

- (3) The splitting of the high-energy phosphate bond of the phosphorylated compound requires Na^+ in the medium and is highly increased by adding K^+ when the medium contains Na^+ , while K^+ alone has practically no effect.
- (4) G-strophanthin which specifically inhibits the active linked transport of Na^+ and K^+ in the intact cell also inhibits the $\text{Na}^+ + \text{K}^+$ activated splitting of the high-energy bond of the phosphorylated compound.
- (5) There is indirect evidence that the particle studied is derived from the surface membrane of the intact cell.
- (6) A particle which contains a system which has the same specificities for Na^+ and K^+ has also been isolated from other tissues where there is an active linked transport of Na^+ and K^+ , namely from brain, kidney and heart muscle.

The relationship of the particulate system to the active linked transport of Na^+ and K^+ across the cell membrane will be discussed.

6 Pharmacological Control of Release of Hormones Including Antidiabetic Drugs. Introductory Remarks. R. COURRIER (France).

7 Pharmacological Actions of the Hypoglycaemic Arylsulphonamides upon the Histophysiology and the Physiology of the Beta-cells of the Islets of Langerhans of the Pancreas. A. LOUBATIERES (France).

The hypoglycaemic arylsulphonamides (thiadiazole or urea derivatives) have a preferential tropism for the pancreas (pancreatotropism) and especially for the beta-cells of the islets of Langerhans (betacytotropism). The betacytotropism is mainly shown by the degranulation of the beta-cells and by other histological modifications demonstrated with electron microscopy.

Hypoglycaemic sulphonamides are betacytotrophic. They produce a hyperplasia of the islets and stimulate the formation of new insulin secretory beta-cells. There follows an increase in the total amount of the beta-cells and an increased capacity of the endocrine pancreas in blood glucose regulation.

We have at the present time strong evidence showing that hypoglycaemic sulphonamides are insulin-secretory stimulating substances. The venous blood coming from the pancreas is more hypoglycaemically active after administration of these drugs than it was before: its "plasma insulin activity" as well as its endogenous insulin content increases. This is the main reason why these drugs are strongly effective in the treatment of human diabetes characterized by sluggishness or relative depression of insulin-secretory process.

The arylsulphonamides manifest an antidiabetic action against meta-alloxanic, meta-hypophyseal or spontaneous diabetes of moderate intensities. They

counteract the establishment of idio-hypophyseal diabetes in a dog. They exert a preventive action against the exhaustive process which occurs "spontaneously" in the beta-cells of the pancreas remnant of a subtotally depancreatized animal. These phenomena are in direct connexion with the actions (stimulation, neoformation, regeneration) exerted by these sulphonamides upon the apparatus of the beta-cells. Clinical trials plead for the possibility of the use of these drugs as prophylactic agents against the development of full diabetes in human beings predisposed to this illness.

8 Experimental Investigations with Sulphonureas (S.U.). A. BÄNDER (Germany).

The effects of oral hypoglycaemic compounds upon the enzyme-system, the liver and the peripheral carbohydrate metabolism do not sufficiently explain the hypoglycaemic action. Experimental animals and patients deprived of the pancreas do not exhibit any hypoglycaemic reaction, provided that the gland is removed, for several days.

There is agreement that the main action is to be found in releasing insulin from the pancreas. How this liberation is effected constitutes a question of paramount interest.

According to results by Wrenshall *et al.*, a large number of the diabetics who develop the disease when adults have a sufficient amount of insulin in the gland, sometimes even more than non-diabetics. There remains the question why these patients are diabetics. Some evidence has been obtained that in these patients there is an abnormal binding of insulin in the pancreas. Thus, the difference in blood sugar curves between non-diabetics and diabetics could be explained.

Experiments of Aiman *et al.* showed that plasma-bound insulin could be released by S.U.

Our own investigations have demonstrated *in vitro* a degranulation of isolated β -cells under the influence of S.U.

Reviewing these observations one may assume that S.U. are exerting their effects by means of physico-chemical properties. It is suggested that these qualities produce a removal of this abnormal binding; in this way adequate amounts of insulin are released.

9 Pharmacological Effects of Some Chemical Compounds of Biosynthesis and Secretion of Thyroid Hormones. R. MICHEL (France).

The main steps in the biosynthesis and secretion of thyroid hormones are: iodide concentration, iodotyrosines formation, iodotyrosines coupling, thyroglobulin proteolysis, enzymatic deiodination of iodotyrosines followed by iodothyronines secretion.

Various chemical compounds modify thyroidal iodine metabolism. Thiocyanate, perchlorate and other isoelectric anions of about the same volume inhibit iodide concentration. They act competitively with I^- which probably fits into some specific