(6) There is no evidence of the existence of a compensatory mechanism between the testes and the thymus.

The work was carried on at the Field Laboratories, Cambridge. The operations were done by F. H. A. Marshall; the weighings and the chief part of the other work by E. T. Halnan. The expenses were defrayed by a grant made by the Board of Agriculture and Fisheries out of funds placed at their disposal by the Development Commission.

Note by G. UDNY YULE.

In view of the disagreement with Prof. Paton's conclusions, Dr. Marshall asked me to investigate the probable errors of some of the comparisons made, with especial reference to the alleged effect of extirpation of the thymus on the growth of the testes.

The problem was not an easy one. A glance at Prof. Paton's figures, or at the corresponding data given by Halnan and Marshall, will show how exceedingly variable are the weights of the testes and how much caution must consequently be used before basing any conclusion on a small difference between the average weights for two groups of some 20 to 30 animals. Considerable differences might be shown even by the averages of groups treated in precisely the same way. Were the animals adult, the "probable error" of the difference between any two observed averages—the amount which it would be as likely as not to exceed owing to mere fluctuations of sampling—might be readily obtained in the ordinary way. But the animals are not adult; the weight of the testes increases very rapidly with the weight of the animal, and the weights of the different individuals themselves vary greatly, so that the two groups of operated and controls are not strictly comparable as a whole.

What I finally decided to do, therefore, was this: To obtain, by known methods, equations expressing as closely as possible the relation between mean weight of the testes and body-weight, for operated and for normal animals, and to see whether the constants in these equations differed more than could be expected owing to the chances of sampling alone. As in Prof. Paton's data the weight of testes did not seem to be a linear function of the body-weight, and it was these data that I first investigated, the logarithm of the testes-weight was substituted for the actual value, and this seemed to give an approximately linear relation, judging from the diagram (fig. 6). The two equations, with the probable errors of the constants which I finally obtained from Prof. Paton's data, including all the 23 normal

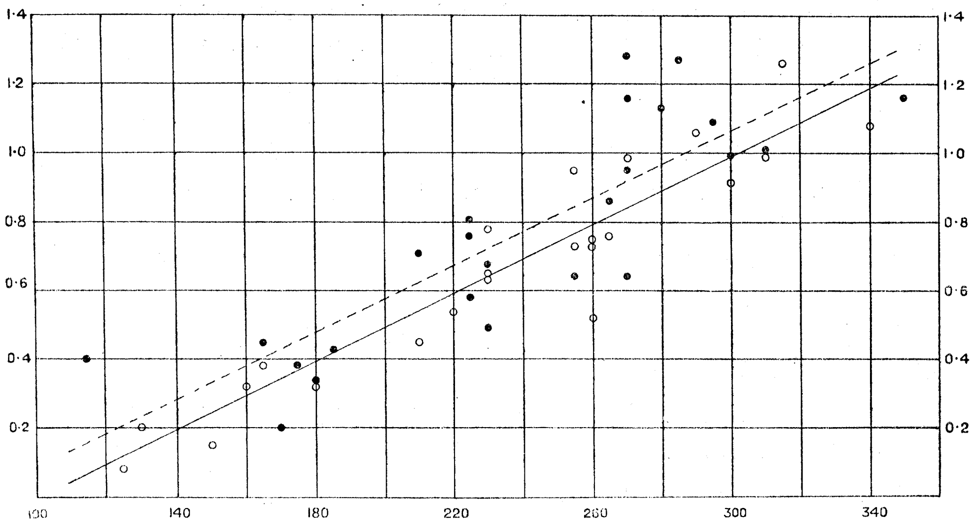

FIG. 6.—Effect of Removal of the Thymus on the Weight of the Testes (Prof. Paton's data).

(Vertical, logarithm of the testes-weight in decigrammes; horizontal, body-weight in grammes. Unbroken line, regression line for normal animals; broken line, regression line for operated animals. Clear circles, normal animals; black circles, operated animals.)

and 24 thymusless animals, were, t being the testes-weight in decigrammes and b the body-weight in grammes :—

Thymusless......... $\log t = (0{\cdot}00489 \pm 0{\cdot}00043)\, b - 0{\cdot}4069 \pm 0{\cdot}1065$,
Controls .... $\log t = (0{\cdot}00503 \pm 0{\cdot}00025)\, b - 0{\cdot}5193 \pm 0{\cdot}0608$.

If the three normals and four thymusless whose body-weights are over 300 grm. be excluded, the results are :—

Thymusless......... $\log t = (0{\cdot}00539 \pm 0{\cdot}00051)\, b - 0{\cdot}5097 \pm 0{\cdot}1203$,
Controls .... $\log t = (0{\cdot}00501 \pm 0{\cdot}00030)\, b - 0{\cdot}5156 \pm 0{\cdot}0815$.

