

PHYSIOLOGY

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In this paper an attempt will be made to describe some of the recent advances in the physiology of both the nervous system and the endocrine glands. While the peculiar interests of the author dictated the selection of material, it is hoped the subjects chosen are of general interest.

The pituitary-adrenal control of the release of antibodies from lymphoid tissue.

One of the more interesting recent contributions to physiology has been the demonstration of a functional relationship between two of the endocrines and the activity of lymphoid tissue. Since the present concepts are based on seemingly unrelated investigations in fields far-removed from each other, it is considered desirable to briefly review the more important points upon which these ideas are based.

As a result of careful correlation of the isolated data of previous workers and crucial experiments of his own, Selye, 1936, introduced the concept of an "alarm reaction," a typical series of events taking place whenever the organism is subjected to severe stresses or damaging agents. (1) As a part of this reaction the lymphoid tissues, lymph nodes, thymus and spleen undergo involution, while the adrenal cortex hypertrophies. It was also established by Selye (2) that the lymphoid tissue changes in the alarm reaction do not take place if either the pituitary or adrenals are absent. The nature of this dependence of the lymphoid tissue on the adrenal and pituitary was shown by Dougherty and White (3) who found that anterior pituitary corticotrophic factor caused atrophy of the lymphoid tissues when injected into intact animals, but not when administered to adrenalectomized animals. They further found that administration of adrenal cortical extract or corticosterone causes involution of lymphoid tissue. These facts taken together with the histochemical finding of a greater secretory activity of the adrenal (3, 6) during the alarm reaction, show that the lymphoid tissue involution comes about because of an increased output of adrenal hormone, the release of which is under the control of the pituitary.

The story does not end at this point, for it has also been observed that a lymphopenia accompanied by an increase in the concentration of the plasma proteins occurs during the alarm reaction (3, 4, 5). The lymphopenia is accounted for by the failure of the involuting lymphoid tissue to deliver ample lymphocytes to the blood stream because of liquefaction and dissolution of stored lymphocytes, while the increased plasma protein is considered to come from the destroyed lymphocytes. Electrophoretic studies have shown that this extra plasma protein consists largely of anti-body containing gamma globulin (6). Confirmation of the importance of the lymphocytes as producers of antibodies has come from the work of Harris et al. (7) and Rich, Lewis and Wintrobe (8) who employed immunological techniques. When these latter findings are taken into account it may be finally said that the pituitary acting through its influence on the adrenal controls the release of antibody globulin from the lymphoid tissues.

Relationships between hormones and enzymes.

An approach to the problem of the mechanisms by which hormones really exert their effects has been made through the study of hormone-enzyme relationships. The logic for undertaking such studies is clear when one considers the fact that hormones alter the metabolism of tissues and that enzymes are ultimately responsible for the energy transfers involved. Since changes in the concentrations of enzymes might well account for the changes in metabolism, the concentrations of various enzymes have been studied in different endocrine states. A number of such relationships have already been demonstrated, e.g., the concentration of cytochrome-c decreases after adrenalectomy and can be restored by the administration of adrenal cortical extract (9), liver alkaline phosphatase concentration is increased in dogs with alloxan diabetes (10) and estrogen injections lower the serum acid phosphates in intact animals (11). Since only a few enzymes in but a small number of endocrine states have been investigated, one expects to see much activity in this field in the future.

One should not leave a consideration of the hormone-enzyme relationships without mentioning the vitamins, several of which (nicotinic acid, thiamine, riboflavin and possibly ascorbic acid) go into the make-up of enzymes and co-enzymes (12, 13, 14). Furthermore, it is known that deficiencies in these vitamins result in lowered concentrations of certain enzymes and co-enzymes and thus decreases in the metabolic activities dependent upon them (12, 13, 14). In view of the fact that the levels of both hormone and vitamin exert an influence on the concentration of enzymes, it is apparent that much future investigation should be carried out to determine the details of the relationships between these three substances.

Adrenal ischemia and hypertension.

It has recently been found that unilateral subtotal ligation of periadrenal blood vessels and tissues results in the development of an hypertension, which is apparent after one to three days and which lasts for months (15). In view of the important facts emerging from the study of the ischemic kidney, one expects thorough exploitation of this ischemic adrenal preparation.

Acetylcholine and conduction of the nerve impulse.

During the past few years a theory relating acetylcholine to the conduction of impulses along nerve fibers has arisen. The facts upon which the theory is based are: (a) Nerve fibers contain and can synthesize acetylcholine (16), (b) nerve fibers contain cholinesterase (17), (c) acetylcholine possesses the ability to depolarize membranes (18, 19, 20). The theory states that the stimulus to the nerve fiber results in the release of acetylcholine which depolarizes the neural membrane rendering it permeable to all ions; this results in the generation of an

action potential which stimulates the adjacent region of the neuron and brings about the release of acetylcholine there, thus repeating the whole process. The cholinesterase present destroys the acetylcholine allowing the membrane to recover its polarization.

The authors of recent experiments (21, 22) suggest a drastic modification of this theory. They state that the action potential is due solely to acetylcholine and that the old Bernstein theory of the polarization of the neural membrane by inorganic ions is untenable.

Synthesis of acetylcholine.

Much recent work has been done to show that the synthesis of acetylcholine by brain and nerve depends upon the presence of both adenosinetriphosphate and an enzyme, cholineacetylase (23).

The autonomic nervous system.

Brief mention should be made of a new concept of the functions of the sympathetic and parasympathetic systems in dually innervated organs. The old ideas of the dual innervation by the sympathetic and parasympathetic systems and the functional antagonisms of these two systems appear to be false. In dually innervated structures such as the iris, the gastro-intestinal tract and the urinary bladder, it has been shown that the sympathetic system exerts its influence solely on the blood vessels and the parasympathetic through actual innervation of the smooth muscle of the organs (24, 25, 26).

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