

# STUDIES ON THE SEX-RATIO AND RELATED PHENOMENA.\*

## V.—THE SEX-RATIO IN MICE, AND ITS VARIATION.

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### I. Introductory.

WITH few exceptions the long periods of gestation and immaturity associated with mammalian reproduction make mammals bad subjects for large scale breeding experiments, and it is only to be expected, therefore, that in but rare cases has the sex-ratio at birth been experimentally determined. In domestic animals our knowledge of the proportions of the sexes at birth, and of the variation in the proportions under different conditions, has largely been obtained by analyses of registration books, whilst of any † sex-ratio of wild mammals there is no accurate information available. In the captive mammals commonly used for breeding experiments (rats, mice, and rabbits), the proportions of the sexes have been determined, but, with the exception of King's<sup>8-11</sup> work on rats, usually in no great detail.

The present paper is an account of some fairly extensive breeding experiments carried out with albino mice. The

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† In any animal there is clearly a sex-ratio any time after sex is first determined. In mammals it is convenient to take conception, birth, and maturity as three salient points in the life-history at which to consider the sex-ratio of a species, and the sex-ratios at these different times are usually known as the primary, secondary, and tertiary respectively, these being the original terms used by Schultz.<sup>23</sup>

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points dealt with cover: the gross sex-ratio, seasonal variation, variation in the sex-ratio in different sizes of litter, and variation at different parities.\*

### 2. Methods.†

A word or two may be said with reference to the normal breeding methods employed in the experiments described below. The mice were left in isolated pairs, and when the doe was obviously pregnant the buck was removed. This prevented much eating of young, and also prevented the doe from becoming pregnant at the œstrous period which follows, in spite of lactation, almost immediately (six to eighteen hours) after parturition. Litters superimposed in this manner were found to be peculiar as regards sex-ratio, and would, therefore, have deranged the normal breeding experiments. Young mice for rearing were weaned at three weeks, and were themselves bred from at about ten weeks. In no case of normal breeding was a male allowed more than one fem. at a time. Polygyny was found to have a certain influence on the sex-ratio.

### 3. The Sex-Ratio in Mice.

Before stating my own results, it may be useful to quote the small amount of previous data which are available. Schultze<sup>24</sup> found approximate equality among over 1000 albino mice, and Copeman and Parsons<sup>2</sup> note that the number of males born is slightly in excess of that of females. With regard to Waltzing mice, Yerkes<sup>21</sup> states that the sexes appear in about equal numbers. It is probable that of these statements only Schultze's has a sufficient experimental basis.

I am indebted to Mr Darling, of the Midland Agricultural College, for the information that in 255 white mice bred by him under normal conditions the sex-ratio was 133.8. My own mice breeding records show that of the 1031 mice bred under normal conditions, 558 were males and 473 were females, a sex-ratio of 118.0. These figures do not include any results

\* "Parity" is a convenient expression for the chronological number of the pregnancy: an obstetric corruption of the suffix found in "primipara," "multipara," etc.

† The work recorded in this paper was carried out in the Zoological Dept., University of Manchester.

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of special experiments (polygyny, superfœtation, dieting, in-breeding, etc.) which were carried on at the same time, and as the numbers are reasonably extensive, the ratio 118.0 must represent something very near the proportions of the sexes at birth in the stock of mice used for these experiments.

Schultze's experiments, the only others conducted on a reasonably large scale, gave a much less proportion of males than this. The reason for this discrepancy is difficult to see, but it would seem that the sex-ratio of different stocks of mice in different places can vary considerably.

The results may now be analysed from different points of view.

### 4. Seasonal Variation.

It may be supposed that the reproductive vigour of the animal is at its maximum during the breeding season, and it is, therefore, of interest to compare the sex-ratio of births resulting from conceptions which take place in the height of the breeding season with the products of extra-breeding season conceptions. In mammals which breed all the year round this comparison is readily made, because the true breeding season is usually easily discernible, but in mammals where breeding is restricted to the breeding season, the periods compared may be the beginning, middle, and end of the breeding season. I know of no existing data relating to the seasonal variation in the sex-ratio of albino mice, but reference may be made to one or two cases of other mammals.

