Variation and Selection; a Reply.

By **W. E. Castle**, Forest Hills (Massachusetts),
Harvard University, Bussey Institution.

(Eingegangen am 1. April 1914.)

In a paper entitled "Studies on variation and selection" recently published in this journal, Dr. and Mrs. HAGEDOORN criticise severely a series of experiments with hooded rats, which I have for some years been conducting with a view to testing the effectiveness of selection. That investigation of this question is worth while will, I think, be questioned by no one, in view of its vital connection with theories of heredity as well as with economic practise; but a difference of opinion may exist as to what methods are best suited to solve the question. Concerning this I wish in passing to say a few words.

The criticism of my methods and results is based wholly on a paper of very general character in which a detailed description of either methods or results was impossible. I have since published jointly with Dr. PHILLIPS a more complete account which, to those who may chance to read it, renders most of these criticisms superfluous, but for the benefit of those who may not read the fuller account referred to, I wish to correct certain wrong impressions which are likely to be received from reading only the account of my critics.

1. I am charged (page 163) with using in my selection experiments foundation stock which was not known to be genetically pure for the character to be studied.

This criticism begs the question at issue. The question under investigation was:—Do pure races exist or can they be produced. Given a pure race to start with, what need would there be of investigating its purity? I began with those rats about whose ancestry I knew most, and endeavored, as my critics did in their own abortive experiments, to obtain races as pure as possible by mating like with like. But I have not yet succeeded (nor did the HAGEDOORN's) in obtaining pure races,

that is those free from variation in the hooded coat-pattern, notwithstanding the fact that selection has been made uniformly in one direction for 15 generations.

2. My critics maintain that I should have inbred my stock. Since the entire stock is descended from a very few individuals (less than a dozen) and we have at no time hesitated to mate together brother and sister, provided they varied in the same direction, but have always used the most extreme individuals (plus or minus) which were available, to mate with each other, it follows that very close inbreeding must have occurred throughout the experiment. What ground my critics had for assuming that inbreeding had not been practised is not clear.

3. The serious charge is made (page 164) and emphasized by italics that I "made no pedigrees of individual rats, but only tables of averages, thoroughly grinding up, as it were, and mixing his results before even looking at them". This statement is untrue. The parentage of each rat is recorded as its description is entered in the record book. Doubtless my critics meant to say no pedigrees had been published, which is a very different matter, but one which presents some difficulty when one is dealing with 20,000 individuals. My critics' use of language is here inexcusably careless.

4. I am further charged (page 170) and again in italics, with failure to "select rigorously". What I said concerning this matter in the paper on which the criticism is based was this, "In each generation the most extreme individuals were selected as parents". This statement apparently has no weight with my critics. I also mentioned the extreme minus variants at the outset of the experiment to have been of grade — 2 (without back-stripe) and am in consequence criticised for using animals of any other grade in the minus series. Had I followed this advice, my experiments would have ended as abruptly as those of my critics, "in a catastrophe", for there was an insufficiency of such animals at the outset, and such extreme variates rarely produced their like. In the first two generations of offspring from minus selected parents there were only 7 in 187 individuals as extreme as — 2 in grade and no two of these of opposite sex were available at the same time for mating with each other. In the next generation there were 16 in 195 young which were as extreme as this in grade, and for the first time a pair of these became available as parents. They produced 9 young, of which only two were as extreme in character as their parents. My critics seem to have adopted the idea that the minus variation must be due to "loss of genes" and so it is inconceivable to

them that a minus variant should produce anything but similar minus variants, if mated with its like. This particular case shows the groundlessness of their assumption. The nine young of the first pair of — 2 parents were actually distributed as follows:—

Grade . . .	— $\frac{3}{4}$,	— 1,	— $1\frac{1}{4}$,	— $1\frac{3}{4}$,	— 2
Frequency . .	1,	2,	3,	1,	2.

(See CASTLE and PHILLIPS, Table 19.)

In this case is seen a marked regression in grade downward, toward 0. Parents of this same grade (— 2) chosen from the minus series at the present time (generation 15) produce more offspring of grades higher than of those lower than grade — 2, that is regression now occurs in the opposite direction, as compared with its original direction. Facts such as these show that the phenomenon of regression as originally described by GALTON is real, not apparent merely, as JOHANSEN's work seems to show, and that the direction of regression with reference to a particular condition can be altered by repeated selection.

5. It is evident that for the array of grades just given an average may be computed which will express the direction and degree of the regression. This average is — 1.36 showing that the regression from the grade of the parents is back toward 0, and in amount 0.64. A comparison with the grade of the offspring of — 2 parents in subsequent generations is instructive. For the first eight generations in which pairs of — 2 parents occur, the average grades of their offspring were as follows. The precise distribution of the offspring in grade is recorded in Tables 19-26, CASTLE and PHILLIPS.

