ANALYSIS OF DIFFERENCES IN THE NUMBERS OF EGGS SHED BY THE TWO OVARIES OF MICE DURING NATURAL OESTRUS OR AFTER SUPEROVULATION

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Summary. The variation in the number of eggs shed by the two ovaries of mice has been examined by statistical analyses of 697 egg counts and 390 corpora lutea counts, made on mice from a variety of outbred strains, both after natural oestrus and after oestrus induced in adults by pregnant mares’ serum (PMS) and human chorionic gonadotrophin (HCG). The numbers of eggs or corpora lutea were distributed between sides approximately at random, the variation conforming fairly closely to a binomial distribution. This was true even after superovulation. There was, however, a slight but significant excess of variation between sides over the random amount in the egg counts, particularly after natural ovulation. Corpora lutea counts differed from egg counts in showing a slight but significant reduction of the variation below the random amount. Several possible reasons for these small deviations from a random distribution are discussed.

The correlation between the numbers of eggs shed by the two ovaries was negative after natural ovulation but positive after superovulation. This difference can be fully accounted for by the random distribution between sides together with the differences of mean and variance between natural ovulation and superovulation. The variation of total egg number was proportional to the mean egg number after natural ovulation. The variation after superovulation was much higher than after natural ovulation, even when the difference of mean was taken into account, and the greater variation of total egg number caused the correlation between sides to be positive after superovulation.

INTRODUCTION

It is a curious, though familiar, fact that the numbers of eggs shed by left and right ovaries of naturally ovulating mice are negatively correlated. That is to

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say, if a mouse sheds fewer than average on one side it is likely to shed more than
average on the other. This fact has been noted by several investigators who
have counted mouse eggs or corpora lutea (e.g. Danforth & de Aberle, 1928;
Hollander & Strong, 1950; Bowman & Roberts, 1958), and it is also true of
rabbits (Adams, 1959) and of guinea-pigs (Eckstein & McKeown, 1955). In
contrast, there is a positive correlation between the numbers of eggs shed by
the two ovaries of mice after induced superovulation (Fowler & Edwards,
unpublished). No one seems to have examined the nature of the correlations,
nor considered what light they may throw on the physiological mechanisms of
ovulation. This is the purpose of the present paper.

The numbers of eggs shed at one oestrus have been shown to be randomly
distributed between the two ovaries in mice and several other species (see
Brambell, 1956). We shall examine the distribution between the two ovaries of
mice in more detail than has been done before, and consider how the correlation
between sides is related to this distribution after both natural ovulation and
induced superovulation. If the distribution of eggs is random, the numbers shed
by each ovary will conform to the expectations of a binomial distribution. A
binomial distribution with respect to the numbers of eggs shed by the left and
right ovaries respectively, means that each egg has a certain probability of
having been shed by, say, the left ovary, and this probability is the same for all
the eggs shed at that oestrus; whatever the physiological mechanism is that
determines the total number of eggs shed at any one oestrus, the ovary from
which each egg is shed is a matter purely of chance.

SOURCES OF DATA

Natural mating was judged by the presence of a vaginal plug. Eggs were
counted on the morning that the vaginal plug was found, by dissection of the
Fallopian tubes. Eggs from mice given superovulation treatments were counted in
the same way, ovulation having been induced by an intraperitoneal injection
(on the right side) of varying doses of pregnant mares’ serum (PMS) followed
after 40 hr by human chorionic gonadotrophin (HCG) (Fowler & Edwards,
1957). Corpora lutea were counted by dissection of the ovaries of pregnant
females, most of them at 16 to 17 days after the vaginal plug, but a few at
earlier stages. All mice were adult and were between 6 and 14 weeks of age.

The data comprise 697 mice counted for eggs and 390 counted for corpora
lutea. The mice came from nine distinct outbred strains and some partially
inbred and crossbred mice derived from them. The designations and character-
istics of the strains are as follows:

NF, NS, NC: selected for large body weight, for small body weight and an
unselected control, respectively, all derived from the same base (Falconer,

CFL, CFS, CRL: selected respectively for high and low 3- to 6-week growth
on normal diet and for high growth on restricted diet, all derived from the same
base (Falconer, 1960a).

JH, JL, JC: selected for large and small litter size and an unselected control,
all derived from the same base as the three ‘C-strains’ above (Falconer, 1955, 1960b).

In addition there were the following miscellaneous groups, all derived from the ‘J-strains’ or the same base, designated for reference in this paper as follows:

JB: crosses between partially inbred lines.
JR: various partially inbred and crossbred mice. ‘Series I’ of Falconer & Roberts (1960).
JF: various partially inbred and non-inbred mice. ‘Series II and III’ of Falconer & Roberts (1960).

Where the strains are referred to separately in the Tables, the generations from which the mice were derived are given in brackets, and the observer who did the counting is indicated by initials. The doses of pms given to induce super-ovulation are also shown.

