122 (1054)

Studies in thyroid transplantation.

I. DATA RELATIVE TO THE PROBLEM OF SECRETORY NERVES.

By **O. T. MANLEY** and **DAVID MARINE.**

[*From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University, Cleveland.*]

During the past two years we have utilized the method of thyroid transplantation in rabbits in the attempt to get further data concerning certain questions in the physiology and pathology of this tissue. One of these questions is that of the necessity or not of specific secretory nerves to the gland. The observations of Anderson, Berkeley and Rhinehart have shown that in the thyroid both vessels and gland cells are abundantly supplied with nerve fibers. Stewart, Francois Frank and others have demonstrated the richness of the vasoconstrictor nerve supply, and Von Cyon demonstrated the presence of vasodilator fibers, both sets of fibers for the most part reaching the gland through the superior laryngeal nerves. More recently Asher and Flack and Ossokin have published physiological evidence which they think supports the view that the gland is under the control of secretory nerves, and Beebe and his associates have found that prolonged stimulation of the thyroid nerves causes a slight reduction in the iodin content which they interpret as indicating the presence of secretory nerves.

The method of transplantation eliminates many of the physiological and technical difficulties and objections of the acute experiments.

It has been found that under certain conditions thyroid tissue may be readily transplanted in widely separated parts of the body, as for example in the adrenal, ovary, subperitoneal tissues, muscle, subcutaneous fascia of the neck, chest and abdomen, and also, though with more difficulty, in the spleen and bone marrow. By transplanting and removing a sufficient amount of the main gland, care being taken to avoid all contact with iodin, we have always obtained compensatory hyperplasia of the remaining

stump, and in addition a simultaneous and similar degree of hyperplasia of any existing transplants independent of their location. Thus we have seen such reactions in ovarian, adrenal and subcutaneous transplants of the chest, neck and abdomen.

Now, if one gives very small doses of some idoin-containing substance, whether by mouth or by the use of a little tincture of iodin as in skin sterilization, involution promptly occurs in from two to three weeks which effects the transplants irrespective of their location in the same way as the main thyroid gland stump is effected. We have seen no exception to this except in cases where the total amount of thyroid tissue was below the level at which iodin will protect against thyroid hyperplasia. Also if iodin is administered prior to or at the time of transplantation, no hyperplasia of either the original gland or transplants occurs until the effect of the iodin has fallen to the level of inducing an insufficiency. Likewise if iodin is administered following transplantation, no hyperplasia ordinarily occurs during the time of such administration. We have followed such thyroid transplants for as long as 271 days.

If now a large part of the transplanted thyroid tissue and of the original gland, thus involuted, is removed, the remaining thyroid transplants and the remaining portion of the stump undergo active hyperplasia for the second time. This is similar in all essentials to the effects seen in dogs following alternate partial thyroid removals and iodin administrations. There is evidence also that transplanted thyroid tissues function. We have observed four rabbits showing marked amelioration of the symptoms of operative myxedema associated with active hyperplasia of subcutaneous abdominal transplants.

In view therefore of the facts that (1) under favorable conditions thyroid tissue may "take" and grow in widely different parts of the body; (2) that such transplanted tissue undergoes hyperplasia simultaneously and is histologically identical with that of the original gland stump; (3) that iodin induces an involution alike in both the transplanted and non-transplanted tissue, we believe (*a*) that the thyroid may function as a true blood-vascular gland in that the stimuli which cause these hyperplasias may reach the gland cells through the blood stream and that

influences causing thyroid involution may be transmitted by the same means; (*b*) that while these observations do not affect the question of the existence of specific secretory fibers, they demonstrate that such fibers are not essential in order that thyroid tissue may exhibit the characteristic morphological and physiological. changes known to be associated with great variations in functional activity; (*c*) that these data emphasize the necessity for additional evidence on the question of specific secretory fibers for the thyroid.

123 (1055)

On the action of sodium chloride in the prevention of proteotoxin shock.

By HANS ZINSSER, CHARLES C. LIEB and JAMES G. DWYER.

[*From the Departments of Bacteriology and Pharmacology, College of Physicians and Surgeons, Columbia University, New York.*]

It was shown by Friedberger and Hartoch that guinea-pigs could be protected against anaphylactic shock by an intravenous injection of hypertonic salt solution immediately preceding the toxic dose of antigen. That this protection is not due, as Friedberger and Hartoch claimed, to the inhibitory action of the salt on the alexin was demonstrated by Ritz, who found that an injection of salt also exerted protective action in animals injected with proteotoxins (the anaphylatoxins of Friedberger).

Dale concluded that the protection afforded by sodium chloride against acute anaphylaxis was due to the decreased irritability of the smooth muscle. He found that if the uterus of a sensitized guinea-pig were suspended in hypertonic salt solution, the addition of the antigen no longer caused the usual anaphylactic reaction. Other stimulating substances, like pilocarpine and pituitary extract, also failed to produce their typical stimulation provided that the uterus was bathed in hypertonic salt solution.

It is the object of the present investigation to show that, when a preliminary injection of salt protects against proteotoxin shock, the absence of reaction is due to the lessened irritability of smooth muscle.

In the first place, it was necessary to confirm, if possible, the