In a separate group ($n = 8$) isolated strip was incubated with Ringer solution containing Atr. This drug did not produce any significant change on the contractile force and the spontaneous rhythm of the strip. Nevertheless, Ach sensitivity was prominently decreased during the oontact time. In spite of repeated washings and additions of Ach to the bath, the antagonistic action of Atr diminished slowly after the removal of this drug. Sensitivity did not return to its original level during 4 h. (Figure 1 Atr). 7 strips were treated with Phe. This substance did not cause any significant change on the physiological parameters of the strip. However, the effect of Ach was inhibited during the contact time (Figure 2, A). After the tissue was washed with fresh solution, decreased sensitivity did not show any significant change (Figure 1, Phe).

Seven strips were exposed to Atr with Car. The spontaneous activity of the strip was initially depressed but later normal rhythmic activity reappeared. Following the washing away of drugs, Ach sensitivity of the strip did not differ significantly from that which is observed in the experimental group where Atr is given alone (Figure 1, Atr + Car). In another separate experimental group, strips ($n = 7$) were treated with Phe and Car. The activity of preparation was initially depressed but later normal function was reestablished. After the washout, the initial antagonistic action of Phe against Ach was significant but it began gradually to diminish (Figure 2, B). At the end of the experiment, the tissue regained nearly its original sensitivity to Ach (Figure 1, Phe + Car).

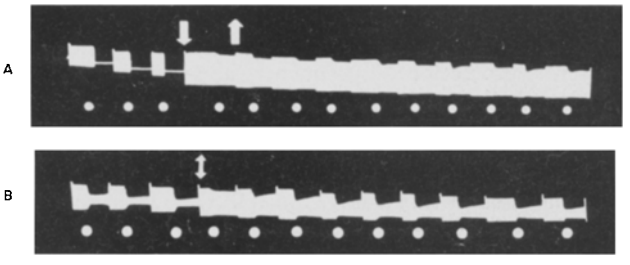

Fig. 2. A) ●, Ach 2 µg/ml; ↓, Phe 250 ng/ml; ↑, washing; B) ↕, Phe 250 ng/ml + 20 µg/ml Car-washing.

Discussion. In this study, we have observed that Car is unable to protect the cholinergic receptor against the action of Atr. However, the same substance prevented the appearance of long-lasting Phe block. These experimental findings led us to the conclusion that 2 antagonists may act on the different receptive sites of cholinergic receptor. Phe and Car probably react with the same receptive site. This may be the common cholinergic site on the receptor macromolecule. Atr possibly combines tightly with a separate special site of cholinergic receptor. This theoretical consideration based on the experimental findings is in agreement with the hypothesis proposed by GOLDSTEIN et al.[4]. In the model considered here for the cholinergic receptor, the binding of Atr and Ach to their respective sites mutually influences the affinity or intrinsic activity of each other. Such an action is reminiscent of the allosteric inhibition in enzymology[7].

Zusammenfassung. Bei Abnahme der Kontraktilität nach Azetylcholin wird am Frosch-Myokard-Modell nachgewiesen, dass Phenoxybenzamin den cholinergischen Rezeptor gegen Atropin «schützt», während Carbachol ohne Wirkung bleibt. Es wird angenommen, dass die beiden Antagonisten an verschiedenen Orten des cholinergischen Rezeptors wirken.

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Stereotopography of the Prolactin Cells of the Rat Pituitary Gland

The relationship between secretory functions and ultrastructure is readily observed in many secretory cells. This applies not only to the synthesis of secretory granules or products but also to their packaging, transport and release. It is well known that granular endoplasmic reticulum surrounds the nucleus on the basal and lateral sides of pancreatic acinar cells[1,2], while the Golgi apparatus, in which maturation and packaging of secretory granules occurs, is located on the apical side of the nucleus[3,4]. The secretory granules then accumulate in the apical region of the cytoplasm and can be observed releasing their product by exocytosis into the lumen of the pancreatic acinus. This secretion scheme is typical for most protein secreting cells[1,3–5], but applies especially to those exocrine or endocrine cells which exhibit a high degree of polarization of their organelles.

A polarization of organelles within cells similar to that observed in the pancreas is often difficult to see in the cells of the anterior pituitary gland. This is probably due to the fact that pituitary cells do not form regular secretory units of structure comparable to the pancreatic acinus since the pituitary glandular associations are composed of several different kinds of cells[6]. Because of this, a three-dimensional analysis of the ultrastructural relationships of intracellular organelles in pituitary cells is justified. This would not only permit a better appreciation of the internal organization of cells, but would also give further information regarding the movement and release of secretory granules from the cytoplasm as well as the extent of functional polarization within the cells. Our previous observations[7] on the pituitary gland of lactating rats suggested that the prolactin cell would be the most suitable cell type for a study of this problem since they have a rapid turnover of secretory products.

