

Elsewhere real progress is found in the direction of simplification, which makes for convenience, saves time, and meets the limitations of memory by instituting more concise methods of making records. Does the law that inheres in nomenclature differ so much from that which obtains in all other vast accumulations of facts? If so, let us have a statement of it, so that we may, by understanding it, attain to acquiescence in the inevitable.

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ON EVIDENCE OF SOMA INFLUENCE ON OFFSPRING
FROM ENGRAFTED OVARIAN TISSUE

TO THE EDITOR OF SCIENCE: In publication No. 144 of the Carnegie Institution of Washington entitled, "On Germinal Transplantation in Vertebrates," by Castle and Phillips, issued March 14, 1911, an attempt is made to overthrow my experiments on transplantation of ovaries in fowls,¹ and Magnus's² experiments of similar character on rabbits, and to establish a claim to priority in the demonstration that offspring may result from transplanted ovaries; and the effect, if any, of soma influence on such offspring. Therefore, I feel it incumbent to call attention briefly to certain of the statements in order that no misunderstanding may result. Since my papers with the experiments are readily available, I shall avoid all unnecessary repetition.

In a word, the situation is as follows:

¹"Results of Removal and Transplantation of Ovaries in Chickens," presented before the American Physiological Society in connection with the seventh meeting of the Congress of American Physicians and Surgeons, Washington, D. C., May 7-9, 1907 (*American Journal of Physiology*, 1907, XIX., xvi-xvii). "Further Results of Transplantation of Ovaries in Chickens," *Journal of Experimental Zoology*, 1908, V., 563. "On Graft Hybrids," presented before the American Breeders' Association, Omaha, December, 1909. "Survival of Engrafted Tissues. I. (A) Ovaries and (B) Testicles," *Journal of Experimental Medicine*, 1910, XII., 269.

²Magnus, "Transplantation af Ovarier med Saerligt Hensyn til Afkommet," *Norsk Magazin for Laegevidenskaben*, 1907, No. 9.

By exchanging the ovaries of fowls and breeding the fowls, I obtained results which seem to show that the transplanted ovaries preserved their reproductive function; and the resulting offspring presented evidence of soma or foster-mother influence. The results are given in detail in my several papers. I may add that since I had no allegiance with any school of theorists, I was not involuntarily partial in observing and recording the results. Whether the results would substantiate either or neither of the theories built largely upon speculation as to the relationship of reproductive tissues to their environment, or whether the character of the offspring would conform to Mendel's results of studies of inheritance in peas, gave me no concern.

The primary object of the experiments was to determine if an engrafted ovary might retain its reproductive function. Therefore, an answer to the question was obtained. And incidentally information on soma influence was secured. Following this, it seemed of additional interest to reverse the matings of the parent stock. And also, by breeding, to study the character of the offspring from the offspring obtained from engrafted ovaries. Unfortunately before this was accomplished, the experiments were terminated by an outbreak of disease among the fowls. But I did not consider then, nor have I since come to believe, that the character of the offspring of the second generation could do more than indicate whether or not soma influence might be evident in the character of the offspring of this generation, that is, the grand chicks. But owing to a degree of familiarity with the general principles of physiological experimentation and interpretation, from the beginning I saw the limitations to the absoluteness of any evidence that might be obtained by continuation of such experiments. For example, before drawing the provisional conclusions in the announcement of my results, the statement was made that "more data must be had on these points before definite conclusions can be drawn."³ Apparently Castle has

³*Journal of Experimental Zoology*, June, 1908, V., p. 570.

overlooked this statement. And I may say that all subsequent statements regarding my results have been made from the same standpoint.

In attempting to interpret my results from the Mendelian standpoint, to overcome the difficulty in concluding that in no instance the offspring were derived from engrafted ovarian tissue, Castle can only see his way clear by speculating as to the result that might have followed had I employed two white cocks in the matings, one cock being a half-breed. But he assumes that only one white cock was used, for, as he points out, I use the expression "*the white rooster*." But since a point of doubt has been raised as to whether one or more white cocks were employed, and since Castle claims that I make no specific statement on this point, I would refer to the table on page 565 of the paper appearing in the *Journal of Experimental Zoology*, which is headed "weights of the chickens were as follows," in which the experiment numbers of the individuals, both male and female, used in the experiment are given, together with their weights.

