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ON THE OCCURRENCE IN THE HOUSE MOUSE OF A MENDELIZING STRUCTURAL DEFECT OF THE RETINA PRODUCING BLINDNESS[1]

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Communicated March 1, 1926

In a previous report[2] the occurrence of an hereditary eye defect in the domestic mouse was briefly described and certain suggestions were made as to its nature and the possible mode of its inheritance. It was described as a "retinal abnormality" (designated in the present paper as "rodless") characterized by the absence of the visual cells (rods) the external nuclear layer, and the external molecular layer. Subsequently it has been found that, in general, the external nuclear layer is not absent entirely but may be clearly demonstrated by differential staining to be reduced to a single row of nuclei which are packed against the internal nuclear layer thus eliminating the external molecular layer. The rods are entirely lacking, as stated. The remainder of the retina is normal in appearance and there are no signs of degenerative change or pathological condition of the tissues. (See Fig. 1.)

Identification.—Because of my inability to recognize this character by external observation, it has been necessary to section a retina from each animal in the families studied, except in the case of F_1 individuals from an outcross, in which the character is never known to occur, since it behaves as a complete recessive.

Function.—On account of difficulties encountered in studying rodent behavior, elaborate apparatus and a system of education were necessary before the functional status of such an eye could be determined. An attempt was made to build up association between "light" and "safety"

as well as "dark" and "electric shock" in animals of rodless inheritance and in controls of a normal strain.

As an example of these tests it may be stated that five control animals became educated well enough to choose lighted holes 180 times in 220 trials, in which they were offered a choice between one lighted and five unlighted holes. They thus chose the lighted hole 143 times oftener than chance alone would have taken them into a lighted hole, the probable error being only 3.71. This deviation is 38.6 times the probable error and shows clearly that the control animals were enabled by sight to choose the lighted hole.

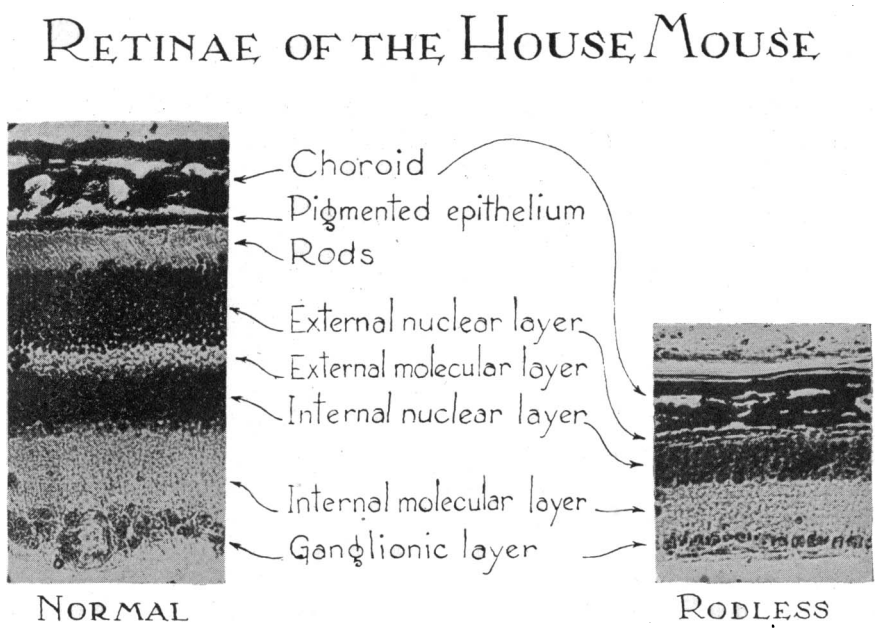

FIGURE 1

In a similar series of tests five rodless animals made 32 correct choices out of a possible 189. Since 32 is almost exactly one-sixth of 189, and in the experiments one in six of the holes was lighted, it is obvious that these animals entered the lighted hole purely by chance, their inability to see making it impossible for them to make a correct choice and thus avoid the ensuing electric shock, which normal seeing mice learned to avoid. The deviation from one-sixth is only 0.5, where the probable error, 3.37, allows for a much greater deviation through chance alone. Hence we are probably correct in assuming that this heritable structural abnormality carries with it total blindness as a functional consequence.

