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1. INTRODUCTION.

The scientific results described in this paper were obtained from experiments begun in the Zoölogical Laboratory of Harvard University and completed in the Laboratory of Genetics of the Bussey Institution. These experiments were made possible by a grant from the Carnegie Institution of Washington to the senior author, for which grateful acknowledgment is hereby made. The authors desire also to thank Dr. Alexis Carrel, of the Rockefeller Institute, for valuable suggestions as to operative technique.

The curiosity of zoologists has long been aroused to know whether the reproductive gland of a vertebrate can be successfully transplanted from the body of one individual to another; and, if so, whether the gland will thereafter function in its new environment; and, if it does, whether the nature of its products will remain unaltered. The fact has repeatedly been pointed out that experiments of this sort, if successful, should afford a crucial test of the Lamarckian and the Weismannian views, respectively, of the relation of the germinal substance to its environment and in particular to the body.

Our own attention was particularly directed to these questions by the remarkable results recently described by Guthrie and Magnus, which seemed to show that transplanted ovaries, in a foreign body, liberate products distinctly influenced in nature by that body. To test the correctness of such a conclusion the experiments described in this paper were undertaken. Since it is known that the environment directly influences the nature of the body, if it can be shown further that the body directly influences the character of the inheritance through the sexual products, the Lamarckian principle is established and that of Weismann is disproved. It is therefore of fundamental importance either to confirm or to disprove the results of the authors mentioned.

We are unable to confirm, we present evidence which tends to disprove, the conclusions reached by Guthrie and Magnus. We do not question the results reported by them, but only the interpretations given by them to that work.

Every biologist is familiar with the able series of essays in which Weismann showed the physiological distinctness of body and germ-plasm. Many will recall also the noteworthy experiments of Heape (1890–1897), by which he showed that influences exerted during gestation do not modify the inher-

itance. Heape's evidence was this: The fertilized egg of a rabbit of one variety (for example a long-haired albino) was removed from the oviduct of the mother before it had become attached to the uterine wall. It was then transferred immediately to the oviduct of a rabbit of a different variety (for example a Belgian hare, which is neither white nor long-haired). In several cases the transferred egg became attached in its new position and passed through all the stages of gestation. Young rabbits produced in this way were both long-haired and albinos like the mother of the eggs, not like the rabbit which bore the young. The foster-mother, indeed, seems not to have influenced the inheritance any more than the corn supplied to cattle determines their breed characters.

Granting all this, a further question remains to be dealt with. The transferred egg was already full-grown and fertilized. If the transfer had been made at an earlier stage while the egg was still growing, would the results have been the same? Might not the *growing egg* have lacked that selective power in assimilation which belongs to the full-grown and fertilized egg? May not the former be subject to modification by the environment, even though the latter is not?

This is the question involved in a study of germinal transplantation. Guthrie believes that he has found evidence of such modification; we question the validity of this evidence, on what grounds will presently appear. On the other hand, we present one clear case of the transplantation of an undeveloped ovary, which later liberated eggs in the body of a foster-mother, but in the young so produced no foster-mother influence is detectable. We therefore question still the existence of foster-mother influence. We maintain with Weismann not only that modifications of the body are not handed on to the germ-plasm, but that the character of the body does not in the least influence the character of the contained germ-plasm, provided only the body affords a suitable medium within which the germ-plasm may exist.

2. REVIEW OF THE LITERATURE ON OVARIAN GRAFTING IN ANIMALS OTHER THAN MAN.

Beginning with the year 1895, a large number of investigators have given attention to ovarian grafting. The results have often been conflicting. They represent the work of physiologists, pathologists, biologists, experimental and clinical surgeons, and lastly of students of heredity. It is impossible here to give space for the discussion of the entire subject. All that is proposed is a brief review of its more important aspects.

As now understood, the term autoplastic grafting means the transfer of tissue within the body of the individual, while homoplastic means the transfer of tissue between individuals of the same species. A third term, heteroplastic grafting, is used to denote a transfer between two individuals of different species or genera.

It is proposed to review very briefly the work done in each of these fields.

Knauer (1896) was the first to report on a series of experiments with animals. He was led to undertake this work through Chrobak, a surgeon who had himself tried feeding ovarian substance to women in whom an artificial menapause, with its attendant train of symptoms, had been brought about by operation. Chrobak's results were not conclusive, and he thought surgical grafting held out more hope of relief in these cases.

In his several papers (1896–1900) Knauer, who worked on rabbits, showed by a series of twelve autografts that the transplanted ovary persisted in its new location even up to three years; that its appearance was normal; that genital atrophy was prevented; and further, that it was possible for animals so operated upon to bear young. He gives details of his very careful technique. The ovaries, after the castration, were placed either in the mesometrium, on the horn of the uterus, or between the fascia and muscles of the abdominal wall.

Grigoryeff (1897) confirmed Knauer's work in all its aspects and reported normal young born from his rabbits after castration and autoplastic removal of both ovaries.

Ribbert (1897–1898) made careful histological examinations of autoplastic ovaries, studying the initial process of destruction followed by reconstruction. As late as 150 days after the operation he found no atrophy.

