The Use of a Pancreatic Extract in Diabetes.¹

By Sir C. S. SHERRINGTON, G.B.E., P.R.S.

IN the words of its charter, repeated at the admission of each new fellow, the Royal Society is described as instituted "for Improving Natural Knowledge." A main means for that "improving" is discovery. In the case of natural knowledge the main road to discovery must lie in research. There are several ways in which research can be encouraged, and one of them lies in providing suitable workers with the means to devote their time freely to investigation. The society is fortunate in possessing now, to a somewhat greater extent than formerly, funds that may be considered as permanently allocated to this fundamental object; for though its existence extends now to more than two and a half centuries, financial help directed to this eminently important aim has come only relatively recently. That it should have now begun may be a sign of the arrival of an Age in some respects new; the beginning of a trend towards wider public interest in and sympathy with research.

Of events in biological science in the past year I may mention one that is attracting attention at this time. In the Physiological Laboratory of Toronto University has been prepared a pancreatic extract possessing striking power over the carbohydrate metabolism of the body. Potent as it is, experience with it is still limited. Work of urgency is required with what may prove to be a desired remedy; the first programme is further investigation of the extract's full properties, with caution as to raising hopes which practice may but partly fulfil. Such are the considerations which weigh with the Canadian—and the discovery is from a Canadian university—to whom the discovery is due. In this country the Medical Research Council has undertaken public-spirited direction of the extract's preparation and of further determination of its properties.

The physiological steps of the discovery may be briefly outlined thus:—Destruction of the pancreas is well known to produce in the dog a diabetes-like condition, rapidly fatal. The liver's store of glycogen is lost, and cannot be renewed by even liberal supply of its normal source, carbohydrate food. Sugar formation from proteins ensues, with rapid wasting of the tissues; at the same time the blood is surcharged with sugar, and the tissues are unable to make use of sugar. In a normal animal, glucose put into the circulation raises the ratio of carbon dioxide expired to oxygen absorbed, because the tissues consume the sugar. But glucose similarly introduced into the depancreatized diabetic animal does not raise the respiratory quotient; the tissues no longer consume the sugar. The inference has long been that the pancreas produces some substance enabling the body to make use of sugar—some substance that in fact should control certain forms of diabetes. At Toronto there seems to have been secured the extraction of that substance.

The pancreas consists of two structures intimately commingled. One, secreting cells set round ducts into which they pour the pancreatic juice, is potently digestive: the other, scattered in tiny islets, is seemingly unrelated to the ducts though closely related to the blood channels. The want of success of pancreatic extracts in mitigating a diabetic condition might be

due to digestive powers of the juice cells destroying an anti-diabetic substance of the islet-cells. Dr. F. G. Banting determined to avoid this possibility by preparing extracts made from the pancreas after its trypsin-yielding cells had been selectively brought to atrophy by ligation of the gland ducts. He and Mr. Best, a collaborator who joined him, overcoming formidable difficulties of technique, succeeded in preparing the required material, and in examining the effect of extract upon diabetic depancreatized dogs. They found the sugar fall both in the blood and urine, and that the animals, instead of dying in three weeks, remained, while treated, in excellent condition.

The further prosecution of the work afterwards engaged other collaborators: to mention them in alphabetical order, Collip, Hepburn, Latchford, MacLeod, and Noble; of these Prof. MacLeod, himself director of the Toronto Physiological Laboratory, is well known as a skilled authority in experiments on carbohydrate metabolism, and Dr. Collip is professor of bio-chemistry in the University of Alberta, though temporarily working at Toronto. With team work, advance has proceeded relatively quickly, and successful extracts are now obtained from ordinary ox and other pancreas.

Of much physiological interest is the fact that the active principle in the extract seems one *normally* controlling the blood-sugar in health, for its injection rapidly lessens the blood-sugar in normal animals. The extract, added to a simple perfusion fluid containing a little glucose and streamed through the isolated rabbit heart, increases three- or fourfold the heart's uptake of sugar from the fluid. The extract sometimes evokes serious nervous disturbances seemingly associated with extreme fall in the amount of the blood-sugar.

Administered to diabetic depancreatized animals, the extract brings reappearance of the liver's glycogen store, while bringing down the sugar excess in the blood and the excretion of sugar and acetone in the urine; and it enables the diabetic organism to consume sugar. It also lessens or prevents hyperglycæmia produced in animals in several other ways.

Gratifying success has already attended the use of this extract in the relief of diabetic patients; much further research is, however, yet needed for development of the methods of extraction and of the routine use of the active principle.

The important physiological advance thus just reached comes as a fit reward to those who have achieved it. It is, of course, the striking result of steady work pursued by many various workers through many earlier years. Such work, we may remember, lay often open to charge by the unenlightened of being merely academic and fruitless, its reward being at the time simply the intrinsic scientific interest of the facts obtained. The Toronto investigators we may be sure would say with Pasteur, "To have the fruit there must have been cultivation of the tree." Part of the merit of the recent successful investigation has been its appreciation of possibilities indicated by previous work. But that merit is after all only a preliminary to the main achievement. The actual achievement is the deserved success of a bold attack conducted with conviction and determination and carried through in the face of formidable experimental difficulties.

¹ From the presidential address delivered to the Royal Society on November 30.