METHODS OF ANALYSIS AND RESULTS

COMPARISON OF LEFT AND RIGHT OVARIES

It is necessary first to find out if the two ovaries shed on the average the same number of eggs, or if there is any overall bias towards the left or right side. Only some of the data can be used for this purpose because in the remainder, though the two ovaries were recorded separately, the left and right sides were not distinguished. The data given in Table 1 come from natural mating in JH, JL and JC (Generations 16, 17, 32, 33), JR and JF. Differences between strains were trivial and the strains are combined in the table. The counts of eggs and of corpora lutea are shown separately, though they gave almost exactly the same result. There is also a smaller amount of data from egg counts in the NF, NC and CFS strains following superovulation, and these gave the same result as natural ovulation. Taken all together, the data show a very slight bias in favour of the right ovary, which yielded 51.65% of all eggs or corpora lutea. The $\chi^2$ testing deviation from 50% is 3.81, which is on the border of significance at the 5% level. The slight bias is therefore probably real. But even if real, the difference from equality is too small to make any appreciable difference to the expectations based on equality. In the analyses that follow, therefore, the overall ratio of left to right is taken to be 50%.

<table>
<thead>
<tr>
<th></th>
<th>No. eggs or corpora lutea</th>
<th>No. eggs or corpora lutea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. mice</td>
<td>Left</td>
</tr>
<tr>
<td>Natural ovulation</td>
<td>159</td>
<td>801</td>
</tr>
<tr>
<td>Eggs</td>
<td>286</td>
<td>1434</td>
</tr>
<tr>
<td>Corpora lutea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superovulation</td>
<td>49</td>
<td>306</td>
</tr>
<tr>
<td>Eggs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>494</td>
<td>2541</td>
</tr>
</tbody>
</table>
Numbers of eggs shed in mice

BINOMIAL DISTRIBUTION OF EGGS BETWEEN THE TWO OVARIES

Expected and observed distributions in the most frequent classes

Since there is no material bias towards left or right we can now disregard the distinction between left and right, and deal with the distributions in terms of the difference between one side and the other. For example, two mice, one with three on the left and five on the right, the other with five on the left and three on the right, are equivalent; both have a difference of two. We may first examine the distributions of these differences among the commonest total egg numbers and see how they agree with the binomial expectation. The commonest total numbers were eight to eleven, each of which is represented by more than fifty mice in the total data on egg counts. The binomial expectation for the differences can be found from statistical tables (e.g. the Tables cited in the reference list). For example, among mice having a total of eight eggs, 27% are expected to have no difference (i.e. four on both sides), 44% are expected to have a difference of two (i.e. 3:5 or 5:3), 22% to have a difference of four (2:6 or 6:2), 6% a difference of six (1:7 or 7:1), and 1% a difference of eight (nil on one side and eight on the other). Table 2 shows the expected and observed

TABLE 2

OBSERVED DISTRIBUTIONS OF DIFFERENCES BETWEEN SIDES FOR COMPARISON WITH THE BINOMIAL EXPECTATIONS

<table>
<thead>
<tr>
<th>Total No.</th>
<th>No. mice</th>
<th>Difference between sides</th>
<th>Mean squared difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0 2 4 6 8 10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exp. 15-0 24-1 12-0 3-4 0-4 –</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>55</td>
<td>Obs. 12 22 15 5 1 –</td>
<td>8</td>
</tr>
<tr>
<td>10</td>
<td>83</td>
<td>Exp. 20-4 34-0 19-5 7-3 1-6 0-2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obs. 19 26 27 8 3 0</td>
<td>12-2</td>
</tr>
<tr>
<td>9</td>
<td>93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>58</td>
<td>Exp. 26-2 18-7 9-3 3-1 0-6 0-1</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obs. 29 17 11 1 0 0</td>
<td>8-7</td>
</tr>
</tbody>
</table>

The figures in the body of the table are numbers of mice expected and observed, the observed numbers coming from all the data on egg-counts combined.

numbers of mice according to the difference between sides. For example, there were fifty-five mice with totals of eight eggs, of which twelve mice had no difference between sides; the expected number with no difference is 27% of fifty-five, which is fifteen. The agreement between the observed and expected numbers is obviously very close.
In order to obtain a comprehensive test of the agreement with the binomial distribution, it is necessary to condense the distribution of differences between sides into a single figure for comparison with expectation. This can be done by making use of the property of a binomial distribution, that the mean of the squared differences is expected to equal the total number. This property can be deduced in the following manner. It is well known that the variance of the numbers observed in one of two binomially distributed classes is npq, a formula that can be found in any statistical text. Applied to the present problem, n is the total number of eggs from both ovaries together; p and q are both $\frac{1}{2}$, as shown in the previous section, so the expected variance reduces to $\frac{1}{4}n$. The ‘variance’ is, by definition, the average squared deviation from the mean number. The deviation of each side is half the difference between the two sides. So we can also express the expected variance in terms of the difference between sides, $d$, as the average of $(\frac{1}{2}d)^2$. Therefore, if $N$ is the number of mice examined, all with the same total number of eggs, $n$, the expectation is that $\Sigma (\frac{1}{2}d)^2/N = \frac{1}{4}n$, or $\Sigma d^2/N = n$. That is, the mean of the squared differences is expected to equal the total, if the distribution is binomial.

