FERTILITY IN MICE.*

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CONTENTS.

1. Introductory.

In spite of the convenience of mice for breeding experiments no particular note seems to have been taken of the fertility of this mammal. The comparatively short periods of immaturity and gestation and the capacity for continuous breeding which characterise mice give an enormous potential fecundity. In practice, however, limiting factors step in, and their theoretical capacity is rarely attained. The question of fecundity and its limitations by various forms of sterility is not touched upon in this note; the data which are presented relate only to the size of litter under normal and various abnormal conditions, and to the factors which govern the number of young born.

2. Data on Fertility in Mice.

Information about the normal litter size in the mouse is not plentiful. As regards its near relative, the rat, data is more abundant and six to seven appears to be the normal size of litter. Such authors as have recorded the litter size in mice have usually paid little special attention to the problem, and their records are too few to be of much service in arriving at a proper idea of the fertility of the species. There are, however, one or two papers which deal with this special point. Prof. Karl Pearson,[8] in his analysis of W. R. F. Weldon's mice records from the point of view of the inherit-

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ance of the sex-ratio, found that the average fertility was 5.65 young per litter. Sumner,[7] Kirkham,[2-8] and Daniel,[1] though all giving the size of a few litters, record no extensive data. Considerable material is given by Robertson and Ray,[6] who state that in their breeding experiments 1242 animals were produced in 241 litters, giving an average size of 5.15. Further, these authors found that the standard deviation of the frequency distribution was 2.2.

Having briefly mentioned existing records, my own data may be discussed.

Normal Litter Size.—The data for normal breeding include details of 1795 mice born in 267 litters, giving an average of 6.72 per litter. The actual frequency distribution is as follows :—

TABLE I.—*Frequency Distribution of Litter Size.*

Size of Litter.	Number of Litters.	Number of Young.
1	5	5
2	13	26
3	16	48
4	17	68
5	19	95
6	50	300
7	41	287
8	48	384
9	22	198
10	19	190
11	13	143
12	2	24
13	1	13
14	1	14
Total	267	1795

A frequency polygon (Fig. 1, p. 23) conveniently represents this distribution.

These records show that litters of 6, 7, and 8 are the most frequent. Indeed, these three sizes of litters account for 139 of the 267 litters under discussion, a percentage of 52.1. Of the rest, 58 (21.7 per cent.) are of larger size, and 70 (26.2 per cent.) smaller. This grouping round the average sizes is well brought out by the fact that the standard deviation of the frequency distribution is only 2.5.

As further analysis of the normal average size of litter, a number of pregnant mice were dissected to see how the

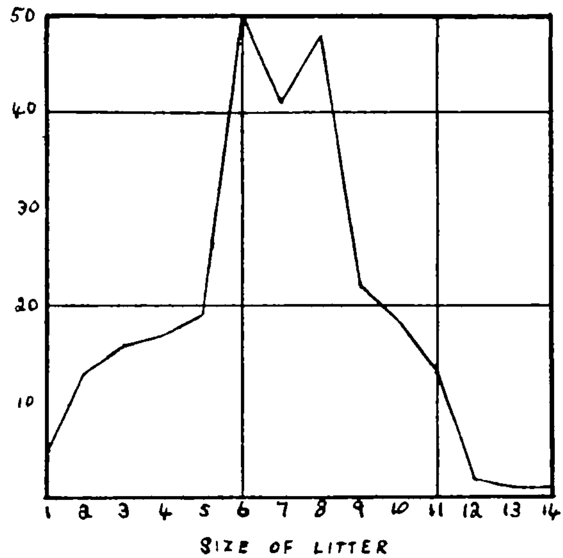

FIG. 1.—Frequency Polygon for Size of Litter.

fœtuses were distributed between the two cornua of the uterus. Table II. gives the results of these dissections :—

TABLE II.—*Distribution of Fœtuses between the two Cornua of the Uterus.*

Mating Number.	Number.	Right Cornu.	Left Cornu.
109	9	5	4
113	12	5	7
124*a*	10	6	4
137	8	4	4
138*a*	11	5	6
166	8	2	6
185	8	6	2
225	6	2	4
B.S. II.	11	6	5
448	7	2	5
475	13	6	7
480	12	7	5
485	1	1	0
Total (13)	116	57	59
Percentage	100	49·2	50·8

The average size of these litters works out at 8.9, which is much higher than the general average. The reason for this is that the mice picked out for dissection were those which were very obviously pregnant, and this, of course, meant a certain amount of selection in the direction of large litters. In spite of this, however, there is no reason why these litters should not give a true idea of the distribution of the fœtuses between the two cornua, and it is evident that as far as these results go, the left and right sides of the female genital apparatus show little or no difference in their capacity for developing fœtuses. In the absence of contradictory material it may be concluded, therefore, that the cornua play very equal parts in the production of a litter.