In man, social conditions have to a great extent obliterated all traces of the primitive breeding season, but there is ample evidence (for detailed argument and references, see Marshall<sup>4</sup>) that one did exist. Actually, the human birth-rate does show a slight seasonal variation, and the sex-ratio has a tendency to vary inversely—to be low for births resulting from conceptions at the season of greatest fecundity, and high at times of lowest birth-rate.<sup>6</sup> It is of interest to note that this feature is much more pronounced in illegitimate births. In Cuba, Heape<sup>7</sup> found a similar thing to exist for both the black and the white population, though the inverse variation between fecundity

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and sex-ratio was much more strongly defined in the black races.

In dogs, Heape<sup>6</sup> found very considerable seasonal variation in the birth-rate, and also that in months of high birth-rate the sex-ratio was much lower than in months of low birth-rate. In fact, for Greyhounds, nearly two males to every female were produced during the months of November and December, when the birth-rate was at its lowest.

In pigs there is little evidence that the seasonal variation in the birth-rate, which is very pronounced, is correlated with any significant variation in the sex-ratio.<sup>18</sup>

Turning to rodents, we have King's<sup>9</sup> very extensive breeding experiments with rats, to show that the sex-ratio is lowest when the reproductive vigour is at its height in March-April-May.

In view of the widespread connection between breeding season and sex-ratio in mammals, I awaited with some interest the result of the analysis of my mice breeding records. In this particular case the birth-rate is no criterion of the breeding season, owing to the fact that the number of breeding pairs was not constant. The animals, however, started to breed in March, and there can be little doubt that this time is the beginning of the breeding season, the height of which is reached in May or June.

The following table shows the monthly sex-ratio from April to October :—

TABLE I.  
*Seasonal Sex-Ratio in Mice.*

Month.	Births.		Sex-ratio.	Percentage of Males with probable Error.
	Males.	Females.		
March . . . .	12	13	...	} 49.7 ± 1.78
April . . . .	42	40	105.0	
May . . . .	44	46	95.7	
June . . . .	78	79	98.8	
July . . . .	88	75	117.4	} 56.5 ± 1.27
August . . . .	138	93	148.5	
September . . . .	100	87	115.0	
October . . . .	56	40	140.0	
Total . . . .	558	473	118.0	54.2 ± 1.04

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A graph will conveniently illustrate this table :—

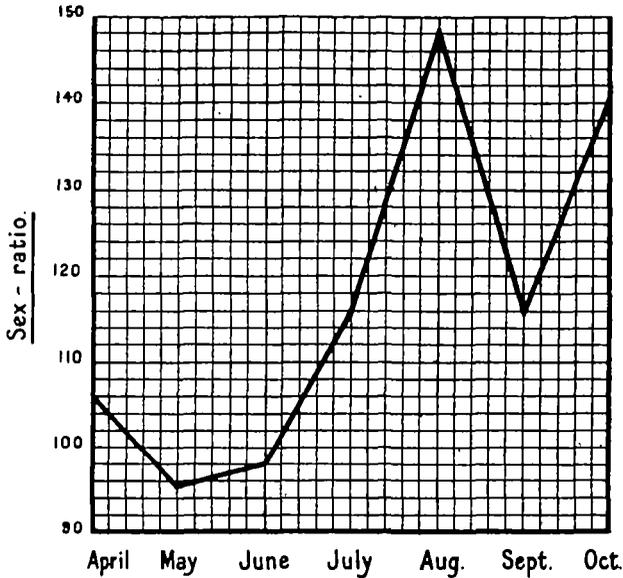


FIG. 1.—Seasonal Sex-Ratio in Mice.

The sex-ratio at the height of the breeding season is thus significantly lower than later, and this result is quite in keeping with the experimental and statistical work which has been cited relating to the seasonal variation in the sex-ratio of mammals.