The probable errors must not be regarded as too precise, since they are obtained on the assumption of normal correlation, but they are likely to give a fair guide to the possible magnitude of fluctuations. That of the coefficient of the body-weight (the regression of the logarithm of the testes-weight on body-weight) is the known value

$$0{\cdot}6745 \,.\, \frac{\sigma_1 \sqrt{(1-r^2)}}{\sigma_2 \sqrt{n}},$$

while for the constant term I find the probable error

$$0{\cdot}6745 \left(\frac{\sigma_1^2}{n}(1-r^2) + \bar{x}_2^2 \frac{\sigma_1^2(1-r^2)}{\sigma_2^2 n} \right)^{\frac{1}{2}}$$

where σ_1 and σ_2 are the standard deviations of $\log t$ and body-weights respectively, r is the correlation between them, n is the number of observations, and $\bar{x}_2$ is the mean body-weight. Further, it may be noted that there is a high negative correlation between errors in the regression and in the constant term. It is clear from the probable errors given that no stress can be laid on the differences observed, which lie well within the range of differences likely to occur owing to fluctuations of sampling alone; equally unlikely or more unlikely differences might have occurred, I find, even had *both* groups been normal, once in some seven or eight trials.

Applying the same method to Halnan and Marshall's data, I find for all the 65 controls and 70 thymusless animals:—

Thymusless......... $\log t = (0{\cdot}00319 \pm 0{\cdot}00020)\, b - 0{\cdot}0384 \pm 0{\cdot}0597$,
Controls .... $\log t = (0{\cdot}00367 \pm 0{\cdot}00015)\, b - 0{\cdot}2032 \pm 0{\cdot}0441$;

and for the 43 controls and 49 thymusless under 300 grm.,

Thymusless......... $\log t = (0{\cdot}00210 \pm 0{\cdot}00069)\, b + 0{\cdot}2195 \pm 0{\cdot}1775$,
Controls .... $\log t = (0{\cdot}00364 \pm 0{\cdot}00057)\, b - 0{\cdot}2098 \pm 0{\cdot}1465$.

The difference between the constant terms in this last case looks large, but the probable errors are also very large, and the difference is less than twice its probable error, viz., 0·2301. Summarising in the same way as before, I find differences as improbable as those observed might have arisen owing to fluctuations of sampling once in some five or six trials. Halnan and Marshall's data, it may be noted, do not include any animals under 200 grm. and few under 250 grm. and give a low correlation between body-weight and log (testes-weight) for the rather narrow available range of the non-adults. Within the short range of body-weight 250–259 grm., there are 22 thymusless and 17 controls, and it may be desirable to give a simple comparison for these to emphasise the magnitude of the probable errors. For controls the mean testes-weight is 0·569, with standard deviation 0·101 grm.; for thymusless, mean 0·519, with standard deviation 0·103. The difference, 0·050, is therefore in the direction indicated by Prof. Paton's views, but no stress can be laid on it, as it is only 2·25 times the probable error of the difference, viz., 0·0222.

Taking Paton's and Halnan and Marshall's data as a whole then, it seems impossible to regard any effect of extirpation of the thymus on the growth of the testes as proved; if there is any such effect it seems clear that it is small. The data stand in complete contrast with those relating to the effect of castration on the growth of the thymus. Within the limits of body-weight in Halnan and Marshall's data, there seems to be little relation between weight of thymus and body-weight, so the means may be compared directly. I find:—

21 castrated animals—mean thymus weight, 0·557 grm.; s.d., 0·1104 grm.

27 controls—mean weight of thymus, 0·331 grm.; s.d., 0·0785 grm.

The difference is 0·226 grm., and is 11·8 times the probable error of the difference, viz., 0·0192.

In the case of Prof. Paton's data respecting the effect of simultaneous removal of the thymus and the testes on the rate of growth, the differences observed between operated and control animals seem to point to definite causation. If his Tables III and IV are pooled together, giving 9 operated animals and 12 controls, the difference between the mean gains in weight (viz., 92·2 and 149·2 grm.) is 4·1 times its probable error. For Lot 4 of Table V there are only five animals a side, but the results are unusually uniform. The mean gains in weight are 65 and 120 grm., and the difference 6·6 times its probable error. This result seems in direct conflict with Halnan and Marshall's experiments; they have pointed out above a possible cause for the divergence.

In the preceding, one or two results in probable errors have been given without proof. I hope to publish the proof elsewhere shortly.

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