In respect to the evidence of soma influence, this was observed in the offspring directly from the transplanted ovaries. Therefore, it is not open to the same doubt as in the case of more indirect or circumstantial evidence. But supposing that such offspring had been bred, and supposing the offspring resulting from this mating (grand chicks) had or had not presented characteristics indistinguishable from the offspring obtained by straight breeding or of hybrids obtained by crossing unoperated fowls of the breeds employed, such results could not affect the conclusions of foster-mother influence in the first generation. It would only show that in the particular individuals presenting feather markings indicating soma influence, that similar feather markings were or were not transmitted to their offspring, or that individuals presenting no such markings might or might not transmit evidence of soma influence to the next generation. Again, the fact that the markings in all cases were not uniform in the

offspring of the first generation, in no way invalidates the results. For all exact knowledge of soma influence must of necessity spring directly from experimental results. Therefore, it can not be assumed that all such offspring must present similar characters either to be acceptable as evidence that an engrafted ovary may preserve its reproductive function, or that such offspring may be influenced by the somatic tissues of the host. That is to say, it is not permissible to assume that all of such offspring would be influenced in the same direction or to the same degree. Nor can it be assumed that evidence of soma influence can be demonstrated in other combinations of fowls, much less in different species of animals.

Seemingly a lack of insight into the underlying physiological principles in such experimentation has led Castle and his collaborator into a misunderstanding, and therefore into stating their belief that my interpretation of the results, and my criticism of a statement of theirs regarding evidence of soma influence,⁴ was due to a failure to grasp fully the laws of inheritance of the character which I used as a criterion. But this is more of a personal matter and therefore of no general interest.

These writers call attention to the fact that Davenport attempted to repeat my experiments on fowls, with the result that in every case spaying was incomplete, and the young from such operated hens showed no influence of the introduced graft. This is far from being an argument against the acceptance of my conclusions, as all that it shows from his interpretation is that the ovaries were incompletely removed in his experiments. But as a matter of fact, his experiments and results, while meagerly reported,⁵ such as they are, might as well lead to the conclusion that he obtained very strong evidence of soma influence. That is, the chicks so closely re-

⁴"Guinea-pig Graft-hybrids," *SCIENCE*, N. S., 1909, XXX., 724.

⁵Davenport, "Inheritance of Plumage Color in Poultry," *Proceedings of the Society for Experimental Biology and Medicine*, 1910, VII., 168.

sembled the foster mother that he was led to ascribe the result to original ovarian tissue of the foster mother. This assumption was based upon another assumption, namely, that chicks from the engrafted ovaries would preserve the characters of the fowl from which the ovaries were obtained. The fallacy of this assumption has been pointed out above.

Davenport did not use standard varieties of fowls, so far as I am able to determine from his statements. This is unfortunate, as it is obviously impossible to discuss his findings from the standpoint of relationship of donor to host. For example, I have shown that engrafted ovaries in fowls do not succeed if the stock is too distantly related.

Davenport states that my results justify the opposite conclusions to those which I have drawn; but since he does not give any reasons nor present any evidence for such a conclusion, it carries no weight other than as a personal opinion.

Castle and Phillips ask that my experiments be repeated before they accept my interpretation of the results. In reply, I ask why they did not employ fowls (chickens) in order to confirm or discredit my experiments. I may say that my first series of fowls, operated on in the summer of 1904, were all lost through lack of proper facilities. The next series, operated on in 1906, were given my undivided attention and furnished the material for my papers. A larger series operated on the following year with the view of extending the observations and investigating new fields opened up by the successful series, were not productive of results in the direction of permitting the study of offspring from engrafted ovaries, but furnished considerable information along other lines which is in part presented in my later papers. Successful breeding of fowls, as every one knows, demands the fulfillment of certain requirements in the way of quarters, and facilities for hatching and raising the chicks, and intelligent attention. As to the first two of these requirements, the third series of experiments clearly proves that the quarters and facilities at my disposal, though after a man-

ner adequate for eight fowls, the number composing the second series of experiments, were not adequate for five times this number, the approximate number that were included in the third series. Also, it was not possible for me to give as much time to the third series as to the second. Immediately following this, I made application to the officers of one of the endowed research funds for support in prosecuting the investigation on a much larger scale, which included the employment of a number of species of animals. But for perfectly good reasons the request was denied. Since that time new experiments have been continuously in progress, but they have been designed with a view of keeping within the limits of my facilities.

