

VARIATION IN THE SIZE OF TRANSPLANTS OF THE PROSTATE AND SEMINAL VESICLE IN THE ANTERIOR CHAMBER OF THE EYE

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PLATE 3

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The transplantation of tissue into the anterior chamber of the eye has been employed as an experimental procedure since 1873, but the increased interest in endocrinology in the past decade has led to greater use of this method. Schochet (1) revived the use of ocular or iridial transplants for a study of endometriosis, and Markee (2) developed methods for continuous study of the tissue in relation to physiological activity. The earlier literature is reviewed by Podleschka and Divorzak (3). Markee and Andersen (4) elaborated quantitative methods for measurement of the size of the transplants and recorded a series of changes with pregnancy. Markee, Pasqualetti and Hinsey (5) applied the method to a study of the effects of transection of the spinal cord on the endometrium. Recently, Buxton (6) and Haterius, Schweizer and Charipper (7) have successfully transplanted the anterior lobe of the pituitary gland into the eye.

Despite a considerable number of published observations upon transplanted female accessory sexual organs in female animals, there is only one observation, that of Heckel and Kretschmer (8), on male accessory sexual organs in male animals. They found that the prostate could be transplanted to the eye in rabbits and that the administration of the anterior pituitary-like hormone of pregnancy urine increased the size of successful transplants.

In the present report, methods of transplantation and variations in the size of seminal vesicular and prostatic transplants under normal conditions are described. In subsequent papers, the effect of parenterally administered hormones and the correlation of the size of the transplant and the blood cholesterol will be given.

Methods

Chinchilla rabbits that weighed about 2000 gm. were used in all experiments except in those with prepuberal animals, which were taken immediately after

weaning. The diet was uniform and consisted of hay, oats, water and fresh green vegetables. The experiments were conducted over a period of 15 months and although the animal room was not at a constant temperature, no variations attributable to season were noted. The rabbits were in separate cages, but in the same room were other rabbits, both male and female, as well as guinea pigs, rats and mice. If an animal contracted snuffles it was not used for experimental observations. All operations were carried out under ether anesthesia and the usual aseptic conditions.

For transplantation, a small piece of the prostate or seminal vesicle was removed through a midline abdominal incision and placed in warm saline solution while the incision was closed. The sclera of the eye was grasped with a forceps and a small incision made into the anterior chamber at the sclerocorneal junction. With a forceps or small eye spoon, a bit of tissue, not over 3 mm. in diameter, was placed in the anterior chamber at the posterior edge of the iris. No preliminary treatment of the cornea with antiseptics was used and no attempt was made to close the incision. After 2 weeks, about 60 per cent of the transplants were well vascularized and could be used for study (Fig. 1).

Daily determinations of size were made by a photographic method (Fig. 2). The rabbit was placed in a vertically sliding box attached to a counterweight so that the eye could be rapidly aligned with the microscope. A monocular microscope with the stage removed and a portable camera with a side observation tube were placed at right angles to the surface of the eye. A 400 watt carbon arc system with a planoconvex lens and a water filter was placed so that the incident ray struck the eye as nearly at a right angle as possible. With this system, satisfactory photographs were secured in 2 to 4 seconds of exposure, with a $\times 8$ ocular and a $\times 3.2$ achromatic objective. The pictures were enlarged and the outline of the transplant drawn. With a planimeter, the square area was determined and recorded on graphs.

Histological study of the transplants in relation to the abdominal prostate and vesicles and the endocrine glands will be reported in a separate paper. An autopsy has been made on all animals and the transplants have been proven to be viable (Fig. 3).

In Fig. 4 a series of daily photographs of the transplant in one animal illustrates the method used.

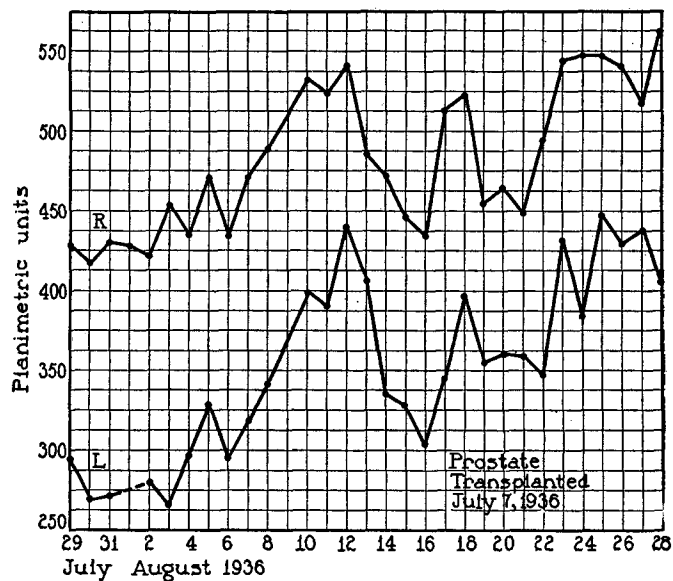
In order to determine the limit of error of the method, 19 photographs of one rabbit were taken over a period of 30 minutes. A statistical analysis of the measurements of these photographs was as follows:

No. of observations.....	19
Sum of observations.....	7271
Mean of observations.....	382.7
Sum of squares of observations.....	2,786,029
Standard deviation.....	13.4
Coefficient of variation.....	3.4%

No differences in the behavior of the prostatic and vesicular transplants have been observed.

RESULTS

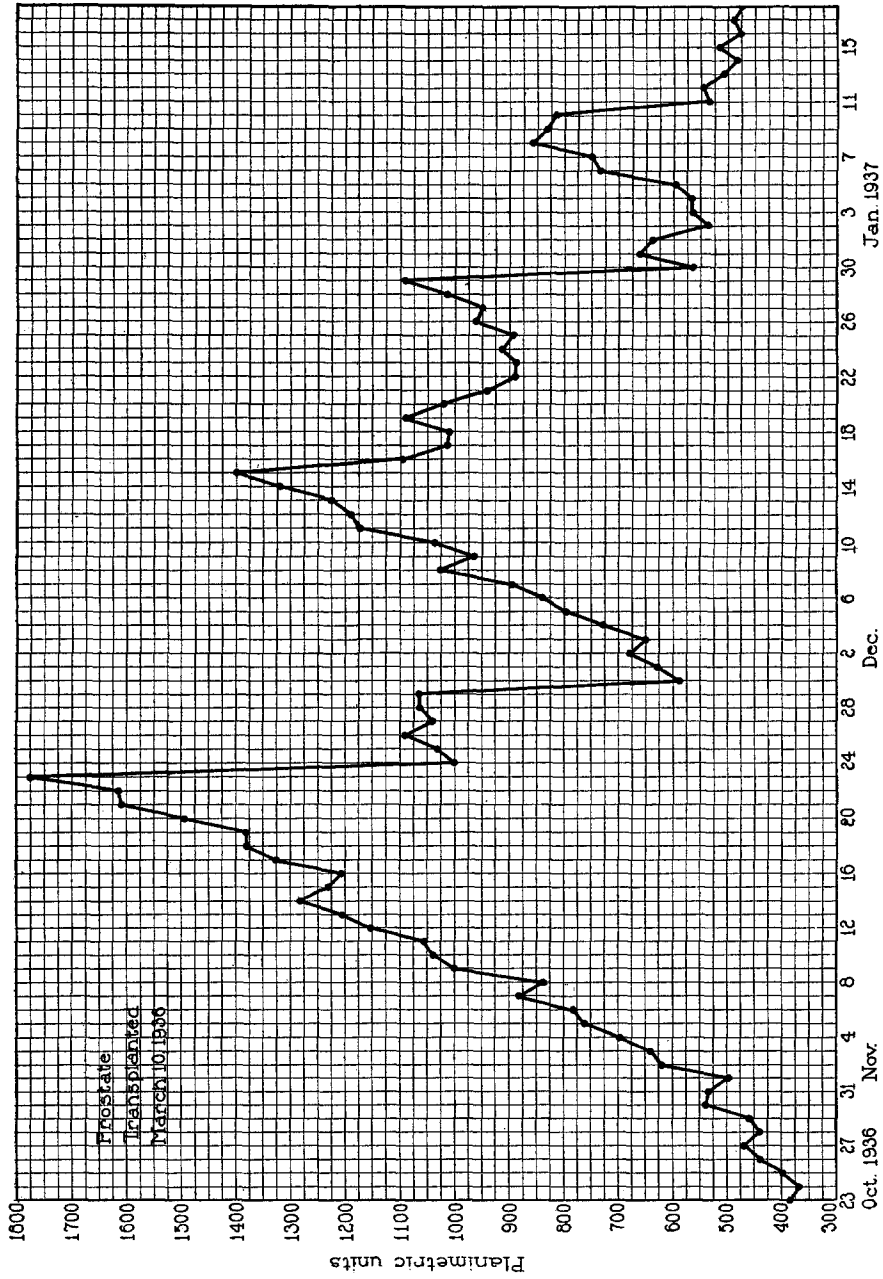
Variation in the Intact Animal.—As shown in Text-fig. 1, there is a variation that exceeds two and one half times the standard deviation of the method and therefore must be considered significant. No regular recurrence or cycle of this variation was observed, even when it was studied over several months. Further, there is no sustained



TEXT-FIG. 1. The daily variation in size of bilateral transplants in a normal rabbit.

growth since the transplants are of approximately the same size after 8 months. When transplants are made into both eyes, the variations in the size of the two are directly correlated. This observation indicates that the change in size represents a physiological phenomenon and is related to the general condition of the animal.

