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AMONG YELLOW MICE.**

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ON A MODIFIED MENDELIAN RATIO AMONG YELLOW MICE. *

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In 1905 Cuénot called the attention of those interested in the experimental study of heredity to the fact that in his experiments he was unable to obtain any homozygous yellow mice. Heterozygous yellows he obtained in abundance, and found that in such animals yellow was dominant to all other color forms, including the gray color of wild house mice. This fact in itself is worthy of note, for among the rodents already experimented on, mice are the only animals in which the yellow coat dominates black or brown.

Cuénot found that in a total of 363 young obtained in yellow \times yellow crosses, 263, or 72.45 per cent., were yellow, and 100, or 27.55 per cent., were of other colors. In view of the fact that the percentage of yellows that he obtained was smaller than the Mendelian expectation by 2.55 per cent., he tested individually the breeding capacity of the yellow animals that he had obtained. In no case was he able to discover an animal which in crosses with gray or black animals would give only yellow young. But if any of the yellows had been homozygous such a result would of course have been obtained, and from the application of the ordinary Mendelian principles we should expect one third of the yellows that he tested to have been of this sort.

It is then perfectly certain that in his experiments homozygous yellows were not formed. With this in mind, he sought an explanation

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of the percentage of yellows that he had obtained. If the homozygous yellow class had simply been wanting entirely, he should have obtained 66.66 per cent. of yellow mice, and the remaining 33.33 per cent. of other colors. Cuénot explained the observed increase above 66.66 per cent. by supposing that all of the "yellow" eggs which would naturally, as a result of random unions of gametes, be fertilized by yellow sperm, fail to be so fertilized, but that some of them subsequently are fertilized by non-yellow sperm and so produce heterozygous yellow young. The proportion of yellow young produced is, accordingly, greater than two thirds but less than three fourths.

Bateson and Punnett commenting on Cuénot's results, point out the fact that even if two gametes bearing the character "yellow" are unable to unite with each other, there should, nevertheless, be no deficiency of yellow young, that is, they should equal 75 per cent. For suppose a *yellow* egg is first approached by a *yellow* sperm. If no union of the two occurs, the egg may still remain capable of producing a yellow zygote, provided it presently meets a *non-yellow* sperm. But this should in all cases be possible, since spermatozoa are regularly present in excess, and the spermatozoa of a yellow mouse are by hypothesis half yellow and half non-yellow in character.

Now the evidence which will presently be offered shows that, contrary to the idea of Cuénot as well as to the suggestion of Bateson and Punnett, the yellow egg which by chance has met a yellow sperm has its career ended thereby. It is not thereafter capable of fertilization by a non-yellow spermatozoon. So it seems probable that the homozygous yellow zygote actually is formed and then perishes, just as in the observations of Baur on an "*aurea*" race of *Antirrhinum*, the homozygous yellow seedling not only forms, but may germinate, yet for lack of assimilating power develops no further, so that all the surviving "*aureas*" are heterozygous and these are to the recessive green plants as 2:1.

In November, 1907, the writers started with a small number of yellow mice in an attempt to obtain a homozygous yellow animal. This quest was not successful, but as the numbers of animals increased and the scope of the experiment became greater, some results were obtained of a striking nature and different enough from previous results to make an extensive study of the subject advisable. Such a study has been carried on during the last two years, and up to date the young in yellow \times yellow crosses have totalled 1,235.

Of these young, as will be seen in the following table, 800 have been yellow and 435 non-yellow. This means that instead of the 75 per cent. heterozygous yellows called for by Bateson and Punnett's hypothesis, or the 72.45 per cent. obtained by Cuénot in 365 young,

there have been obtained 64.77 per cent. yellow, a deviation of only 1.23 per cent. from the 66.66 per cent. that we should expect if the homozygous yellow class is entirely absent.

The result observed by us, 64.77 per cent. yellow in 1,235 young, is a wide deviation from 75 per cent., but close enough to 66.66 per cent. to enable us to say with considerable certainty that the homozygous yellow class is entirely lacking and is not replaced by heterozygous animals of the same color.