I do not propose to enter into a discussion of Castle and Phillips's results in this place, save to challenge their assertion that theirs is the first critical case of successful ovarian transplantation from the standpoint discussed above, on record. This statement I make in view of the fundamental considerations also above stated, as well as from an examination of their protocols. For example, they used mongrel stock. Therefore, any evidence furnished by the character of the offspring would be of doubtful value. This is true particularly as regards soma influence; and as cross-breeding was not employed, any evidence of soma influence in the offspring would have been obscured by the character of the male parent.

Also it is not proven that the offspring may not have come from ovarian tissue of the host left in site after operation. Indeed, an interpretation of their results from the numerical standpoint, a criterion employed by them in interpreting their results from the Mendelian standpoint, it would be as fair to conclude that in all of their pigs that became pregnant no post-mortem findings are given. And after operation that this was due to incomplete removal of ovarian tissue. For they state that of the five animals in this group, the results in three were due to ovarian tissues generated from the host. Of the two animals left in the successful group, for one

denying soma influence, the results in this case might as well lead to the conclusion that the offspring were from ovarian tissue of the mother, as from the engrafted ovarian tissue. Also in the remaining animal, from the description given of the post-mortem findings it is impossible to conclude that the mother's ovarian tissue was completely removed on both sides. This objection the authors endeavor to surmount by stating that the mass of ovarian tissue found at the site from which the right ovary was removed, was apparently strongly encapsulated, so that no ovum could be discharged even if it came to maturity. Such a conclusion is of course incompatible with the evidence, for few experienced pathologists, from the evidence presented, would care to make such a definite statement as to the retention of liberated ova.

Similarly, their statements regarding the regeneration of ovarian tissue are too absolute. For example, in certain cases where both ovaries were removed and ovaries from another animal engrafted in the neighborhood, as to the horn of the uterus, the absence of ovarian tissue at the site of implantation, and the presence of ovarian tissue at the site of removal of the animal's own ovaries is not proof that the former degenerated, and the latter regenerated. For it is possible that the implanted ovaries might have come in contact with the raw surface left after removal of the original ovaries, and become attached thereto. And since the engrafted ovaries were secured in place by means of exceedingly fine strands of unraveled silk, it is by no means certain that they could not have broken away from their moorings, owing to a cutting out of the tissues or a slipping of the knots, or even a breaking of the thread; though the latter accident would probably be less liable to occur.

These are merely some points that it is unsafe to leave out of account in concluding that such experiments are critical in the absolute sense, and I wish to say that I do not urge them as invalidating their results. In fact I consider that they have added at least one more confirmatory observation upon the reproductive functioning of transplanted

ovaries, probably two, and possibly five. For the evidence does not absolutely rule out the animals which they have placed in the group in which they think regeneration of the ovarian tissue occurred. But it should not be forgotten that conclusions based upon indirect evidence, though appearing absolute, are never wholly free from at least a shadow of doubt. To accept this statement, it is only necessary to trace almost any biological subject developed from indirect experimentation a little way back into the literature. Indeed, teachings based upon such conclusions have passed without question through generations, to be later overthrown. And since the element of indirectness has not been eliminated in the experimental investigation of ovarian transplantation, I have stated that my results *seem* to lead to certain conclusions. And the same applies to Castle and Phillips's results as regards functioning of engrafted ovaries.

As to their interpretation of the results from the Mendelian standpoint, the nature of some objections to their conclusions has been discussed above. In addition, I would say that it is unfortunate that they did not preserve the individuals furnishing an ovary for engrafting, leaving the other ovary in place and then breeding this female to the same male used upon the female carrying the engrafted ovary. From their paper it would seem that they look chiefly to the second generation for evidence of soma influence, the index for detecting such influence being based upon the assumption that such influence would show in the second generation. The fallacy of this assumption has also been considered above.

In conclusion, I desire to say that the continuation and extension of these experiments is of the greatest interest and importance, and I hope that Professor Castle and his pupil may see their way clear to continuing them on a larger scale, using purer varieties of animals, including fowls of not too distantly related varieties.

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