Fish, Rubinstein, Halban, Herlitzka, Basso, Carmichael, Katsch, Stilling, Limon, and others also proved that autoplastic grafting is possible. From their work one comes to the conclusion that autografts of whole ovaries on animals should nearly always be successful, provided the technique is careful and the ovary not too large or too old. Success does not appear to depend upon the new position of the ovary. It will grow anywhere where nourishment is assured, and will even establish itself at times when merely dropped into the peritoneal cavity. In connection with this, one must remember the experiment of Lode, who injected the ova of *Ascaris* into the abdominal cavity of animals and afterwards recovered these from the fallopian tubes and uterus.

Among all these workers Arendt raises the only dissenting voice. He concludes that neither autoplastic nor homoplastic ovarian grafting is possible. He criticizes Knauer's work and the clinical work of Glass, Morris, Montprofit, and others, but his conclusions are clearly too sweeping.

We have ourselves obtained several normal young from a rabbit whose own ovaries were grafted onto the uterine horns. Both the ovaries were found large and healthy in their new position at the end of nine months.

In studying the results of homoplastic grafting we obtain, however, a very different picture and are forced to conclude that the success in this group depends not only on good technique, but also perhaps on the relationship of the two stocks, and certainly on the intimate chemical tolerance of the

opposed tissues. Thus the results are greatly at variance. No doubt the stock used by some of the workers in this field has been more or less closely related. The ratio of success in such cases to the degree of relationship of the opposing tissues has not been worked out, so far as we are aware.

It is necessary to criticize workers in this group on the ground that many cases are considered successful if the ovary is found more or less normal after short intervals—days or weeks. This is no adequate test, as in many of these cases degeneration is ultimately complete.

Knauer's results with his thirteen operations of homoplastic grafting were negative except in two cases, in which the findings were by no means conclusive. In spite of this Knauer thought that homoplastic grafts were possible, though difficult.

Fish (1899) experimented upon twenty rabbits with, he says, successful results. He had hoped to establish the fact that conception is possible subsequent to homoplastic ovarian transplantation, but in this he was disappointed. His experiment is not given in detail.

Foa (1900–1901) was led to undertake experiments in homoplastic grafting, at the suggestion of Celisea, as a means of settling the controversy between the Neo-Lamarckians and the Neo-Darwinians. He does not give details of each experiment, and their number appears to have been small. His grafts were made onto the original ovarian sites. With this method one might question whether regenerated tissue could be distinguished from grafted tissue. His conclusions were that homoplastic grafting was practical, especially when ovaries of new-born animals were used as material to be grafted. He thought that such material, planted into older animals, grew much faster than normally and soon arrived at the growth stage of the host, and he cites an experiment in support of this view. It is possible, however, that regeneration of older tissue may have occurred in such cases rather than accelerated development of introduced tissue. He says also that ovaries of a new-born animal immediately degenerate when placed in an older animal whose own ovaries have ceased to function. His findings inclined him to the belief that there can not be such independence of germinative material as the doctrine of Weismann would have us believe. Experiments in which he hoped to show the influence of the foster-mother upon foreign germinative material have not been heard from.

Guthrie (1908) did homoplastic grafting of ovaries in chickens and obtained young from his grafted animals. He concludes that the homoplastic ovaries function normally and produce young. He thinks that the color characteristics of the fœtuses and of the chicks may be influenced by the foster-mother. The detailed observations made may be summarized as follows:

Two pure-bred black single-comb Leghorn and two white single-comb Leghorn pullets were operated upon, and a third pullet of each sort was

kept as control. In the operations the ovary of a black pullet was exchanged with that of a white one. Six months after the operation the birds, which had now begun to lay, were mated, with the following results in chicks or fœtuses:

1. The control black hen mated with a black cock produced thirteen black chicks with light breasts and throats.

2. Black hen B 2, which had received an ovary from a white pullet and was mated with a white cock, produced nine white chicks and eleven white ones having black spots on heads, wings, or backs.

3. Black hen B 3, which had received an ovary from a white pullet and was mated with a black cock, produced four ordinary black chicks (with light under surfaces) and two chicks described as being "black with white legs."

4. The control white hen mated with a white cock produced eighteen white chicks.

5. White hen W 2, which had received an ovary from a black pullet and was mated with a white cock, produced three white chicks, one chick white with black spots, and one ordinary black.

6. White hen W 3, which had received an ovary from a black pullet and was mated with a black cock, produced twelve white chicks spotted with white on head, wings, or back.

The conclusions to be drawn from these observations will be discussed elsewhere in this paper.

Magnus (1907) transferred the ovaries from an albino to a black rabbit with apparent success. The black rabbit was mated with an albino male five months after the operation and a month later bore two young, one black and the other an albino. Two months later she died pregnant, and in the uterus were found two dark-colored embryos and five light-red ones supposed to be albinos. No ovary was found on one side of the body, but on the other side was a well-developed and functional ovary bearing corpora lutea. Magnus supposes that all the embryos produced were derived from eggs liberated by the transplanted ovary, but in view of our own experience we are inclined to question this interpretation.

Ten other rabbits similarly grafted by Magnus produced no young, though three of them gave indications by their sexual activity that they contained living ovarian tissue.

Among other authors who have reported successful results with homoplastic grafting in animals may be mentioned: Schaus, Basso, Mauclaire, McCone, and Lukaschewitsch.

McCone gives the case of the birth of five well-formed offspring in a rabbit from the grafted ovary of another rabbit, but the evidence that the functioning ovary was an introduced ovary is far from complete. Pregnancy took place four months after complete castration and transplantation from another member of the same species. The other authors report no young.