Seasonal Variation.—The seasonal variation in fertility is shown in the following table:—

TABLE III.—*Seasonal Variation in Fertility.*

	Number of Litters.	Number of Young.	Average Size of Litter.
January	10	61	6·1
February	18	113	6·3
March	5	25	5·0
April	16	91	5·7
May	14	100	7·1
June	29	187	6·4
July	39	296	7·6
August	51	384	7·5
September	42	260	6·2
October	25	153	6·1
November	4	29	7·2
December	14	96	6·9
Total	267	1795	6·72

As such these figures are erratic, but when grouped into three-month periods a greater coherence is found:—

TABLE IV.—*Seasonal Fertility of Three-Month Periods.*

Period.	Number of Litters.	Number of Mice.	Average Size of Litter.
January to March	33	199	6·03
April to June	59	378	6·40
July to September	132	940	7·12
October to December	43	278	6·45
Total	267	1795	6·72

This table may be expressed graphically :—

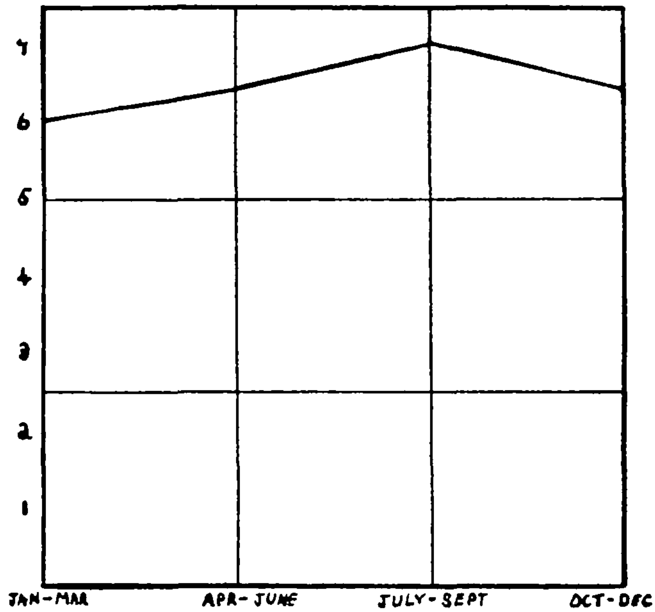

FIG. 2.—Seasonal Fertility in Mice.

These results indicate that the highest fertility is attained at the end of the summer, but at the same time there is no great variation and any great significance can not be attached to these figures. What they do show is that under laboratory management mice show good fertility all the year round.

If, as is most probable, normal seasonal variation in fertility is an environmental effect, the artificial maintenance of approximately constant conditions in which these experimental animals were finally kept is probably adequate explanation of this result.

Parity.*—The influence of parity upon fertility is shown in the following table :—

TABLE V.—*Parity and Size of Litter.*

Parity.	Number of Mice.	Number of Litters.	Average Size of Litter.
1	504	81	6·2
2	191	25	7·6
3	171	27	6·3
3 and over	191	31	6·2
Total	1057	164	6·5

* A convenient expression for the chronological number of the pregnancy.

These results show that what might be expected, namely, that the second litters are largest, and that after the second the average size decreases again.

Influence of Concurrent Lactation.—Mice will become pregnant at the œstrus period which follows within eighteen hours of parturition, and the fertility of these litters developed during the lactation of the previous litter is of interest from several points of view.

The data bearing on this point give the following results :—

TABLE VI.—*Size of Litter produced during Lactation.*

Size of Litter.	Number of Litters.	Number of Young.
2	4	8
3	1	3
4	1	4
5	2	10
6	7	42
7	6	42
8	3	24
9	3	27
10	1	10
11	2	22
Total	30	192

This gives an average size of litter of 6.4, which is slightly lower than that found for normal matings.