Materials and methods. The pituitary glands were obtained from young, adult rats (Sprague-Dawley) which were in various stages of lactation. Details as to the experimental procedures used in our studies of prolactin

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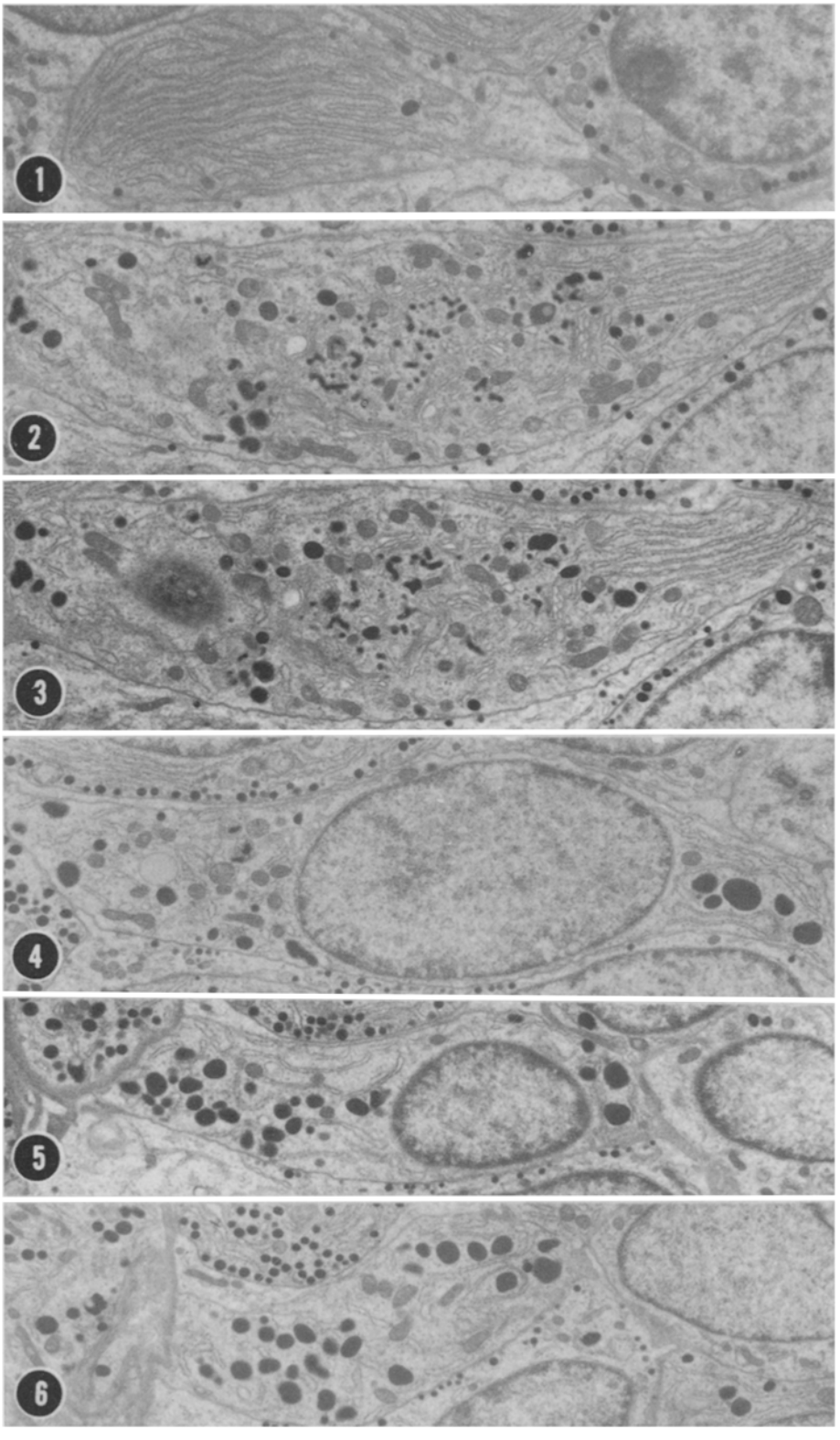

These six micrographs are from serial sections of the same prolactin cell. The position of each section is the series is indicated. ×6,800. 1. In this region of the cell, the rough surfaced endoplasmic reticulum is well developed (Section No. 20). 2. At this level, the Golgi apparatus, mitochondria and a few secretory granules are observed. The rough endoplasmic reticulum is not as extensively developed here as it was in Figure 1 (Section No. 60). 3. A similar cellular organization as in Figure 2 is noted here except for the appearance of the nucleus (Section No. 65). 4. A few cisternae of rough surfaced endoplasmic reticulum are present; however, the Golgi apparatus is no longer visible (Section No. 90). 5. The abundance of secretory granules is clearly illustrated along with evidence of granular extrusion (Section No. 120). 6. Same as in Figure 5 (Section No. 130).

cells, in relation to changes induced by the suckling stimulus, are given in an earlier report from this laboratory[7]. The electron micrographs used in the present analysis of the stereotopography of prolactin cells were prepared from a tissue block from an animal killed on the sixth day of lactation. Several cells contained within two hundred serial sections (silver grey to gold) were analyzed, but one was selected to illustrate the high degree of polarization which can be seen when the stereotopography of an entire cell is examined.

