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PERMEABILITY OF BIOLOGICAL BARRIERS OF THE ENDOCRINE ORGANS FOR SERUM PROTEINS IN GUINEA PIGS

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Transport of macromolecules both into and out of the parenchyma of a gland is interesting in connection with regulation of the functions of these organs by the aid of peptide hormones, and also in connection with transport of the actual hormones produced by these glands. Penetration of proteins is also important for the development of pathological processes in organs of the endocrine system. However, the blood-tissue barriers in the endocrine glands have received little study.

The aim of this investigation was to study the permeability of barriers of the thyroid and parathyroid, thymus, and adrenal glands, the pancreas, the testes, and ovaries for autologous native and heterologous serum proteins.

EXPERIMENTAL METHOD

Experiments were carried out on healthy guinea pigs. Penetration of autologous serum proteins of the animals was studied in tissues of the endocrine glands with the aid of fluorescent antibodies by the standard method [2], using antisera against albumins, globulins, and whole serum proteins of guinea pigs with an antibody titer of up to 1:20,000 according to dilution of the antigen in Ouchterlony's test. Penetration of heterologous serum proteins was investigated with the aid of horse serum labeled with fluorescein isothiocyanate (FITC), 1 and 10 h after intravenous injection of a 3% solution of serum proteins in a dose of 1 ml/100 g body weight. After luminescence investigation, the sections were stained along with parallel sections with hematoxylin and eosin.

EXPERIMENTAL RESULTS

Autologous and heterologous serum proteins penetrated through the vessels of the thyroid and parathyroid glands into the interstices and were detected in the fibers and cytoplasm of the connective tissue cells. Serum antigenic proteins were distributed in the parathyroid gland among the interstitial tissues between secretory cells, surrounding them on all sides. In the thyroid gland, autologous and heterologous serum proteins penetrated to make contact with the interstitial surface of the follicular epithelium. These proteins were detected in the cytoplasm of the follicular epithelium, particularly in the low epithelium, and also in the colloid of some follicles. The number of follicles into whose lumen autologous and heterologous serum proteins penetrated varied in different animals from a few to half of the total number. The arrangement of follicles containing and not containing serum proteins in a section through tissue of the thyroid gland was not uniform. In the thymus, autologous and heterologous serum proteins penetrated from the vessels into the interlobular connective tissue, and spread through it to make contact with the surface epitheliocytes of the cortical

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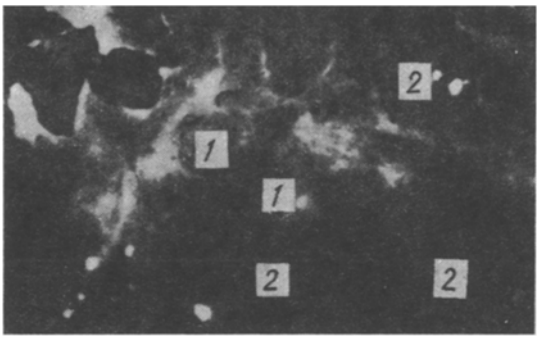

Fig. 1. Fluorescence of horse serum proteins labeled with FITC in thyroid gland tissue 1 h after injection. 1) Follicles containing labeled serum proteins; 2) follicles not containing serum proteins. Fluorescence of proteins detected in interstices, in the cavity of some follicles, and in the cytoplasm of the epithelial cells of these follicles. Objective 20, homal 3.

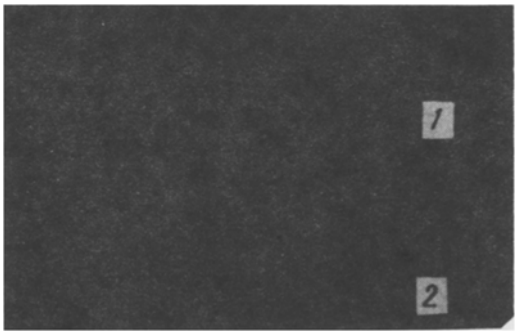

Fig. 2. Fluorescence of autologous native globulins in guinea pig thymus tissue. 1) Connective tissue of thymus capsule; 2) cortex of thymus. Fluorescence of autologous globulins detected in fibers of capsule, on surface of cortical thymocytes and, in some places, between surface thymocytes, but absent in the deeper layers of the thymus.

part of the thymus, but were not found in the cortical part in deeper layers of cells. Serum proteins were determined in vessels of the cortical part but were absent in the tissue outside the vessels. Autologous and heterologous serum proteins penetrated from the vessels into the tissue of the medullary part of the thymus. Albumins and globulins of the animal's own serum were present in some Hassall's corpuscles. In the pancreas, endogenous serum proteins penetrated from the vessels in the islets of Langerhans between the islet cells and were detected in the cytoplasm of some cells in the form of diffuse homogeneous luminescence. Heterologous serum proteins, unlike endogenous, were found only in solitary islets, where they were also observed to leave the vessels between the islet cells. In the adrenals autologous serum proteins of the animals penetrated into fibers of the capsule, and together with them they passed into the cortical substance and surrounded groups of cells in the glomerulus layer, but none were found either between these cells within the glomerulus or in the cells themselves. In the zona fasciculata endogenous serum proteins penetrated from the vessels into fibers of the interstitial tissue and spread between the cells of this layer. In the zona reticularis, adjacent to the zona fasciculata, penetration of these proteins also was found, and in the middle and lower parts of the zona reticularis endogenous serum proteins were detected in the lumen of the vessels and in the cytoplasm of the endothelium, but were absent outside the vessels between the secretory cells and in those cells. Endogenous serum proteins penetrated widely from the vessels of the medullary part of the adrenals and were detected in connective tissue fibers; in some places they penetrated between the cells and were present in the cytoplasm of some cells. Heterologous serum proteins at both times of observation, like endogenous proteins, were detected in fibers of the capsule and zona glomerulosa,

