that he was perfectly convinced that we had obtained sufficient evidence to prove the presence of insulin. We had a list of a dozen other studies which we wished to make but he insisted that we obtain more and more evidence on the fundamental point, that is, that the potent anti-diabetic material could be consistently extracted from dog and beef pancreas and that this would eliminate the signs of diabetes and keep completely depancreatized dogs alive as long as they were given one injection a day.

We presented our results before the Physiological Society in Toronto in November 1921, and before the American Physiological Society in December 1921. In both cases the reception of our findings was enthusiastic and most encouraging.

In early January I made a special extract from beef pancreas, purified it with alcohol and fat solvents, sterilized it by passing through a Berkfeld filter and then tested the final product on diabetic dogs. It was very potent.

As I have stated elsewhere, I have always felt it regrettable that we did not use an extract of foetal calf pancreas because this was at least ten times as potent as that made from whole beef material.

On the 10th of January, 1922, Banting and I gave each other injections of our insulin. There were no untoward effects except a mild soreness of our arms. On the following day the material was taken to the Toronto General Hospital where a 14-year old boy, Leonard Thompson, became the first diabetic to receive insulin. The first patient in the United States was James Havens of Rochester, New York. He became a celebrated artist and lived to have a fine family.

Our travels in some 70 different countries have brought us into contact with many, many thousands of diabetics. The statisticians tell us that figures based on the world-wide consumption of insulin indicate that some 130,000,000 diabetics have had their lives prolonged by insulin. The number, of course, is steadily increasing.

All this work which I have described, up to the clinical application of insulin, was carried out on dogs and this is only one of the many, many thousand series of experiments which testify to the importance of dogs in medical research.

In other work which led to the discovery of the vitamin choline which prevents fatty changes and cirrhosis in the liver, dogs were used in our laboratory. In other experiments on the purification and the use of heparin in preventing thrombosis, this species was also utilized. The same is true of much of the work on histamine which led to the discovery of the enzyme histaminase.

Fred Banting and I had two great hopes in 1921 and 1922. One, that the dramatic recovery of diabetic animals could be consistently produced by insulin in human patients. This, of course, is in general true although one is acutely conscious of the problems in the treatment of the human cases which have not as yet been solved. But great progress is being made not only in learning more about the etiology of diabetes and the mechanism of production of the complications but in the development of new methods which may make possible the more physiological administration of the hormone.

We were also hopeful that insulin would be an important agent in metabolic research. Volumes could be written on this subject and indeed I think one could say that no other physiological agent has been instrumental in revealing as much about the intermediate metabolism of carbohydrates, proteins and fats, as this hormone has. It has been important in enzymology, in the study of cell permeability and many other fields which I must not attempt to list.

Fred Banting and I got a great thrill out of the recovery of all diabetics, many of whom we knew personally. Perhaps the most interesting was that of Dr. George R. Minot, of Boston, who was a sever diabetic. He responded well to insulin and then devoted his life to medical research. His discovery of the liver treatment of pernicious anemia (with Murphy and Whipple) is another of the great romances of medicine. Patients who have been successfully treated with vitamin B₁₂, have undoubtedly made great contributions to science and the arts. This is the beginning of one of the pyramids of scientific romance and certainly scores, perhaps hundreds of others, have been built during the last half century.

EDITOR'S NOTE: Dr. Charles H. Best, the co-discoverer of insulin, was asked to prepare this statement because of the recent great interest in the Congress of the United States in restricting or even prohibiting the use of dogs in biomedical research. More than fifteen separate bills with nearly one hundred sponsors have been introduced into the 1974 session of the Congress dealing in one way or another with this question.

The Physiologist, as the house organ of the American Physiological Society which numbers among its 4,500 members the majority of the scientists in the United States who are concerned with the use of animals in scientific research, seems to be the appropriate place to publish the dramatic story of the way in which the dog became man's best friend for the tens of millions of diabetics who would not otherwise have been alive today, and the hundreds of millions who would die in the future if the use of dogs in the discovery of insulin had not been permissible.

It is hoped that this essay or at least its essential story may reach hundreds of thousands of people. Too many people believe that the study of living animals in the search for knowledge about disease is inhumane or even unnecessary. It is fortunate that one of the two primary players in the drama of the development of insulin in 1921 has given us this account in his own words.

Dr. Best has not only had a brilliant career in physiological research with many useful applications to medicine in addition to the discovery of insulin, but he has played a major role in the development of science on an international scale. He was President of the International Union of Physiological Sciences. He is a member of numerous National Academies and a Fellow of the Royal Society of London, and has received almost innumerable medals and honorary degrees. He is also the co-author of two of the most valuable textbooks in the field of physiology; one for prospective physicians and another for non-specialists. His contributions to physiology have been exceeded only by his contributions to humanity.