Results. On the basis of our previous studies, as well as the present observations on sections of the pituitary gland, we observed a marked polymorphism of the prolactin cells. Some cells were large and oval, or spherical in shape, while others were elongated and possessed cytoplasmic processes directed toward the capillaries. By studying the prolactin cells in serial sections, we observed a distinct polarization of their organelles. This was particularly striking in cases of prolactin cells of the elongated variety such as the one illustrated in Figures 1–6. Parallel lamellae of granular endoplasmic reticulum were concentrated at one pole of the cell (Figure 1). The Golgi apparatus was in close association with this concentration of granular endoplasmic reticulum (Figures 2 and 3), while the mature secretory granules were localized at the opposite pole of the cell (Figures 5 and 6). Evidence of granular extrusion by exocytosis was noted almost exclusively at the vascular pole of the cell where the granules were concentrated. The nucleus (Figures 3, 4 and 5) was eccentrically located in the cytoplasm, with its largest profiles seen in sections near the Golgi apparatus (Figure 4).

Discussion. On the basis of our observations, we propose that the cellular organelles of prolactin cells in lactating rats have a characteristic topographical orientation. On one side of these cells granular endoplasmic reticulum is concentrated and is in close association with the Golgi apparatus, while secretory granules are concentrated at the opposite pole in the region of the cell closest to a capillary. This scheme probably prevails in all prolactin cells, with only slight modifications to fit their shape. However, it is easier to appreciate this ultrastructural organization in elongated forms of prolactin cells, in which the organization is similar to that commonly seen in pancreatic acinar cells.

It is well known that prolactin cells of suckling animals secrete large amounts of prolactin[7–9]. The distribution of secretory granules in these cells appears to be different from that of some other types of pituitary cells, particularly the corticotroph, or ACTH cell[6, 10], in which the granules are aligned near the entire periphery of the cell. This suggests the possibility of different mechanisms of granule transport and release from pituitary cells. Presumably, these processes are related to differences in the size of the secretory granules, and perhaps to cytoplasmic channels which may depend on viscosity gradients in the cytoplasm. Recent publications[11] indicate that considerable variation in viscosity of the cytoplasm may exist within the same cell. At present we do not have any information about the viscosity of the cytoplasm of prolactin cells. However, it is reasonable to assume that channels of low viscosity, through which the granules might move, may be formed in the cytoplasm. Such channels would facilitate the transport of secretory granules in prolactin cells. Our observations on serial sections suggest that analysis of the functions of pituitary cells by electron microscopy must be conducted with extreme care because different thin sections of the same cell may reveal quite different morphological features. They also suggest that a study of the organizational patterns of organelles involved in cell secretion may give clues concerning variations in the mode of cell secretion.

Résumé. L'orientation des organelles dans les cellules de l'hypophyse antérieure a été étudiée sur des coupes en série pour la microscopie électronique. Une polarisation importante des éléments de l'appareil sécrétoire fut observée dans quelques cellules à prolactine. En conclusion, l'étude de la distribution topographique des organelles peut fournir des informations sur les variations du mode de sécrétion cellulaire.

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Über den Ursprung der Flügelmuskulatur. Experimentelle Untersuchungen mit Wachtel- und Hühnerembryonen

Nach LILLIE[1] beginnt die Entwicklung der Flügelanlagen beim Hühnerembryo nach einer Bebrütungszeit von 50–60 Stunden (Stadium 16 nach HAMBURGER und HAMILTON) mit einer Verdickung der Somatopleura in Höhe der Somiten 14–20. Die Frage, ob das Extremitätenmesenchym ausschliesslich aus der Somatopleura hervorgeht, oder ob Somitenzellen in den Differenzierungsprozess der Extremitätenanlage miteinbezogen werden, wird von den Untersuchern kontrovers beurteilt. Das gilt in besonderem Masse für die Entwicklung der Extremitätenmuskulatur. FISCHEL[2] vertritt die Auffassung, dass bei Vögeln und Säugetieren Somitenzellen in die Extremitätenanlage einwandern und sich dort zu Muskelzellen differenzieren. Zu einem ähnlichen Ergebnis kommt ZECHEL[3] aufgrund der Untersuchung menschlicher

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