Mean grade of the offspring of parents of grade — 2.

Generation	Grade of Offspring	Number of Offspring
4	— 1.36	9
5	— 1.52	109
6	— 1.58	283
7	— 1.72	969
8	— 1.81	1170
9	— 1.90	811
10	— 1.96	478
11	— 2.08	51

It will be observed that upon repeated selection away from 0, the regression toward 0 grows less and less until in generation 11 it coincides with the direction of the selection.

This case illustrates what my critics object to most of all, the use of statistical methods in genetic analysis. This they regard as a "lamentable error" because it seeks first to get an unbiased view of the facts, before attempting to explain them. In their own words, (page 171), "For as the statistical method concerns itself exclusively with results and absolutely neglects the causes of variation, it must hopelessly tangle up these causes."

They object to my averaging the parental grades, when these do not exactly coincide with each other, urging the possible lack of homogeneity in the material averaged. Thus, parents of mean grade 0 might be respectively of grades -2 and $+2$, which on a hypothesis of genes should give a very different result from parents both of grade 0. This is a valid objection, which I have continuously held in view, and have met in the best practical way I could devise. When the two parents in a mating were not of identical grade, the difference between them has in no case been large, except in the series of crosses, which is tabulated by itself and is entirely distinct from the straight selection series. In a considerable number of matings the grade of the male parent has been slightly higher than that of the female because polygamy was allowed among our rats, one male being mated with two or three females simultaneously. This made possible a more rigorous selection of male than of female parents, a smaller number of males being required. In assembling the observations, it seemed proper that the grade of both parents should influence the classification of the offspring. Thus, when both parents are of grade 2, it is obvious that the offspring should be placed in the row, parents 2; again, when both parents are of grade $2\frac{1}{4}$, the offspring should be placed in the row, parents $2\frac{1}{4}$. In a case in which one parent is of grade 2 and the other of grade $2\frac{1}{4}$, we have split the difference between them and have placed the offspring in a row, parents $2\frac{1}{8}$. While this is described as the "mean grade of the parents", it is obvious that it does not constitute any such a vicious average as the average blackness of a mixture of all black and all white birds, the hypothetical case advanced by the HAGEDOORNS.

The parents, in our experiments, are in all cases as extreme, plus or minus, as are available in the respective series, and the parental differences averaged are small. They are such in amount as have been disregarded altogether by the HAGEDOORNS in dealing with their own observations recorded in their Figures 3 and 4.

If one objects to averaging the grades of the offspring, he may, if he chooses, deal with them unaveraged; they are presented in our tables in such form that each reader may do as he likes about it.

6. The HAGEDOORNS consider their method of recording the young by pictures superior to ours of recording them by grades. Having employed both methods extensively, I cannot concur in their view. The picture method is satisfactory, if one is dealing with a small number of observations or those of a preliminary character only, but becomes insupportably laborious when one deals with large numbers. With such definitely localized areas of white and black as the hooded rat presents, it is easy to devise a system of standard stages or grades to guide one in classifying the animals. Even if one pictures every rat (an impossible task, when numbers are large) the day of classifying the young is only postponed thereby. Sooner or later some classification must be made, if quantitative variation is to receive any consideration whatever, if only into the HAGEDOORNS' categories of "light" and "dark" hooded. Carefully prepared grades allow of more accurate description than such categories, and may subsequently be dealt with statistically, unless like the HAGEDOORNS one steadfastly refuses to use such tools of investigation and insists on making all his excavations with the bare hands, scorning pick and shovel.

7. A counter criticism.

In 1911, Dr. HAGEDOORN took occasion to criticise briefly (in the Mendel Festschrift) my selection experiments with rats, referring to experiments of his own as a basis for showing the unsoundness of mine. The passage in full is as follows:—

"The experiments of Castle on the amount of black in the coat of hooded rats have been interpreted by their author to show that selection on continuous variation within a strain can shift the mean of the variation-curve. I am repeating these experiments, and as I have only bred some few hundreds I am not yet prepared to state how many genetic factors can constitute the difference between a dark rat and a light one. But I find, that selection has effect only in so far as one chooses between individuals differing in genetic constitution, but is without effect when the choice is made between individuals with the same genetic factors, but differing through the effect of non-genetic ones".

I have awaited with some curiosity, but up to this time without comment, some further account of HAGEDOORNS "few hundreds" of rats and their "genetic" and "non-genetic" factors. Spurred on by my silence and my continued adherence to the idea that selection is effective in

modifying characters which Mendelize, Dr. and Mrs. HAGEDOORN now publish their complete data. They say (page 165):

"The records, however complete, were far from giving us a clear oversight over the results so far obtained. When, however, Prof. CASTLE published his paper in the American Breeders Magazine, and thus showed still to adhere to the belief, that he had, by selection, modified a gene (or in his own words a unit-character) we thought it worth while to put the pictures of our rats together, and arrange them in pedigrees, to show clearly what selection had accomplished in the few generations we had bred."