The mean of the squared differences found among the mice with total egg numbers of eight to eleven are shown at the right of Table 2. Three of them are a little in excess of expectation and one is below. Whether the discrepancies are significant or not will be considered later.

*Expected and observed distributions in all classes*

The first point to be examined with the mean squared difference is whether the inequality of the numbers of eggs shed by the two ovaries varies according to the total number of eggs. It might be expected that there would be a limit to the number of eggs that one ovary could shed at one time. This would tend to reduce the average difference between sides when large numbers of eggs were ovulated, particularly with superovulation. For the purpose of this analysis all the data on egg counts from all stocks and treatments were put together. Similarly, all the data on corpora lutea counts were put together, but not combined with the egg data. The mean squared difference between sides was then computed for all mice having the same total number of eggs. These total egg numbers ranged from two to fifty-four, but the lower and higher numbers were represented by too few mice to give reliable comparisons between the observed and expected mean squared difference. The data were therefore grouped as follows. For each total egg number the mean squared difference between sides was divided by the total egg number: this ratio $(\frac{d^2}{n})$ will be unity if the distribution is binomial. The ratios of the classes to be grouped together were then averaged, with weighting according to the numbers of mice. The ratios obtained are shown in Text-fig. 1, from which the following conclusions can be drawn:

1. The inequality between sides is not less when the number of eggs is large, and the distribution between sides is approximately binomial over the whole of the range of egg numbers. There is, perhaps, a suggestion that the inequality tends to increase with the higher egg numbers, but this tendency, when tested by a regression analysis, was not significant.
(2) With corpora lutea counts the inequality between sides tends to decrease as the total number increases. The first point, representing mice with five to seven corpora lutea, may be spuriously high: it included four mice with all the corpora lutea in one ovary and none in the other— one with five, one with six and two with seven. Even if this point is included, however, the tendency to decrease is not significant. (The computed regression is: \(0.057 \pm 0.036\).)

(3) Most of the points representing egg counts show a difference between sides greater than expectation, and most of the points representing corpora lutea counts show a difference less than expectation. The next point to be examined must, therefore, be the overall agreement with the binomial expectation.

**Significance tests on departures from expected ratios**

In order to test the overall agreement with the binomial expectation, it is necessary to condense the measure of the inequality between sides still further by combining the mean squared difference from all mice irrespective of the total number of eggs. This will also enable us to compare strains and treatments. The measure of inequality that seems most appropriate is again the ratio of the mean of squared differences to the total number of eggs, which has an expectation of 1. Combination of different totals has been done by summation of all squared differences and division of this by the sum of all totals, i.e. \(\Sigma d^2/\Sigma n\). This ratio weights the measure by the number of eggs counted rather than by the number of mice examined. The ratios obtained for the different strains and treatments are given in Tables 3 and 4.

The test of significance of the departures from the expected value of 1 for this ratio \(\Sigma d^2/\Sigma n\) was made by a method described by Robertson (1951). The basis of this method is an estimate of the heterogeneity between mice in their left-right difference, which may be explained in words as follows. The mean proportion of the eggs shed at one ovulation that come from one of the ovaries, say the left, is \(\frac{1}{2}\) (very nearly). Individual mice, however, vary widely round this mean ratio. How much of this variation represents real differences between the mice, over and above the chance variation expected from a binomial distribution? This real variation between mice is the ‘heterogeneity’ that the method
TABLE 3