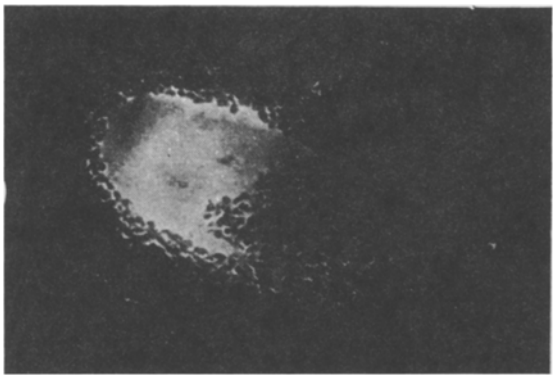

Fig. 3. Fluorescence of horse serum proteins labeled with FITC in follicles of guinea pig ovary 1 h after intravenous injection. Fluorescence of labeled heterologous proteins observed between cells of follicle and in cavity of follicle. Fluorescence microscopy. Objective 20, homal 3.

and also in fibers of the medullary layer of the adrenals. However, heterologous proteins were rarely found in some vessels and were not found outside the vessels in the zona fasciculata and zona reticularis.

Significant differences in serum protein penetration were found in the ovaries and testes. Endogenous and heterologous serum proteins penetrated through the vessel walls of both organs into the interstitial tissue. In the testes serum proteins spread from the interstices through the tissue layers between the myoid cells [3] in the walls of the seminiferous tubules, to make contact with the basal surface of the cells of the seminiferous tubules, but they penetrated neither into those cells nor between them, and were not found in the lumen of the seminiferous tubules. This character of distribution of serum proteins in the testes is a reflection of the blood-testicular barrier. By contrast with the testes, in the ovaries serum proteins, including globulins, not only moved out of the interstitial cells, but also spread between the follicular cells, penetrated into the lumen of the follicles and, from thence, into the corona radiata, and into the zona pellucida, and were detected in the cytoplasm of the ovum. Autologous serum proteins occupied part of the cells of the follicular epithelium and cells of the corona radiata. Heterologous serum proteins penetrated within 1 h after intravenous injection into the follicle by the same path as endogenous serum proteins, and were detected both in the follicular fluid and in the cytoplasm of some follicular cells, and in the corona radiata and zona pellucida. The same pattern of distribution of heterologous serum proteins was observed 10 h after injection, when the intensity of luminescence and the zones of spread of these proteins in most other organs were considerably reduced. This is evidence of the special status of the ovaries for permeability for serum proteins.

The results of this investigation showed that vessels of the endocrine organs are permeable for proteins. This applies both to autologous and heterologous serum proteins. Meanwhile, the pathways of extravascular transport of proteins into tissues of the endocrine organs may differ significantly. The following versions of extravascular penetration of serum proteins can be distinguished in terms of the classification put forward by the writer previously [1]: in the parathyroid gland, in the islets of Langerhans of the pancreas, in the medulla of the thymus and adrenals, and also in the ovary, penetration of proteins is observed between the secretory cells, so that the latter are surrounded on all sides by a zone of their spread. The proteins occupy part of the cells of these organs and can be detected in the cytoplasm of the cells. The vessels and tissue formations in these organs perform a barrier function, because the outflow of blood cells into the tissue is prevented and the quantity of substances leaving also is controlled. A different situation is observed in the thyroid gland. In this organ serum proteins pass from the vessels into the stroma and spread until they make direct contact with the follicular epithelium, but the latter structure prevents further penetration of the serum proteins. In this case the epithelium of the follicles itself plays the role of barrier and bounds the zones in the tissue (the cavity of the follicles) in which proteins do not penetrate. Since in this case part of the surface of the epithelium is isolated from contact with proteins, this type of

barrier may be a partially isolating barrier. Since serum proteins are found in some follicles, which probably depends on the functional state of the follicular epithelium, this partially isolating barrier in the thyroid gland may be interpreted as functionally dependent, or variable. The study of protein transport in the thymus also indicates that here the barrier role may be played by the parenchymatous cells, and the barrier effect is observed constantly. For that reason the barrier in the thymus along the boundary between the interlobular connective tissue and the surface thymocytes and between the blood vessels in the cortex of the thymus and the perivascular thymocytes can be regarded as a partially isolating, functionally constant type. The third variety of barrier is present in the testes. The sustentocytes of the seminiferous tubules isolate the spermatogonia and sex cells from contact with serum proteins. This type of barrier can be classed as isolating at the level of the secondary cells of the organ. Just as in the thymus, blood vessels in the adrenal cortex are of the fenestrating type, and no tight junctions are present between the endothelial cells; however, in the zona reticularis of the adrenals serum proteins are not detected between the secretory cells. Probably a phenomenon of a partially isolating barrier is observed here, possibly connected with the particular features of extravascular transport within the tissues.

Thus the barrier role in organs of the endocrine system is played not only by blood vessels which are permeable for proteins. The barrier function with respect to proteins is performed also by the parenchyma, on which the particular nature of permeability in the given organ and the type of barrier depend.

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