DYNAMICS OF MEMBRANOUS STRUCTURES OF THE ACINAR CELLS

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UDC 612.34.014.21

The results of an ultrastructural study of the acinar apparatus of the pancreas during secretory activity are described. Membranous structures of the acinar cells circulate from the basal to the apical surface of the plasma membrane and, after liberation of the secretion, are incorporated into structures of the Golgi complex. The authors consider that this circulation of the membranous structures indicates their interchangeability and their possible reuse after corresponding modification.

The idea of an exchange of membranous structures between the superficial and inner segments of the cell is at present under wide discussion. It is closely linked with the problem of how membranes are formed and with the aid of which cell organoids. This is an extremely important section of cytology in which our knowledge is still very limited.

The surface membranes of the endothelial cell, as Fawcett [6] points out, being intensively used in the course of pinocytosis, phagocytosis, the transport of materials through the cell, and so on, would be worn out were they not replaced at an equivalent rate. The question of the exchange, circulation, exchangeability, and reuse of membranes in secretory glandular cells is a particularly acute problem [1].

During the liberation of secretion by a merocrine type of process many new membranous structures are constantly being incorporated into the apical membrane, and this ought evidently to be accompanied by a limitless increase in size of the ducts. However, no appreciable increase in the lumen of the ducts is observed under ordinary conditions. The question arises what is the disposal of the excess of membranous structures in the apical part of the cell. The suggestion has been made that this excess of membranes is reused by the cell through the backward movement of the membranes into the cytoplasm [10]. However, it is not yet clear how this reutilization of the surface membranes of the cell takes place. Some workers [10, 5, 3] point to the possibility of a reserved flow of membranes by endocytosis, while others [6-8] suggest that this process takes place at the molecular level or that the membranes are used as a building material for synthesis de novo [4, 11].

The object of this investigation was to examine the possibility of circulation of the membranous structures of the cytoplasm and of the bounding cell membrane of the exocrine cells of the pancreas during their metabolic activity at the ultrastructural level.

EXPERIMENTAL METHOD

The exocrine part of the pancreas of male Wistar albino rats during activation (pilocarpine, secretin, pancreozymin) or inhibition (atropine, morphine, trasylol) of secretion and after the intake of food (a balanced diet or one consisting chiefly of proteins, carbohydrates, and lipids), formed the test object.

Department of Pathological Anatomy, N. V. Sklifosovskii Research Institute of Emergency Aid, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 77, No. 4, pp. 121-125, April, 1974. Original article submitted May 23, 1973.

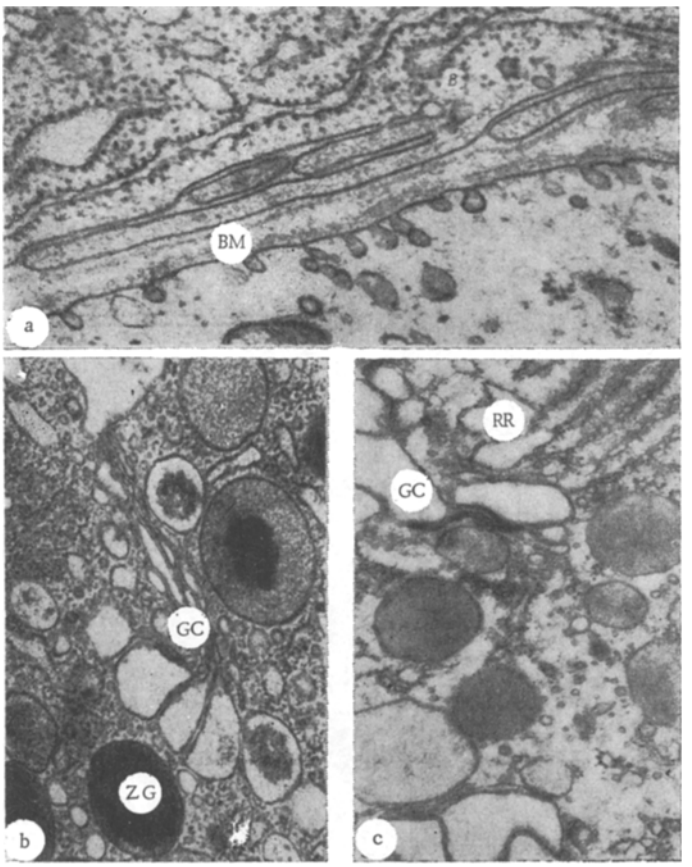

Fig. 1. Flow of cytoplasmic membranes in the direction from the basal to the apical zone: a) small, smooth vesicles (V) at apices of folds of basal surface of plasma membrane (BM). 60,000×; b) formation of zymogen granules (ZG) in Golgi complex and their shedding into the cytoplasm, 42,000×; c) transformation of membranes of rough reticulum (RR) into smooth membranes of the Golgi complex (GC), 38,000×.