### 5. Variation according to Size of Litter.

It is difficult to suppose that the size of litter in ordinarily polytocous animals can have any definite or constant effect on the sex-ratio, and though data in mice seem to have been hitherto lacking, work on other mammals suggests no constant relationship. Multiple births in animals which are normally monotocous are obviously peculiar, and have, in fact, a peculiar sex-ratio,<sup>26</sup> but such cases are not referred to in the present paper.

Wentworth,<sup>26</sup> working on dogs and pigs, found no relationship between litter size and sex-ratio, a conclusion also arrived at by King<sup>9</sup> for rats, and Parker and Bullard,<sup>16</sup> and also Machens<sup>18</sup> for pigs. Some work of my own on pigs<sup>19</sup> seemed to suggest that the average

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sized litters have a lower sex-ratio than extreme sizes, but the connection was only loose, and fuller statistics<sup>20</sup> have not confirmed this view.

My mice records bearing on this point are summed up in the following table:—

TABLE II.

*Sex-Ratio and Litter Size in Mice.*

Size of Litter.	Number of Litters.	Number of Mice.	Sexes.		Percentage of Total Litters.	Sex-ratio.	Percentage of Males with probable Error.
			Males.	Females.			
1	3	3	1	2	19.75	41 ♂	45.5 ± 3.53
2	8	16	6	10		49 ♀	
3	9	27	13	14		= 83.7	
4	11	44	21	23			
5	9	45	25	20	62.98	369 ♂	54.6 ± 1.28
6	32	192	105	87		306 ♀	
7	26	182	97	85		= 120.5	
8	32	256	142	114			
9	12	108	59	49	17.27	148 ♂	55.6 ± 2.05
10	8	80	42	38		118 ♀	
11	6	66	41	25			
12	1	12	6	6		= 125.4	
Total	157	1031	558	473	100	118.0	54.2 ± 1.04

The numbers occurring at each litter size are not large enough to give a sex-ratio of any value, so the results are analysed in the above table in three groups, litter sizes 1 to 4, 5 to 8, and 9 to 12; the aggregates in each group amounting to workable numbers. At the same time the percentage of the total litters occurring in each group is given in order that the relative frequency may be seen. Group 5 to 8 includes nearly two-thirds of the total litters and, therefore, includes all the average sizes of litters. This correlates well with the fact that in this group the sex-ratio is very near the over-all average of 118.0. The extreme groups, 1 to 4 and 9 to 12, each comprise little more than one-sixth of the total litters, and clearly contain mostly atypical sizes of litters. The sex-ratio of group 1 to 4, 83.7, is significantly abnormal, while that of group 9 to 12 is less so at 125.4.

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These results give rise to the suggestion that the sex-ratio increases with litter size, but such a conclusion is probably misleading, and the question will be discussed later.

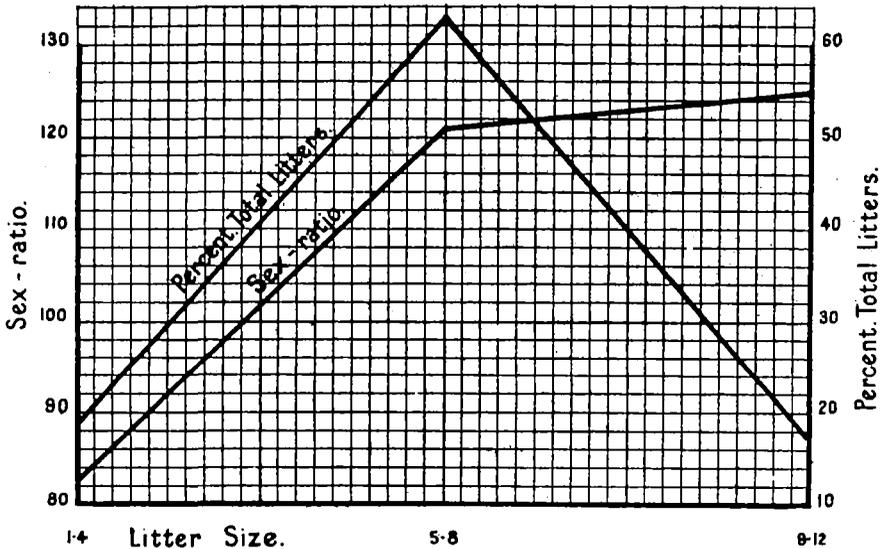


FIG. 2.—Sex-ratio and Litter Size in Mice.