A still more striking result is obtained by adding to the total of young obtained in the experiment above mentioned the 363 young of Cuénot's experiments. We then have 66.52 per cent. yellow young in a total of 1,598, a deviation of only 0.14 per cent. from the expected 66.66 per cent.

A table showing the progress of the experiment follows, to which is appended in similar form a statement of Cuénot's results:

Ledger No.	Yellow Young	Non-yellow Young	Total Young	Per Cent. Yellow
1 - 5,400	423	238	661	63.99
5,401 - 5,514	22	11	33	66.66
5,515 - 5,824	97	45	142	68.30
5,825 - 6,437	184	110	294	62.58
6,438 - 6,621	74	31	105	70.47
Total	800	435	1,235	64.77
Cuénot's results	263	100	363	72.45
Grand total	1,063	535	1,598	66.52

To state in another way the closeness of agreement between the expected and the observed percentages of yellow young, we may say that the ratio of 800 yellow to 435 non-yellow obtained in our experiments equals 1.943 yellow to 1.057 non-yellow, the deviation from the 2:1 ratio being 0.057. Now the theoretical "average error" in the case of a Mendelian 2:1 ratio based on the given number of observations (1,235) as calculated by Johannsen's formula (1909, p. 403) is ± 0.013 , which is slightly less than the observed error. If, however, Cuénot's totals are added to ours, the deviation from the 2:1 ratio is reduced to 0.005, while the theoretical "average error" (for 1,598 observations) is ± 0.011 . The observed deviation is therefore well within the limit of error and so points strongly to the 2:1 ratio as the true ratio.

Cuénot (1908) found that when yellow mice are mated *inter se*, smaller litters of young are obtained than when yellow mice are mated with non-yellow ones. This observation we can confirm from a study of larger numbers than were reported in Cuénot's experiments. The

averages reported by Cuénot in the respective cases, based on a careful count of 50 litters of either sort, are 3.38 and 3.74, respectively. From yellow \times yellow matings we have obtained 277 litters including 1,305 young, an average of 4.71 young to a litter. From yellow \times non-yellow matings, 325 litters have been obtained, including 1,812 young, an average of 5.57 young to a litter. These averages are considerably higher than Cuénot's indicating either a healthier stock of animals or better experimental conditions. Qualitatively, however, the results obtained in the two cases are completely in accord. The yellow \times non-yellow matings produced larger litters than the yellow \times yellow matings, but not so much larger as we should expect if homozygous yellow zygotes simply perished without otherwise affecting the character of the litter. For, in that case, the two categories of litters should be to each other in average size as 3:4, but we find that they were really as 3.38:4. The litters of yellow \times yellow parents, instead of being 25 per cent. smaller, are only 15.5 per cent. smaller than those of yellow \times non-yellow parents. In other words, when 100 pure yellow zygotes perish, they cause 38 other zygotes to develop in their stead. How can this be brought about? Cuénot supposes that some of the potential pure yellow combinations really become heterozygous yellow combinations and so swell the size of the litter. But in that case the total percentage of yellows should exceed 66.66 per cent., which it does not in our experience. We are forced, therefore, to conclude that the perishing of a pure yellow zygote makes possible the development of a certain number of *other* fertilized eggs.

Two ways may be suggested in which this might come about. First, more eggs may normally be liberated at an ovulation than there are young born subsequently. In that case, failure of some eggs to become attached to the uterus may make the chances greater that the remainder will become attached, or the perishing of some may make the chances greater that the rest will successfully complete their development. Or secondly, the production of a relatively small number of young at one birth may lead indirectly to more free ovulation subsequently, and so to the production of a larger litter at a second birth. It should be possible to test the validity of both these hypotheses experimentally.

The result here described for yellow mice, in common with that of Baur in the case of *Antirrhinum*, would seem to show that a Mendelian class may be formed and afterwards be lost by failure to develop. In other words, a physiological inability to develop may permanently modify a Mendelian ratio, causing the loss of an entire class.

As regards the matter of selective fertilization of the egg discussed by Wilson and Morgan in connection with this case, it is evident that nothing of the sort here occurs.

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