ANALYSES OF EGG COUNTS AND CORPORA LUTEA COUNTS FOLLOWING NATURAL OVULATION, CLASSIFIED ACCORDING TO THE STRAIN

<table>
<thead>
<tr>
<th>Strain</th>
<th>Observer</th>
<th>No. mice</th>
<th>Mean No. eggs (α)</th>
<th>Variance of total egg No. (σ²n)</th>
<th>Σ d²/n</th>
<th>Heterogeneity (H×10³)</th>
<th>Standard error of H (σH×10³)</th>
<th>H/σH</th>
<th>Correlation betw. sides</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egg counts</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NF (36 to 40)</td>
<td>R.E.F.</td>
<td>33</td>
<td>11.1</td>
<td>2.86</td>
<td>1.06</td>
<td>14.4</td>
<td>57.3</td>
<td>0.25</td>
<td>-61</td>
</tr>
<tr>
<td>NS (29 to 32)</td>
<td>R.E.F.</td>
<td>13</td>
<td>4.9</td>
<td>1.23</td>
<td>0.54</td>
<td>-291.7</td>
<td>228.2</td>
<td>-1.28</td>
<td>-35</td>
</tr>
<tr>
<td>NC (21 to 25)</td>
<td>R.E.F.</td>
<td>24</td>
<td>7.5</td>
<td>2.87</td>
<td>0.89</td>
<td>-40.5</td>
<td>100.6</td>
<td>-0.40</td>
<td>-40</td>
</tr>
<tr>
<td>CFL (17 to 19)</td>
<td>R.G.E.</td>
<td>21</td>
<td>14.9</td>
<td>2.13</td>
<td>0.65</td>
<td>-63.0</td>
<td>33.5</td>
<td>-1.18</td>
<td>-64</td>
</tr>
<tr>
<td>CFS (17 to 20)</td>
<td>R.G.E.</td>
<td>29</td>
<td>8.9</td>
<td>2.50</td>
<td>1.28</td>
<td>84.8</td>
<td>76.7</td>
<td>-1.10</td>
<td>-64</td>
</tr>
<tr>
<td>CRL (17 to 20)</td>
<td>R.G.E.</td>
<td>23</td>
<td>16.0</td>
<td>5.09</td>
<td>0.97</td>
<td>5.3</td>
<td>47.1</td>
<td>-0.11</td>
<td>-51</td>
</tr>
<tr>
<td>JH (18 to 19)</td>
<td>R.G.E.</td>
<td>27</td>
<td>11.7</td>
<td>4.62</td>
<td>1.57</td>
<td>129.3</td>
<td>59.9</td>
<td>2.16*</td>
<td>-60</td>
</tr>
<tr>
<td>JH (16 to 17)</td>
<td>D.S.F.</td>
<td>45</td>
<td>10.4</td>
<td>2.20</td>
<td>0.85</td>
<td>-37.8</td>
<td>52.7</td>
<td>-0.72</td>
<td>-60</td>
</tr>
<tr>
<td>JH (32)</td>
<td>D.S.F.</td>
<td>30</td>
<td>13.7</td>
<td>4.22</td>
<td>1.73</td>
<td>139.5</td>
<td>48.4</td>
<td>2.88*</td>
<td>-70</td>
</tr>
<tr>
<td>JL (18 to 19)</td>
<td>R.G.E.</td>
<td>25</td>
<td>10.1</td>
<td>2.03</td>
<td>1.09</td>
<td>23.5</td>
<td>73.1</td>
<td>0.32</td>
<td>-69</td>
</tr>
<tr>
<td>JL (16 to 17)</td>
<td>D.S.F.</td>
<td>34</td>
<td>8.5</td>
<td>1.39</td>
<td>1.22</td>
<td>72.3</td>
<td>75.2</td>
<td>0.96</td>
<td>-77</td>
</tr>
<tr>
<td>JL (32)</td>
<td>D.S.F.</td>
<td>30</td>
<td>10.3</td>
<td>2.12</td>
<td>1.60</td>
<td>79.2</td>
<td>79.9</td>
<td>0.99</td>
<td>-72</td>
</tr>
<tr>
<td>JC (32)</td>
<td>D.S.F.</td>
<td>30</td>
<td>8.9</td>
<td>2.13</td>
<td>1.66</td>
<td>210.1</td>
<td>75.6</td>
<td>2.78*</td>
<td>-75</td>
</tr>
<tr>
<td>All</td>
<td></td>
<td>354</td>
<td>10.61</td>
<td>2.736</td>
<td>1.175</td>
<td>41.7</td>
<td>17.8</td>
<td>2.34*</td>
<td>-64</td>
</tr>
<tr>
<td>Corpora luteca</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JH (33)</td>
<td>D.S.F.</td>
<td>38</td>
<td>13.1</td>
<td>5.79</td>
<td>0.53</td>
<td>-94.1</td>
<td>44.1</td>
<td>-2.13*</td>
<td>-09</td>
</tr>
<tr>
<td>JL (33)</td>
<td>D.S.F.</td>
<td>67</td>
<td>9.9</td>
<td>3.09</td>
<td>0.95</td>
<td>-12.2</td>
<td>45.1</td>
<td>-0.27</td>
<td>-51</td>
</tr>
<tr>
<td>JC (33)</td>
<td>D.S.F.</td>
<td>37</td>
<td>9.1</td>
<td>1.52</td>
<td>0.95</td>
<td>-16.3</td>
<td>67.2</td>
<td>-0.24</td>
<td>-70</td>
</tr>
<tr>
<td>JR</td>
<td>R.C.R.</td>
<td>144</td>
<td>10.1</td>
<td>3.76</td>
<td>0.93</td>
<td>-18.7</td>
<td>36.2</td>
<td>-0.62</td>
<td>-43</td>
</tr>
<tr>
<td>JF</td>
<td>D.S.F.</td>
<td>104</td>
<td>11.0</td>
<td>7.19</td>
<td>0.65</td>
<td>82.8</td>
<td>32.2</td>
<td>2.57*</td>
<td>+01</td>
</tr>
<tr>
<td>All</td>
<td></td>
<td>390</td>
<td>10.48</td>
<td>4.550</td>
<td>0.81</td>
<td>-48.0</td>
<td>17.5</td>
<td>-2.75*</td>
<td>-30</td>
</tr>
</tbody>
</table>

* Heterogeneity significantly different from zero: P = 0.05 or less.