Polygyny.—In polygynous matings the size of the litter was found to be very near normal :—

TABLE VII.—*Size of Litter in Polygynous Matings.*

Size of Litter.	Number of Litters.	Number of Young.
2	2	4
3	2	6
4	3	13
5	4	20
6	5	30
7	10	70
8	5	40
9	1	9
10	2	20
11	1	11
12	...	...
13	1	13
Total	36	236

These litters have an average size of just over 6.5.

3. Discussion.

Any consideration of fertility and variation in fertility must be based on the factors which govern the number of young at birth.

Looked at in the widest manner complete sterility may be due to:—

(1) Inability of the adult organisms to produce gametes.
(2) Inability of the adults to effect fertilisation.
(3) Inability of the mother to carry the young through a period of gestation.

For purposes of discussion these three types of sterility may be respectively called (1) primary, (2) secondary, (3) tertiary. Since, however, the real object of this paper is not to discuss complete sterility, but to consider limitations to fertility, it is clear that these factors must be examined rather more closely. Decreased fertility may be due to:—

(1) Decrease in the number of gametes produced. In practice this is limited to the female, because if the male is capable of producing spermatozoa at all, they are usually produced in numbers sufficient to ensure the largest litter which can be borne by the female.
(2) The mortality during gestation becoming larger, even if not total.

The causes of secondary sterility hardly arise as causes of slightly decreased fertility, because where fertilisation can be effected at all a large litter can, other things being equal, be conceived as well as a small one. The two factors which govern fertility are normally, therefore:—

(1) The number of ova ovulated.
(2) The amount of pre-natal mortality.

The approximate number of ova ovulated is normally a function of the particular species in question. In the horse, the cow, and the human subject one is the rule. The dog and the cat produce about 3 to 5, the rabbit, rat, and mouse 5 to 10, whilst the pig is probably the most prolific with 8 to 15 at an ovulation. Nevertheless, great individual variation occurs, though the extreme sizes are aberrant in each case, and the standard deviation from the mean would, I think, be found not to be great if sufficient corpora lutea counts could be made to complete a frequency distribution.

In counts made for eight mice litters the corpora lutea totalled 82, an average of 10.2. Here again, as in the work on the distribution of fœtuses, this cannot be taken as an average for the number of corpora lutea, because only mice which were obviously pregnant were dissected and this tended towards selection in the direction of large litters. Hence, when compared with the average size of litter at birth the difference cannot be entirely put down to fœtal mortality. By comparing the individual counts, however, with the individual litter sizes at birth a mortality percentage of 9.8 was arrived at (Parkes [4]).* In other mammals prenatal mortality, whether resulting in re-absorption or in abortion, is known to be, on occasions, much greater than this, and it is clear that high initial fertility at conception may be very much lowered by the time of birth, in exactly the same way as good fertility at birth may be discounted from the point of view of specific survival by a high mortality during early life.

The factors which govern the number of eggs ovulated are, as pointed out above, primarily specific; but it is also clear that strains showing low and high fertility occur in one species, and this fact points to an hereditary factor in individual fertility. In addition, there is the necessity for good nutrition, without which the most potentially prolific ovary will fail to function to the full.

The factors controlling the amount of prenatal mortality are little known, and in the present state of the knowledge of the subject little good can be done by discussion. A brief mention of the possible causes of prenatal mortality may be found in a previous paper (Parkes [4]).

Since there are two known factors governing the size of litter at birth, variation in fertility at birth may be the product of variation in either of these factors, *i.e.* variation in the number of eggs ovulated, or variation in the amount of pre-

* This calculation involved the assumption that all eggs ovulated are fertilised. The validity of this assumption is considered in the paper referred to above.

natal mortality. If both of these vary together, the variation may be cumulative or compensating. For instance, high initial fertility may be discounted by a high rate of mortality during gestation, and a low initial fertility may be mitigated by a low mortality. High initial fertility, on the other hand, is accentuated by low mortality, and low initial fertility is accentuated by a high mortality.

The variations described above may now be considered in the light of these premises.