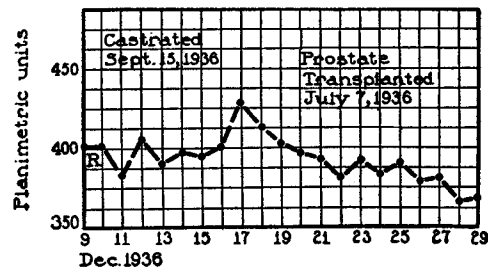
In addition to this deviation of from 20 to 40 per cent of mean size, a marked increase of size with eventual return to the original dimensions after 2 months was noted in one animal (Text-fig. 2). This



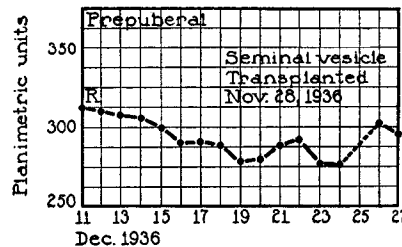
TEXT-FIG. 2. Marked variation in one animal characterized by gradual increase and precipitous decrease.

period was during the winter months and there was no adequate explanation of the change. The variation in size was characterized by gradual increase and precipitous decrease with a loss of as much as 30 per cent of the total size in 24 hours, and occurred only once in eight rabbits, which were observed for from 6 to 8 months, and in fifteen which were observed for shorter periods.

The Effect of Castration.—In all mammals the removal of the testes (9) results in a decrease in the size of the prostate and the epithelium



TEXT-FIG. 3. The size from day to day of a transplant in a castrated rabbit.



TEXT-FIG. 4. The size from day to day of a transplant in a prepuberal rabbit.

and stroma undergo atrophy. This conclusion is entirely supported by the observations on eye transplants. There is a prompt fall within 48 hours and after 10 days the size is approximately 40 per cent of the precastration average value. During the decrease, which gradually loses velocity, there are temporary periods of increase in size. After several months the irregularity in size from day to day is markedly diminished or absent (Text-fig. 3). This indicates that the testis is responsible for the daily variation.

Transplants in Prepuberal Animals.—In rabbits in which the testes

are intra-abdominal or within the canal, variation is at a minimum (Text-fig. 4). Because the accessory sexual organs of the prepuberal animal are not developed, this observation gives further confirmation to the conclusion that the internal secretion of the adult testis varies from day to day and that this variation is reflected in the size of prostatic transplants.

DISCUSSION

In an evaluation of the results outlined above, it is necessary to bear in mind that the tissue under investigation is in a position where it is deprived of the normal nerve and blood supply. With transplants in one eye, this "out-of-placeness" might be considered as an explanation of the variation, but the close positive correlation of the size of bilateral transplants makes it likely that the variation is the result of a general humoral change. The prompt decrease of size and lack of irregularity from day to day after castration and the minimal irregularity before puberty point directly to the testis as the source of the humoral substance.

In view of the immense literature which has accumulated on the general topic of the endocrinology of the sexual organs, it is remarkable that variation in the male accessory sexual organs has not been previously described. In fact, C. R. Moore (9) states that "hormone production in mammals, not strictly seasonal breeders, appears to be a continuous process. . . ." The reason for this discrepancy is probably to be found in the methods employed for study. The prostate and vesicles in the abdomen are held within a fibrous tissue capsule and surrounded by other organs. In the anterior chamber, the small piece of tissue has no definite capsule and is suspended within a fluid which may be readily absorbed or secreted to allow for changes in size. The method described here is in all likelihood an extremely sensitive indicator of stimulation or depression and will reveal changes not detectable by the usual methods.

The nature of the histological changes in the transplant is under investigation and will be described in a separate communication. When the transplant is largest, the blood vessels are more conspicuous in number and size and no areas within the transplant appear as though acini had filled with secretion. Visible congestion and per-

haps an associated edema are sufficient to account for the changes observed. It cannot be denied, however, that contraction and relaxation of the smooth muscle is also in part responsible. It is not related to local tissue hypersensitiveness, such as that described by Seegal and Seegal (10), since it is a continuous phenomenon and the sections which have been studied show no evidence of inflammation.

SUMMARY

1. A method is described with which the two-dimensional size of a transplant in the anterior chamber of the eye may be measured daily with a high degree of accuracy.