The figures in brackets after the strain designations refer to the generation from which the mice came. The combined values entered for 'all' strains are weighted averages.
Numbers of eggs shed in mice

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Alternatively, the variation of the ratios actually found might be less than would be expected on a chance basis. In that case, the 'heterogeneity' would be negative. The method provides a standard error for the estimate of heterogeneity, from which the significance of differences from the binomial expectation can be assessed. The heterogeneity, $H$, is estimated as follows:

$$H = \frac{2 \Sigma (d^2 - n)}{8 \Sigma n(n - 1)},$$

where $d$ is the difference between sides and $n$ is the total number of eggs from each mouse. We have already seen that, if the distribution is binomial, $d^2$ will equal $n$. Therefore an excess of inequality between sides will appear as a positive heterogeneity; and if, conversely, the number of eggs from the two ovaries are more alike than would be expected by chance, this will appear as a negative heterogeneity. The sampling variance of the estimate of the heterogeneity is

$$\sigma^2_H = \frac{1}{8 \Sigma n(n - 1)},$$

and the standard error is the square root of this.

The estimates of heterogeneity and their standard errors found in the different strains and treatments are listed in Tables 3 and 4. The three main groups of

<table>
<thead>
<tr>
<th>Strain or dosage</th>
<th>$\Sigma d^2$</th>
<th>Heterogeneity ($H \times 10^4$)</th>
<th>Standard error of $H$ ($\sigma_H \times 10^4$)</th>
<th>$H/\sigma_H$</th>
<th>Correlation betw. sides</th>
</tr>
</thead>
<tbody>
<tr>
<td>NF (36-40)</td>
<td>54</td>
<td>0.99</td>
<td>1.7</td>
<td>29.3</td>
<td>-0.06</td>
</tr>
<tr>
<td>NS (29-32)</td>
<td>45</td>
<td>1.58</td>
<td>137.5</td>
<td>52.4</td>
<td>2.62*</td>
</tr>
<tr>
<td>NC (22-26)</td>
<td>45</td>
<td>0.75</td>
<td>28.6</td>
<td>28.8</td>
<td>-0.99</td>
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<td>CFL (17-20)</td>
<td>49</td>
<td>1.34</td>
<td>31.8</td>
<td>21.5</td>
<td>1.48</td>
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<td>CFS (16-20)</td>
<td>24</td>
<td>0.62</td>
<td>48.9</td>
<td>44.8</td>
<td>-1.09</td>
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<td>JH (18-19)</td>
<td>25</td>
<td>0.96</td>
<td>4.3</td>
<td>30.0</td>
<td>-0.14</td>
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<td>JL (18-19)</td>
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<td>1.22</td>
<td>19.4</td>
<td>31.5</td>
<td>0.62</td>
</tr>
<tr>
<td>JR</td>
<td>82</td>
<td>1.06</td>
<td>6.7</td>
<td>18.9</td>
<td>0.36</td>
</tr>
<tr>
<td>All</td>
<td>343</td>
<td>1.08</td>
<td>8.9</td>
<td>9.8</td>
<td>0.90</td>
</tr>
<tr>
<td>½ i.u.</td>
<td>9</td>
<td>1.22</td>
<td>77.8</td>
<td>166.7</td>
<td>0.47</td>
</tr>
<tr>
<td>⅛ i.u.</td>
<td>62</td>
<td>1.20</td>
<td>47.1</td>
<td>43.6</td>
<td>1.08</td>
</tr>
<tr>
<td>⅛ i.u.</td>
<td>103</td>
<td>0.99</td>
<td>1.1</td>
<td>26.0</td>
<td>-0.04</td>
</tr>
<tr>
<td>3 i.u.</td>
<td>147</td>
<td>1.02</td>
<td>2.2</td>
<td>12.2</td>
<td>0.18</td>
</tr>
<tr>
<td>6 i.u.</td>
<td>16</td>
<td>1.49</td>
<td>33.5</td>
<td>25.7</td>
<td>1.30</td>
</tr>
</tbody>
</table>

* Heterogeneity significantly different from zero: $P = 0.05$ or less.
All observations by R.G.E. or R.E.F.
difference between sides to the total number of eggs \((\Sigma d^2/\Sigma n)\) is 1.175 instead of the expected 1.0. The heterogeneity variance between mice is 2.34 times its standard error, and so the excess of inequality, though very small, is significant at the 2% level. Corpora lutea counts following natural ovulation show, in contrast, significantly less variation between sides than would be expected by chance. The ratio \(\Sigma d^2/\Sigma n\) is 0.808 and the (negative) heterogeneity variance is 2.75 times its standard error, which is significant at the 1% level. Since egg counts and corpora lutea differ significantly from expectation in opposite directions it is clear that they differ from each other significantly. The difference of heterogeneity between the two sets of data is 3.6 times its standard error and is significant at the 0.1% level. Finally, the egg counts after superovulation show a slight but non-significant excess of variation between sides. The ratio \(\Sigma d^2/\Sigma n\) is 1.08, and the heterogeneity variance is less than its standard error. The difference of heterogeneity between the naturally ovulating and superovulated mice is not significant: it is 1.6 times its standard error and this has a probability of 10%. We cannot conclude, therefore, that the inequality between sides is really less in superovulated than in naturally ovulating mice.

