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HORMONES AND CHOLINERGIC AGENTS IN INSULIN SECRETION *IN VITRO*

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Chapter IV

Summary

A number of recent studies indicate that insulin release may be partially controlled through the adenylcyclase system in the pancreatic beta cell. Two agents, theophylline and glucagon, are known to increase the cellular level of cyclic 3'5'-AMP in islets of Langerhans. It has been postulated that the increased level of cyclic nucleotide induced by these compounds is responsible for their stimulant effect on insulin release.

The objectives of the present study were a.) to examine the effect on insulin secretion of agents and hormones which are known to act on the adenylcyclase system in other tissues; and b.) to study the effects of cholinergic agents on insulin release from the pancreas of the rat, rabbit, dog and man.

Theophylline and glucagon were found to stimulate insulin release from the rat pancreas. ACTH and TSH have a similar but much weaker effect. These agents have no effect on secretion in the absence or at low concentrations of glucose, but they augment the stimulant effect of a high glucose concentration. Carbachol, a cholinergic agent, has no effect on secretion induced by glucose in low concentration from the pancreas of the rat. On the other hand, at high glucose concentrations carbachol consistently depresses

the stimulant effect of glucose. The effects in rat pancreas appear to be unique for in the pancreas of the rabbit, dog, and man carbachol augments the effect of glucose especially, and most consistently, at a high glucose concentration.

Theophylline, glucagon, ACTH, and TSH increase intracellular cyclic 3'5'-AMP in other tissues, and cholinergic agents decrease activity of the adenylcyclase system in the heart. Findings in the present study suggest that insulin secretion from rat pancreas could be partially regulated by the cellular level of cyclic 3'5'-AMP. Thus, theophylline, glucagon, ACTH, and TSH could augment and carbachol could inhibit secretion by respectively increasing or decreasing the cellular level of cyclic 3'5'-AMP.