## *Section IV. The Beta Cell and Its Responses*

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# The Secretion of Insulin

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A new teaching film entitled "The Secretion of Insulin"* was shown in place of a formal presentation. This movie illustrates a proposed model of the biologic events in the formation, storage and release of insulin in beta cells of the rat pancreas.

The proposed sequence of events is as follows: intracellular glucose metabolism signals the initiation of proinsulin synthesis in the endoplasmic reticulum; proinsulin is transferred either directly from the endoplasmic reticulum to the Golgi complex or is transported to the Golgi in sacs of the endoplasmic reticulum; the conversion of proinsulin to insulin probably occurs in the Golgi complex; mature beta granules are released from the Golgi complex and are enclosed by smooth membranous sacs; some of these beta granules become crystalline and apparently are micro-crystals of zinc insulin; the mature beta granules released from the Golgi complex either remain free in the cytoplasm or become attached to the microtubular system of the beta cell; glucose metabolism initiates the entry of calcium which triggers a change in physical conformation of the microtubules with resultant displacement of the granules to the cell surface; the membranous sacs encasing the granules fuse with the plasma membrane and the granules are released in tandem by emiocytosis at specific loci on the plasma membrane resulting in the formation of concavities and cytoplasmic projections between the sites of release of beta granules.

This proposed scheme of beta cell secretion serves as a working model that can be tested and modified by further investigations. Many parts of the model are firmly established whereas other aspects are tentative concepts. The established portions include the formation of proinsulin in the endoplasmic reticulum, the involvement of the Golgi complex in the formation of beta granules, the essential requirement of calcium for insulin secretion and the stimulation of calcium uptake by intracellular glucose metabolism in the beta cell and the release of beta granules by emiocytosis.

Some of the major aspects which remain to be resolved are the biochemical events involved in the initiation of proinsulin synthesis, the enzyme or enzyme system responsible for the transformation of proinsulin to insulin, the precise intracellular localization of this transformation and the role of the microtubular-microfilament system in the intracellular transport of beta granules. In regard to the microtubular-microfilament system, the evidence accumulated thus far indicates that this system is responsible for the translocation of the beta granules following glucose stimulation; this same system may be involved in the secretion of hormones from the thyroid, pituitary and adrenal medulla. Further investigations in our laboratory indicate that the microtubular system is involved in both the first and second phase of insulin secretion in vitro by perifusion.

Many questions remain to be answered. If and when the missing pieces of the puzzle are to be found, it may be possible to determine the cause of diabetes and, with such knowledge, eventually its cure.

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* Available from Eli Lilly and Company, Audio-Visual Film Library, P.O. Box 814, Indianapolis, Indiana 46206.