2. The size of transplants of the prostate and seminal vesicles varies from day to day and objective evidence indicates that this variation is related to physiologically active testicular tissue.

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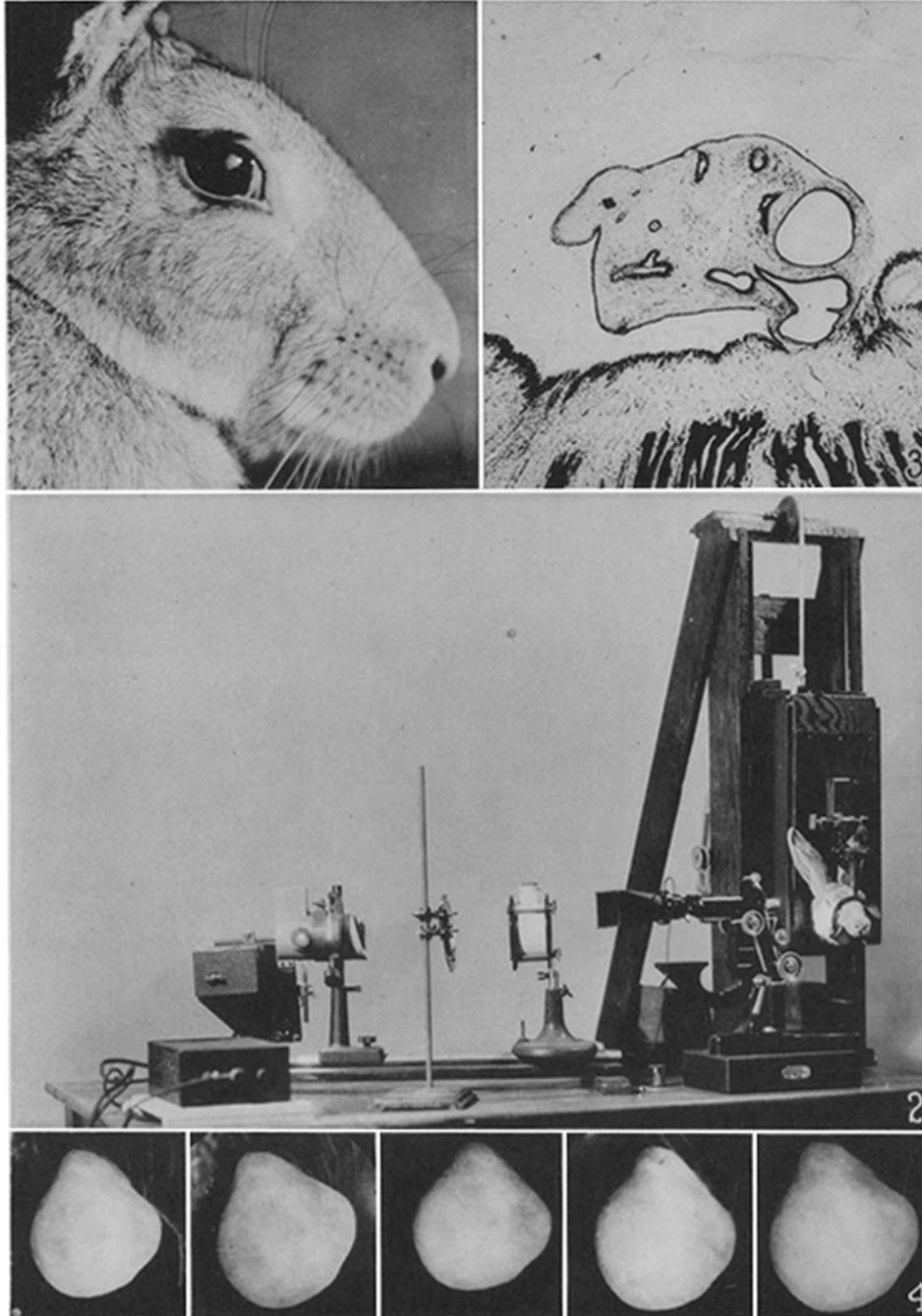
EXPLANATION OF PLATE 3

FIG. 1. Photograph of a rabbit to show the transplant in the eye.

FIG. 2. The apparatus used in these experiments. The details are explained in the text.

FIG. 3. A low power photograph of a transplant of prostate to show the tissue attached by a pedicle to the iris. Hematoxylin and eosin. $\times 19$.

FIG. 4. A series of photographs of a transplant to illustrate the changes in its size. The dates, from left to right, are Jan. 3, 13, 15, 23 and 30, 1937.



(Moore *et al.*: Prostatic and vesicular transplants in eye)