The range of estimates of heterogeneity obtained from the separate strains may seem from an examination of Table 3 to be rather large; the estimates range from \(-1.28\) to \(+2.88\) times their individual standard errors. Also, there seems possibly to be a difference between observers, R. E. F. and R. G. E. obtaining low heterogeneities and D. S. F. high ones. Are these differences between strains and between observers, in respect of the estimates of heterogeneity, statistically significant? Table 5 shows \(\chi^2\) tests of these differences, the \(\chi^2\) values being obtained as follows. If the ratios of \(H/\sigma_H\) (given in Table 3) are normally distributed, then the squares of the ratios will be distributed as \(\chi^2\). Summation of \((H/\sigma_H)^2\) over, say, \(n\) strains gives a total \(\chi^2\) with \(n\) degrees of freedom. Subtraction of the value of \((H/\sigma_H)^2\) for all strains combined gives a \(\chi^2\) with \((n-1)\) degrees of freedom which tests the significance of differences in \(H\) between strains. Table 5 shows that the differences between strains in egg counts following natural ovulation are significant at the 5% level, and the differences between observers approach significance at this level. Observers

---

**Table 5**

Comparisons of Strains and Observers in Respect of the Estimates of Heterogeneity

<table>
<thead>
<tr>
<th></th>
<th>d.f.</th>
<th>(\chi^2)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural ovulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egg counts:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>between strains</td>
<td>12</td>
<td>22.2</td>
<td>0.05-02</td>
</tr>
<tr>
<td>between observers*</td>
<td>1</td>
<td>3.6</td>
<td>0.1-05</td>
</tr>
<tr>
<td>Corpora lutea:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>between strains</td>
<td>4</td>
<td>4.1</td>
<td>0.5-3</td>
</tr>
<tr>
<td>Superovulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between strains</td>
<td>7</td>
<td>10.9</td>
<td>0.2-1</td>
</tr>
<tr>
<td>Between doses</td>
<td>4</td>
<td>2.3</td>
<td>0.7-5</td>
</tr>
</tbody>
</table>

and strains are, however, confounded in the analysis, and the apparent difference between observers could well arise from the differences between strains, since only two strains were common to both observers.

The conclusions from the foregoing analyses are that the difference between the numbers of eggs shed from the two ovaries is on the average a little greater than would be expected by chance, but the difference between the corpora lutea counted in the two ovaries is less than would be expected by chance and less than that of the eggs shed. The deviations from chance expectation are, however, very small and the distribution of eggs between the two ovaries is very close to the binomial expectation.

**CORRELATION BETWEEN LEFT AND RIGHT SIDES**

The starting point for the present study was the correlation between the numbers of eggs from the two ovaries. How are the observed correlations related to the binomial distribution which has been demonstrated? The sign and magnitude of the correlation must depend on the relative magnitude of the variation between sides and the variation of total egg number between individual mice. Thus, if all mice shed the same total number of eggs there would be perfect negative correlation-between sides; if, on the other hand, there were no differences between the two sides but mice varied in total egg number, then there would be perfect positive correlation between sides. The object of this section, therefore, is to deduce the theoretically expected correlation in terms of these two sources of variation and then to show that the observed correlations follow the expected pattern.

The correlation coefficient, \( r \), can be expressed in terms of the variance of the total egg number, \( n \) and the variance of the difference between sides, \( d \), thus:

\[
\begin{align*}
    r &= \frac{\sigma_n^2 - \sigma_d^2}{\sigma_n^2 + \sigma_d^2} \\
    &= \frac{\sigma_n^2 - \sigma_d^2}{\sigma_n^2 + \sigma_d^2} . . . . . . . . . . . . . . . . \quad (1)
\end{align*}
\]

This expression can be derived as follows. Let \( L \) and \( R \) be the number of eggs on the left and right sides of any mouse. Let \( d = L - R \), the sign of the difference now being taken into account. Then \( L = \frac{1}{2}(n+d) \) and \( R = \frac{1}{2}(n-d) \). The sums are \( \Sigma L = \frac{1}{2}(\Sigma n + \Sigma d) \), \( \Sigma R = \frac{1}{2}(\Sigma n - \Sigma d) \), and the sum of products is \( \Sigma LR = \frac{1}{4}(\Sigma n + \Sigma d)(\Sigma n - \Sigma d) \). The covariance is

\[
\text{cov}_{LR} = \frac{1}{N-1} \left( \Sigma LR - \frac{\Sigma L \Sigma R}{N} \right),
\]

where \( N \) is the number of mice. Writing \( L \) and \( R \) in terms of \( n \) and \( d \) gives

\[
\begin{align*}
    \text{cov}_{LR} &= \frac{1}{N-1} \left[ \frac{1}{4}(\Sigma n^2 - \Sigma d^2) - \frac{1}{4} \left( \frac{\Sigma n^2 - (\Sigma d)^2}{N} \right) \right] \\
    &= \frac{1}{4} \cdot \frac{1}{N-1} \left\{ \left[ \Sigma n^2 - \frac{(\Sigma n)^2}{N} \right] - \left[ \Sigma d^2 - \frac{(\Sigma d)^2}{N} \right] \right\} \\
    &= \frac{1}{4} \sigma_n^2 - \sigma_d^2).
\end{align*}
\]