Sex Ratios.—Early tabulations of sex ratios are as follows:

Of homozygous rodless stock, bred *inter se*, 164 offspring were produced,

of which 86 were females and 78 were males. The deviation from the expected equality of the sexes is 4, the probable error being 4.3. Hence the sex ratio is entirely normal.

Of 125 F_2 rodless animals from crosses to normal strains, 62 were female and 63 male, again a normal sex distribution.

Back-cross rodless offspring totaling 244, consisted of 115 females and 129 males. The deviation from equality of the sexes is 7, or 1.3 times the probable error, 5.2, a result which is without statistical significance.

Accordingly everything indicates that the rodless character is neither sex-linked nor sex-limited.

Mendelizing Nature.—The early conclusion that the character is inherited as a Mendelian recessive was based on the data of a pedigree containing 31 individuals. No evidence to the contrary has been found in a population of over 2000 individuals examined since.

Viability.—In an F_2 population of 468 there were 351 normals expected and 343 found, 117 rodless expected and 125 found. The deviation is 1.2 times the probable error.

In back-cross animals totaling 511 there were expected 255.5 of each type, while 267 normals and 224 rodless were obtained. The deviation is 1.5 times the probable error, which is statistically insignificant, as are all previous deviations.

These ratios are evidently those of a Mendelizing recessive character bearing no lethal tendency.

Linkage.—Back-cross tests for linkage have been made involving albinism, dilution, brown, pink-eye, recessive spotting and agouti.

These give the following ratios of numbers of individuals in cross-over classes to numbers of individuals in non-cross-over classes:

For albinism, 26:20, dilution, 39:36; brown, 13:18; pink-eye, 17:19; recessive spotting, 26:20; agouti, 49:54. The deviations from equality are in no case significantly greater than the probable error.

A few data have been secured from tests for linkage with short-ears, kinky-tail, waltzing and dominant spotting. All results so far bespeak free segregation between rodless retina and all the characters enumerated. It is probable, therefore, that we are dealing with a character belonging to a new linkage group in mice.

Variations.—In the progeny of an outcross two other types have arisen, differing from the original abnormality in that one bears about 3 rows of nuclei in the external nuclear layer and the other about 6 rows. Strains are being established for study of the relationships involved, which suggest the possibility of modifying factors.

Embryology.—Studies upon the embryogenesis of the character have not progressed far enough to warrant the drawing of definite conclusions but the indications at present are of interest.

One is unable to recognize the character in sections of new-born mice, the development of the rodless eye not having deviated in a noticeable manner from the normal. At the thirteenth day, however, the difference is apparent. During this period in the normal animal the external and internal nuclear layers separate and the rods become differentiated. Histological examination of several series of retinae from this period would suggest that the rods are developed about the 6th day. This makes it probable that the rodless retina ceases growth about the 4th or 5th day of post-natal life.

Summary.—Summarily, it may be stated that this retinal anomaly, characterized by complete absence of rods and external molecular layer and reduction of the external nuclear layer, results in total blindness in the individual. It affects both sexes alike, breeds as a Mendelizing recessive, carries no lethal action and probably represents a new linkage group. It is possibly affected by modifying factors (as it varies quantitatively) and appears to result from a post-natal inhibition of differentiation in the nervous tissue ordinarily destined to produce the sensory receptor mechanism of the eye.

[1] Read before the Genetics Section of the American Society of Naturalists, December 28, 1925.

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VITAL STATISTICS OF THE NATIONAL ACADEMY OF SCIENCES. V. THE GROWTH OF THE ACADEMY

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Communicated March 5, 1926

The growth of the National Academy in total living membership can be ascertained by adding each year, to the living membership of the year before, the algebraic sum of the elections and deaths of the year in question. Thus, if at the end of the calendar year 1891 there were 97 members of the Academy, and during the calendar year 1892 there were 3 persons elected, and 7 persons died, the living strength of the Academy at the end of the calendar year 1892 was $97-4 = 93$. Proceeding in this manner throughout the history of the organization gives the living membership on December 31st of each calendar year. For the practical purpose of getting a picture of the manner in which the Academy has grown since its inaugura-