### 6. Variation according to Parity.

A correlation of the sex-ratio at birth with the number of the pregnancy has many times been noted for man, where a continuous drop in the sex-ratio at each succeeding pregnancy is found.<sup>4, 5, 13, 15, 22</sup>

King<sup>9</sup> found the same sort of thing to obtain in rats, and in mice, with which we are specially concerned in this paper, Copeman and Parsons<sup>2</sup> say that the proportion of males is greater in first births than in subsequent ones.

My own mice records are incomplete on this point, owing to the fact that I did not immediately begin to note the parity. I have, however, records of about 400 animals, and these work out as shown in Table III.

The very high total sex-ratio is accounted for by the fact that the particular births in which the parity was noted largely occurred in the second half of the breeding season (see section on variation of the sex-ratio during the breeding season). Even so, however, the variation between first and

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subsequent births though barely significant is in the opposite direction to Copeman and Parson's results, and opposite to what we know to happen in other mammals. It is probable, however, that this result is accounted for by the fact that most of the second and higher births occurred right at the end of the breeding season when the sex-ratio is at its highest. All things considered, these particular data relating to sex-ratio parity are somewhat unsatisfactory, and this experiment stands in need of repetition.

TABLE III.  
*Sex-Ratio and Parity in Mice.*

	Totals.	Sexes.		Sex-ratio.	Percentage of Males with probable Errors.
		Males.	Females.		
First births . . .	242	134	108	124.2	55.4 ± 2.14
Subsequent births .	190	114	76	150.0	60.0 ± 2.39
Total . . .	432	248	184	134.9	57.3 ± 1.60

### 7. Discussion.

In all considerations of the variation in the sex-ratio at birth, whether it is variation between species or in different cases of the same species, it is essential to consider the question in the light of the two factors which govern the sex-ratio at birth, namely:—

- (a) The sex-ratio at conception.
- (b) The amount and sex-incidence of the mortality occurring before birth.

Variation in the sex-ratio at birth can clearly be the product of variation in either or both of these, and as determinants of the proportions of the sexes at birth they merit some little attention. In mammals it is almost certain that pre-natal mortality falls preponderatingly upon the males, and in mice this is undoubtedly the case.<sup>17</sup> This means that if there is an excess of males at birth there must have been an even greater excess at conception, and as from the chromosome theory it would be expected that the sexes would be conceived in equal numbers, this fact needs explanation. Most probably

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the quantitative differentiation which exists between the X- and Y-spermatozoa in many mammals—mouse, rat, man,<sup>21</sup> dog,<sup>22</sup> horse, bull, and pig<sup>28, 29, 30</sup>—supplies this.

The constant difference between the sex-ratio of different species presents a problem of some magnitude, but it is improbable that it is caused by a constant difference in the amount of pre-natal mortality, and this leaves as a source of the difference the second factor, the ratio at conception. If, as is most probably the case, this ratio depends on the differential mobility and vitality of the X- and Y-spermatozoa, it may be supposed that owing to the amount of difference between the two types of spermatozoa varying in different species, the result of this difference, the disproportion of the sexes at conception, may also vary. That is to say, in cases where the Y-spermatozoon is only very slightly smaller and lighter than the X-spermatozoon, it will not have so great an advantage as in cases where it is much smaller and lighter, and consequently the excess of males at conception will be less.

The question of seasonal variation may be approached in the same manner. Düsing<sup>5</sup> contended that there was some seasonal variation in the amount of pre-natal mortality,\* but later observers, Davis,<sup>3</sup> Sozinskey,<sup>25</sup> and Whipple,<sup>27</sup> have contradicted this. In any case it seems that there is no appreciable seasonal variation. This factor, therefore, may be ruled out as causing the seasonal variation in the secondary sex-ratio. I suggest that this variation originates in variation in the proportions of the sexes at conception. In animals with a marked breeding season, the spermatozoa must towards the end be matured in comparatively unfavourable conditions, and such conditions very likely have a greater lethal effect on the apparently less hardy X-spermatozoa than on the apparently more hardy Y-spermatozoa.