The variance of the numbers on the two sides will be equal, so \( \sigma_L \sigma_R = \sigma_L^2 = \sigma_R^2 = \text{variance of} \ \frac{1}{2}(n \pm d) = \frac{1}{4}(\sigma_n^2 + \sigma_d^2 \pm 2 \text{cov}_{nd}) \). The covariance terms will
cancel out because half will be positive and half negative and of equal magnitude. Thus \( \sigma_L \sigma_R = \frac{1}{2} (\sigma_n^2 + \sigma_d^2) \). The correlation between left and right sides is

\[
    r_{LR} = \frac{\text{COV}_{LR}}{\sigma_L \sigma_R} = \frac{\sigma_n^2 - \sigma_d^2}{\sigma_n^2 + \sigma_d^2}
\]

The above expression for the correlation rests on no assumption other than that the variances of the numbers shed by left and by right ovaries are equal, which is a reasonable supposition to make. This formula was used to calculate the observed correlations, and these are given in Tables 3 and 4. Table 3 refers to natural ovulation and the correlations found in each strain are given. Those based on egg counts are all negative and range from \(-0.35\) to \(-0.77\); those based on corpora lutea counts range from \(+0.01\) to \(-0.70\). Table 4 refers to superovulation and the correlations found after each dosage level are given. They are about zero after the two low dosages and are positive after the higher dosages, the highest value being \(+0.63\).

If we apply the conclusion, arrived at in the previous section, that the distribution of eggs between the two sides is binomial, or nearly so, we can arrive at an expression for the correlation between sides in terms of the variance and mean of the total egg number. Since the mean number of eggs shed by left and by right ovaries is equal \((\bar{d} = 0)\) it follows that the variance of the difference, \(\sigma^2_d\), is equal to the mean squared difference, \(\Sigma d^2/N\). This, as was explained earlier, is equal to the total number of eggs, \(n\), if the distribution between sides is binomial. We can therefore substitute the mean of the total egg number, \(\bar{n}\), for the variance of the difference, \(\sigma^2_d\), in equation (1), and write the correlation in the form

\[
    r = \frac{\sigma_n^2 - \bar{n}}{\sigma_n^2 + \bar{n}}
\]

This formula shows that, with a binomial distribution between sides, the correlation will be negative when the variance is less than the mean, and positive when the variance exceeds the mean.

The expected correlations, calculated from Equation 2, are given in Tables 3 and 4. The observed correlations deviate from the expected correlations only in so far as the mean squared difference between sides deviates from the total egg number. The close correspondence between the observed and expected correlations therefore provides no new information: it merely reflects the close agreement with the binomial distribution which has already been established.

The way in which the expected correlation depends on the variance and the mean may be more easily appreciated from the graphical representation in Text-fig. 2. This shows each strain and treatment plotted according to its variance and mean of total egg number. The superovulation data are here subdivided into both strains and treatments, as in Table 6, so that there is a point for each strain at each dosage level with which it was treated. Some of these points are based on rather few animals and they are consequently rather widely scattered. The correlations expected are related to the positions of points on the graphs by Equation 2, and straight lines are drawn to mark the positions of various levels of the correlation coefficient. The positions of the
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points in relation to these lines show how the expected correlations vary from natural ovulation to superovulation, and with increasing dosages of PMS.

The fact that the correlations change from negative in naturally ovulating mice to positive after superovulation is purely the consequence of the relatively greater variance of total egg number after superovulation, together with the binomial distribution between sides. This effect of superovulation on the variance may be of physiological interest, and it will now be examined in more detail.

**Text-fig. 2. Variance of total egg number (left+right) plotted against the mean egg number.** Each point refers to a strain or treatment. The straight lines represent various values of the expected correlation between left and right ovaries, as explained in the text. (a) Superovulation. Dosage: * = $\frac{1}{2}$ i.u.; $\bigcirc$ = $\frac{1}{4}$ i.u.; $\bigtriangleup$ = 1 i.u.; $\blacktriangle$ = 3 i.u.; $\bullet$ = 6 i.u. (b) Natural ovulation (● = egg counts; ○ = corpora lutea counts).
Table 6
Means and variances of total egg numbers following superovulation, classified by both strains and dosage

<table>
<thead>
<tr>
<th>Dosage of PMS (i.u.)</th>
<th>1/2</th>
<th>1</th>
<th>3</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain</td>
<td>N</td>
<td>$\bar{n}$</td>
<td>$\sigma^2_n$</td>
<td>N</td>
</tr>
<tr>
<td>NF</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>17</td>
</tr>
<tr>
<td>NS</td>
<td>9</td>
<td>7.0</td>
<td>9.0</td>
<td>14</td>
</tr>
<tr>
<td>NC</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9</td>
</tr>
<tr>
<td>CFL</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>15</td>
</tr>
<tr>
<td>CFS</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7</td>
</tr>
<tr>
<td>JH</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>JL</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>JB</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>All</td>
<td>9</td>
<td>7.0</td>
<td>9.0</td>
<td>62</td>
</tr>
</tbody>
</table>

* Excluding seven mice that gave no eggs.