For electron-microscopic investigation the pancreatic tissue was fixed by Palade's method in 1% osmic acid solution, dehydrated in alcohols, and embedded in methacrylate mixture, Araldite, and Epon. Ultrathin sections were cut on the LKB-8800 microtome and stained with lead citrate by Reynolds' method. The material was examined in the UEMV-100B and 100K electron microscopes.

EXPERIMENTAL RESULTS

The exocrine cells of the pancreas are a convenient model for studying the circulation of membranes for the processes of intake of the original materials and synthesis of the digestive enzymes take place in particular cell territories: the intake of the materials in the basement membrane of the cell, synthesis of the primary secretion in the rough endoplasmic reticulum, in the basal portion of the cytoplasm, the formation of the secretory granules in the Golgi complex, and the liberation of the finished digestive enzymes into the lumen of the duct in the apical portion. There is thus a natural flow of elements of the cytoplasm in the direction from the basal surface of the plasma membrane toward the apical surface.

On activation of the first phase of the secretory cycle (the intake of nutrient materials) numerous folds or invaginations are formed in the basement membrane of the acinar cells, with the separation of tiny smooth vesicles from their apices to become incorporated into the membranes of the cytoplasm (Fig. 1a).

Primary synthesis of digestive enzymes in the exocrine cells of the pancreas is known to take place at the level of the smooth membranes of the ergastoplasm, after which the secretory "semifinished product"

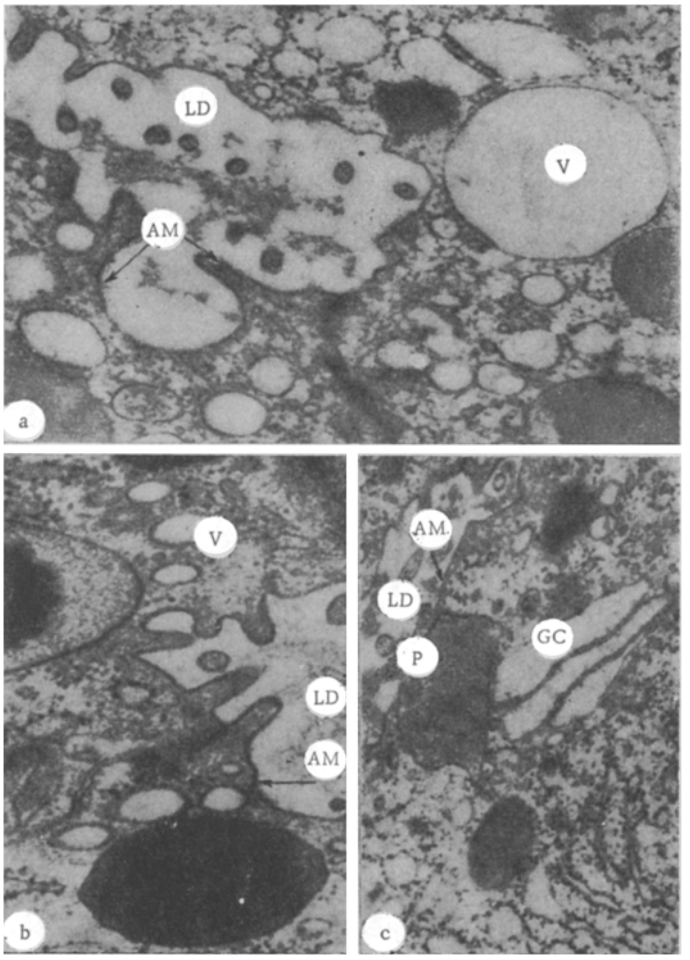

Fig. 2. Incorporation of fragments of apical plasma membrane into the system of cytoplasmic membranes: a) large invaginations and vacuoles (V) of apical cell membrane (AM). LD) Lumen of duct, 40,000×; b) small smooth vacuoles (V) separating from apical membrane, 48,000×; c) fusion of membrane of vacuoles of Golgi complex (GC) with apical membrane (AM), with the formation of a pore (P), 54,000×.

enters the lumen of the cisterns of the rough reticulum, from which it is transported into the zone of the Golgi complex. There is no direct communication between the channels of the rough endoplasmic reticulum and the Golgi complex.