In wild mice the breeding season is limited to the summer months, and it might be expected, therefore, that their cultivated relations, albino mice, would show the greatest fertility at the time of year corresponding to the primitive breeding season. This appears to be so in so far as mice kept in quarters where the temperature is not regulated only breed during the summer, but while they are breeding the size of litter does not show any great variation. My original mouse room had no arrangements for maintaining an equitable temperature during the cold weather, and from November to February no litters were born. In March the average size of litter was 5.0, and in September and October just over 6, as against the July average of 8.2. On removal, however, to quarters where the temperature could be kept regularly between 55° F. and 65° F. the animals bred throughout the winter with a fertility very little below the average. In other respects, food, etc., conditions were identical, and there appears to be strong ground for believing that the cessation of breeding during the winter months was a temperature effect, and that a similar explanation covers the rise in fertility during the summer. There is little evidence of seasonal variation in the amount of fœtal mortality in any species of mammal (for discussion see Parkes[6]), and the small seasonal variations in litter size found undoubtedly arise from variations in the initial fertility at ovulation.

The results relating to the influence of parity on fertility agree with what is known of other mammals, including man, *i.e.* that the female is most fertile in the first part of the period of full maturity. It has not yet been experimentally determined for mice whether this variation is due to alteration of the number of ova produced or to difference in the amount of fœtal mortality, but, if an analogy may be made with the human female, it may be supposed that the latter factor does at least play a part in determining the fertility at different parities.

In a previous paper[4] it has been shown that the mortality in gestations which are concurrent with lactation may be as much as double the normal, and this would appear to be an adequate explanation of the smaller size of litter found in such cases. In fact, the very small decrease in the size of litter does not seem to reflect adequately the greater mortality, and it is not improbable that the number of eggs ovulated at the immediate post-partum œstrus is slightly greater than normal. It has been impracticable, however, to actually investigate this point owing to difficulty of obtaining fair samples of pregnant animals—even a careful watch often fails to detect pregnancies with only one or two fœtuses.

It has been mentioned above that it would be supposed that normally the male has little influence on the size of litter; he is usually capable of producing a full-size litter or is sterile. This being so, therefore, it was not to be expected that polygyny would have any very remarkable effect on fertility, and the average fertility, 6.5, of 36 polygynous litters is not much below the normal average, any difference being easily accounted for by the slightly inferior conditions under which polygynous animals unavoidably live.

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4. Summary.

1. The average size of 267 litters of albino mice totalling 1795 animals was 6.72; in addition, the distribution of fertility between the two cornua of the uterus was found to be very even.

2. Seasonal variation in fertility was found to be slightly in favour of the summer months. Without artificially maintaining an optimum temperature, the mice were found not to breed in the months November to February.

3. Of consecutive pregnancies the second was found to produce the largest number of young, while concurrent lactation was found to decrease the size of litter, as also, to a lesser degree, did polygyny.

4. The interpretation of these results is attempted in the light of the two factors which govern the size of litter at birth, *i.e.* the number of ova ovulated and the amount of prenatal mortality.

5. References.

[1] Daniel (1910), "Observations on the Period of Gestation in White Mice," *Journ. Exp. Zool.*, **9**.

[2] Kirkham (1916-17), "Prolonged Gestation Period in Suckling Mice," *Anat. Rec.*, **11**.

[3] Kirkham (1918), "Observations on the Relation between Suckling and the Rate of Embryonic Development in Mice," *Journ. Exp. Zool.*, **27**.

[4] Parkes (1923), "Studies on the Sex-ratio and Related Phenomena. (1) Fœtal Retrogression in Mice," *Proc. Roy. Soc.*, B., **95**.

[5] Parkes (1924), "Studies on the Sex-ratio and Related Phenomena. (5) The Sex-ratio in Mice and its Variations," *Brit. Journ. Exp. Biol.*, **1**.

[6] Robertson and Ray (1916), "Experimental Studies on Growth. II. The Normal Growth of the White Mouse," *Journ. Biol. Chem.*, **24**.

[7] Sumner (1916), "Superfetation and Deferred Fertilisation among Mice," *Biol. Bull.*, **30**.

[8] Weldon (1906-7), "On Heredity in Mice from the Records of the late W. R. F. Weldon. Pt. I. On the Inheritance of the Sex-ratio and the Size of Litter," *Biometrica*, **5**.