Turning to the size of litter records, the results must be analysed in the light of the two factors which govern the size of litter, namely, the number of ova ovulated and the amount of mortality between conception and birth. It will be seen at once that the number of ova fertilised can hardly affect the

\* The only data of seasonal variation in the amount of pre-natal death relate to still-births, but, as shown elsewhere,<sup>15</sup> these are strictly comparable with earlier mortality.

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sex-ratio at birth, whereas the amount of mortality during gestation certainly does.

The very low sex-ratio of mouse litters of 1 to 4 is, I think, explained by the supposition that such small litters must have been depleted by heavy pre-natal mortality. I am at present investigating this point by corpora lutea counts, but I may mention here that on one occasion I examined a rabbit in which there were only two normal foetuses and one atrophic one, whereas the corpora lutea numbered eleven. Since ovulation is not spontaneous in the rabbit this discrepancy could hardly have been caused by non-fertilisation of the ova, and, since the case occurred right at the beginning of the breeding season, corpora from a previous pregnancy could scarcely have been present (see also <sup>17</sup>). I judge that the same kind of thing happened in the case of the abnormally small litters of mice, and if so the very low sex-ratio associated with such litters would be accounted for. In the same way, the abnormally large litters can have been subjected to but little pre-natal mortality (the number of ova ovulated rarely seems to be more than twelve or fourteen), and the consequent conservation of males would produce the high sex-ratio apparently characteristic of such litters.

It was mentioned above that investigations on sex-ratio and litter size in other mammals have given no results. These other investigations, however, seem to have all been statistical analyses of herd and stud books, to which, it may safely be said, records of very abnormally sized litters do not find their way. A pig-breeder, for instance, does not advertise the fact that his pigs produce litters of two and three, and when very large litters are produced the least promising are usually killed immediately without being recorded, so that the sow may rear the rest comfortably. As the clue to the connection between sex-ratio and litter size has to be sought in the extreme sizes of litters, pig records and records of other commercial animals form but poor material for the elucidation of this subject, and the negative and erratic results obtained in such cases are readily understandable.

Lastly, the nature of the influence of the parity on the sex-ratio may be discussed. The number of the pregnancy

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appertains solely to the female, and the connection between the sex-ratio at birth and the parity has often been used as evidence against the chromosome theory, which, in mammals, relegates sex heterozygosity to the male. It has, however, been shown almost conclusively<sup>18</sup> that in man the variation of the sex-ratio at different parities is brought about by variation in the amount of selective post-conceptual elimination of fœtuses, and not by influence exerted at fertilisation. Whether this is the same in other mammals is not yet certain, but in view of the similarity in different mammals of many phenomena of reproduction, the probability is that it will be found to be so.

Possible explanations of all the results described above have now been made, and, while the explanations cannot in all cases be said to have the authenticity of the experimental facts described in the other sections of the paper, it may be hoped that the discussion of possibilities has not failed to serve some useful purpose.

### 8. Summary.

(1) The sex-ratio of over 1000 albino mice born in 157 litters worked out at 118 males per 100 females. In the records which I was able to secure of 255 other mice the ratio was 133.8.

Both these ratios are above other experimental determinations of the sex-ratio in mice.

(2) The seasonal variation in the new breeding records here presented is quite in keeping with work on other mammals, *i.e.* the ratio is lowest in the height of the breeding season and highest at the extreme end.

(3) The data relating to size of litter and sex-ratio show that abnormally small litters have a very low ratio compared with the average, and that abnormally large litters have a sex-ratio rather higher than the average.

(4) The sex-ratio is known in some cases to fall with each successive pregnancy, but in the present case the ratio of first births is lower than in subsequent ones.

(5) The interpretation of these facts, on the dual basis of the chromosome theory of sex determination and the sexually selective pre-natal mortality which is known to occur, is attempted.

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