At this stage of intracellular transport, at the boundary between the rough endoplasmic reticulum and the Golgi complex the phenomenon of transformation of the rough ergastoplasmic membranes into smooth is encountered. Distinct parts of the rough membranes lose their ribosomes and form vesicular evaginations, from which small vesicles are constantly being shed. Sometimes these vesicles stretch out into a chain forming what is apparently a bridge between the rough tubules and the smooth vesicles of the Golgi complex (Fig. 1c).

The molecular basis of this transformation of the membranes is not yet clear. From the physiological point of view the phenomenon of internal pinocytosis, by means of which the synthesized product is transported from the cisterns of the rough reticulum into the system of smooth laminae and vacuoles of the Golgi complex.

One of the functions of the Golgi complex is to provide a limiting membrane for the secretory granules. During accumulation and condensation of the secretion the Golgi cisterns are constantly dilating and

subsequently splitting off vacuoles of different electron densities (Fig. 1b). As the secretion finally matures the zymogen granules incorporated into the membrane are displaced into the apical portion of the cytoplasm.

At this level the next stage in transport of membranes supplied with a natural label (osmiophilic secretion) from the system of the Golgi complex toward the apical cell membrane can thus be observed.

Further conversions of the membranes of the secretory granules depend on the type of liberation of the secretion [2]. Exocrine cells are characterized by a merocrine type of secretion, of which there are two varieties: with liberation of secretion through pores invisible in the electron microscope and with the liberation of secretion through wide pores.

In the first case after discharge of the secretion an "empty" vacuole, surrounded by a smooth membrane, remains in the cytoplasm. In the other type (merocrine secretion) the membranes of the zymogen granules are incorporated into the apical plasma membrane to form numerous invaginations resembling bays. In this type the secretory granule acquires the properties of a cell membrane and its three-layered structure becomes clearly visible, while in turn, new secretory granules may be emptied into the "bay."

After discharge of the secretion a moderate degree of dilatation of the lumen of the central acinar ducts is observed, but at the same time the apical membrane forms many round invaginations, often penetrating deeply into the cytoplasm and separating as large vacuoles (Fig. 2a). Elsewhere in the zone of the apical plasmalemma multiple invaginations are formed, from which small smooth vesicles resembling pinocytotic vesicles are shed and penetrate singly or in chains into the apical cytoplasm or lie in the submembranous zone (Fig. 2b).

After discharge of the secretion three types of smooth vesicles can thus be observed in the zone of the apical plasmalemma: 1) vacuoles emptied of their secretion after discharge of the contents through the "intact" membrane, 2) large vacuoles, 3) small vesicles, formed by separation from invaginations of the apical membrane.

The question of the functional role of these vacuoles and the possibility of reuse of their membranes in the system of smooth vesicles of the Golgi complex and rough reticulum of the cytoplasm accordingly arises.

No conclusive evidence is available that the three types of vacuoles can be reincorporated into the system of membranes of the Golgi complex or rough reticulum. However, there is indirect evidence that reuse of the elements of the bounding membrane of the cytoplasm can take place. Direct contact between the vacuoles of the Golgi complex and the apical cytolemma is possible, with discharge of the contents of the vacuole and incorporation of its membrane into the apical cytolemma (Fig. 2c). Consequently, reincorporation of elements of the apical cytolemma into the system of the Golgi complex can take place to overcome the deficiency of membranes arising in the course of secretion. After liberation of the secretions the localization of the Golgi complex changes and it moves closer to the apical plasmalemma, thus facilitating incorporation of the apical plasmalemma into its system.

These facts show, in the writers' view, that the membranous structures of the cell possess extraordinary plasticity. However, the interchangeability of the membranes is undoubtedly connected with changes in their molecular structure [9] which cannot be detected by electron-microscopic analysis.

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