Now what do these pictured records "show clearly"? The reader may refer to Fig. 3 and see for himself. They show first, that the "some few hundreds" of Dr. HAGEDOORN'S 1911 paper have dwindled down to 59 offspring (omitting four albinos) distributed) in the "few generations" mentioned, as follows¹):

Generation	Number of matings	Number of offspring	Remarks
P ₁	1	11	Unselected
F _{1/2} (mother of unrecorded pedigree)	1	7	
F ₁	4	26	First selection.
F _{1 1/2}	1	9	Selected son bred to mother.
P _{2 1/2}	1	6	Second selection.

Two full selections were made, the latter, however producing only a single litter of 6 young. This seems rather a slender basis for generalization on the effects of continued selection. So far as the records show anything, they support what I have stated on various occasions, that the darker individuals of a litter produce darker offspring and vice versa.

Regarding the P₁ generation the authors say "The variation in this family is discontinuous." But on referring to the pictures one may well inquire at what point the discontinuity comes in. Is it at 126, 53, 52, 51, or 48? There is no apparent break in the series of pictures as arranged in order of increasing blackness. Is there "non-genetic" blackness here which obscures the supposed discontinuity? If so, what

¹) I leave out of consideration here the three matings shown in Fig. 4, which involve in every case the "Irish" pattern and accordingly have nothing to do with the straight selection series.

is the evidence of its existence? Nothing is said about this matter subsequent to the 1911 paper. In the present paper the authors are following another clew. They adopt a gene hypothesis to account for the quantitative variation exhibited by the eleven young and their descendants. A purely statistical treatment of the series, that to the authors reprehensible method, which "concerns itself exclusively with results and absolutely neglects the causes of variation", would reveal no discontinuity here. It would arrange the animals in a series of stages of increasing blackness and would classify each animal in terms of these definite quantitative stages. Such treatment would not preclude the subsequent application to the series of any biological hypothesis one chooses to test by it. But the HAGEDOORNS will have none of this. Their vaunted analytical method begins with a preconceived idea. In 1911 it was "non-genetic factors"; today, when dealing with the same series of observations, it is a gene, which they name B. This makes the hooded rat blacker. Hence the darkest hooded rats are supposed to be homozygous for this factor, the intermediate ones heterozygous, and the lightest ones to lack it entirely.

Fortunately for this theory, the "catastrophe" which brought the HAGEDOORNS rat colony to an end, made it impossible to test the theory by breeding from the supposed homozygous recessives, the lightest hooded individuals. To have obtained from them as parents young much darker than themselves would undoubtedly have given the theory a jolt. For the authors state that on the gene hypothesis "selection in the opposite direction will never succeed in bringing the lost genes back, and therefore it would be impossible in an inbred family to bring it [the minus selected race] back to its starting-point. Still, this would be as easy, if selection in reality changed the germinal bases underlying the character in question." My own extensive experience with reference to this particular point shows that return selection from a minus selected race is as easy as progress in the opposite direction. I therefore regret that the HAGEDOORNS were not able themselves to give this matter an experimental test.

We have in America a type of scientist who does things part way, but gives the impression of full accomplishment. One of these climbed part way up a mountain not previously ascended and subsequently exhibited as evidence of his feat a photograph showing a view of the plain below as seen from the mountain. It remained for a companion later to disclose the fact that the picture was taken part way up the mountain. The same man who climbed the mountain also sought the

pole later on, and went there part way. Again it remained for others to ascertain what part of the way he had gone. His own impression seems to have been that he had gone the whole way. Expert assistance was later required to determine whether his impressions had been well founded.

Some of us who have witnessed this and other similar occurrences, and have had the bitter experience of seeing our first formed hypotheses proved false, have become sceptical about part way work and part way theories. We entertain a suspicion that the genotype theory may be a view of heredity from altogether too low and restricted a point of outlook, and prefer to climb a little higher up the mountain of investigation before we place our camera for a final panoramic view of heredity.

Bibliography.

- CASTLE, W. E., 1912: Some biological principles of animal breeding. *The American Breeders Magazine*, vol. 3, pp. 270—282.
- and JOHN C. PHILLIPS, 1914: Piebald rats and selection; an experimental test of the effectiveness of selection and of the theory of gametic purity in Mendelian crosses. Publication No. 195, Carnegie Inst. of Wash., 56 pp., 4 plates.
- HAGEDOORN, A. L., 1911: The interrelation of genetic and non-genetic factors in development. *Verh. d. naturf. Verein Brünn*, Bd. 49, pp. 1—18.
- and A. C., 1914: Studies on variation and selection. *This Zeitschrift*, Bd. 11, Heft 3, pp. 145—183.
-