STUDIES IN THE PHYSIOLOGY OF THE THYMUS

EXPERIMENTAL attempts to determine the function of the thymus gland have been in progress nearly a century. The approach has been by one of four methods: (1) Thymectomy; (2) the use of thymus extracts; (3) thymo-toxic sera; (4) x-ray destruction of the thymus.

Of these, thymectomy appears to have been most popular. We selected the x-ray approach because we felt it offered the best means of destroying the thymus. The rat was chosen as the first animal for study for a number of reasons that are not pertinent here. All animals used were of the Wistar strain and were maintained on the standard Wistar diet.

Following numerous experiments, we found that approximately 2,200 R delivered to the skin over the thymus destroyed the gland completely. The animals were treated through an eight millimeter anterior portal over the thymus which, before treatment, was localized fluoroscopically. The rest of the animal was adequately protected from any x-ray exposure. Another important feature of our approach was the age of the animal when treatment was started. All rats were treated within forty-eight hours after birth, 550 R being delivered to the skin over the thymus on four successive days. We believe that this has been one of the most important factors that permitted reproducible results in successive litters. It is our opinion that the conflicting results reported in the thymus literature of the past century were, in a large measure, due to the different age periods of the animals on which experiments were started.

Following thymus destruction early in the life of the rat, we saw a number of striking changes, some of which we feel have been observed long enough to justify a report. All observations were made on litter mates. Both sexes showed a slowing up of general bodily development as measured by weekly weight curves. For approximately three weeks after birth, no appreciable difference in the weights of the treated and control animals was noted; whereas, a spreading of the weight curves was generally observed after this period. This was more consistent and more marked in the male group.

The most striking organ changes were noted in the gonads, particularly in the male. With complete destruction of the thymus, the development of the testicle was practically arrested. Especially striking was the microscopic picture. In that of the treated animal, there was almost a complete disappearance of the germ cells, with no attempt at spermatogenesis.

The effect on the female gonad was relatively very slight. Although grossly somewhat smaller in the treated animal in most instances, no real differences from the control ovary could be seen microscopically. The estrus cycle remained normal in all our animals. When mating was effected, we again saw the striking differences between the sexes in those animals in which the thymus had been destroyed. No successful mating was obtained with treated male and treated female. The same was true when treated male was crossed with control female. In all instances in which we mated a treated female with a control male, litters were successfully cast, which up to the present are not inferior to those cast by the control animals.

Studies of the effect of thymus destruction on all the other endocrine glands are still being carried out as well as numerous control observations. While sufficient time has not elapsed to permit a detailed examination of all the other glands, certain striking changes in some of them have already been noted. In computing the organ-weight and body-weight ratios, findings consistently showed that in the male animals there was a striking decrease in the weight of the testicles with a relative increase in weight of the pituitary and adrenals, but these ratio changes were not consistent in the female group. In the male, we saw the development of the typical picture of the castrate pituitary, with its hypertrophied vacuolated basophiles. This, however, was not found in the female pituitary. At the moment, we believe these pituitary effects are secondary to the testicular changes, since these changes represent essentially a physiological castration.

In spite of the fact that the thymus was effectively destroyed in both sexes, the marked effects on the testicle and the lack of striking changes in the ovary, the failure to influence the estrus cycle, the sterile male and the failure to alter the reproductive function in the female, the typical castrate pituitary in the former and the relatively unchanged pituitary in the latter, the less striking general body-weight changes and the absence of any consistency of organ-weight and body-weight ratio changes in the female prompted us to consider the possibility that the thymus functionally plays a different rôle in the two sexes.

Certainly our data indicate a close relationship between the function of the thymus and the proper development of the testes.

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