All observations by R.G.E. or R.E.F. $N=$ number of mice; $\bar{n}=$ mean number of eggs (left+right); $\sigma^2_n=$ variance of egg number. The combined values at the foot are weighted averages.
DOSSAGE EFFECT IN SUPEROVULATION

Consideration of the variance of total egg number and its relation to the mean egg number leads to a conclusion that is of interest in connection with superovulation. Text-fig. 2 shows that the variance increases as the mean increases, both with superovulated and naturally ovulating mice. (In this section, 'variance', 'mean' and 'egg number' all refer to total egg number, i.e. the sum of the numbers from the two ovaries). Text-fig. 2 shows also that the variance is very much greater after superovulation than after natural ovulation (see above). Is this increased variance consistent with the greater mean, or does the superovulation itself cause a greater variability?

The answer to this question can be seen most clearly from a consideration of the coefficient of variation, i.e. the ratio of standard deviation to mean egg number ($\sigma_n/n$), though as will be seen later this is not the most appropriate measure of variation for making the comparison. The coefficients of variation are plotted against the mean egg numbers in Text-fig. 3 from the data contained in Tables 3 and 6. Each point represents a strain, and the different dosages used to induce superovulation are shown separately. Over the range of mean egg numbers covered by natural ovulation, where a direct comparison can be made, the coefficient of variation is considerably higher after superovulation than after natural ovulation. Superovulation therefore causes an additional source of variation not present in natural ovulation, even when the mean egg numbers are the same. Another conclusion to be drawn from Text-fig. 3 is that the coefficient of variation of egg number after natural ovulation is not constant, but declines as the mean increases. This trend is statistically significant at the 1% level. The regression of the coefficient of variation on the mean egg number is $-0.0082 \pm 0.0025$ ($t_{111} = 3.3; P = 0.01$). After superovulation, in contrast, the coefficient of variation does not decline as the egg number increases. The regression is $+0.0005 \pm 0.003$, and the two regression coefficients are significantly different from each other at the 5% level. Thus, not only is the variation relatively greater after superovulation than after natural ovulation, but the form of the relationship between the variation and the mean is different. The

![Text-fig. 3. Relationship between coefficient of variation and mean egg number in different strains and after different dosages of pms. • = natural; △ = ½ i.u.; ○ = ⅔ i.u.; △ = 1 i.u.; △ = 3 i.u.; ● = 6 i.u.](image-url)
interpretation of this different relationship is complicated by the fact that the differences in mean egg number following superovulation are associated with differences of dosage, and the amount of variation may be influenced by the dosage level, as distinct from the mean number of eggs shed. If the relationship is examined within each of the three intermediate dosage levels, which are represented by several strains, it is found that there is a tendency for the coefficient of variation to decline with increasing mean, just as with natural ovulation. The mean regression, within dosage levels, of the coefficient of variation on the mean egg number is $-0.107 \pm 0.073$, which is nearly the same as with natural ovulation. The regression is, however, not significantly different from zero, and it can only be taken as a suggestion that the coefficient of variation may follow the same relationship with the mean within any one dosage level as it does in naturally ovulating mice. The empirical fact demonstrated by the graph is that the coefficient of variation is the same at all dosage levels, whereas it is less with high natural egg numbers than with low.

Since the coefficient of variation is not constant in naturally ovulating mice, this measure of variation is not a suitable one for the comparison of variation in groups with different mean egg numbers. A suitable measure is the ratio of variance to mean ($\sigma^2/n$). This ratio was found to remain constant over the range of mean egg numbers for natural ovulation in the data. The regression of the ratio on the mean egg number was $+0.003 \pm 0.0077$. The ratio of variance to mean therefore seems to provide the more appropriate measure of variation for an assessment of the effects of dosage level on the variability of egg number following superovulation. The ratio of variance to mean is plotted in Text-fig. 4 against the dosage. The ratio for each dosage level is the overall mean of the ratios for each strain tested at that dosage, weighted by the number of mice. The ratio for natural ovulation is shown against a dosage of 0. If the variation after superovulation behaved as it does after natural ovulation, and if the only effect of higher doses was to produce a higher mean egg number, then the

![Text-fig. 4. Ratio of variance to mean egg number in relation to dosage of PMS.](image-url)
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ratio of variance to mean would be expected to remain constant over all doses and to have a value equal to that after natural ovulation. Text-fig. 4 shows clearly that it is above the level for natural ovulation at the lowest doses and that it increases very much at the higher doses. The dosage of PMS required to induce a mean ovulation rate equal to the natural rate was calculated for the N- and C-strains used in this work by Fowler & Edwards (1960) from regressions of total egg number on dosage. The values obtained were below ½ i.u. for the NS (small) strain and between 0·4 and 1·2 i.u. for the other N- and C-strains. At dosages of ½ to 1 i.u., the variance is five to ten times as great as after natural ovulation. At a dose of 3 i.u., the variance is twenty-four times as great as it would be if the same mean egg number were produced by natural ovulation. Thus the induction of superovulation by PMS introduces an additional source of variation which is not present in naturally ovulating mice, and this additional variation increases with higher doses of PMS.

The conclusions about the relationship between variation and mean egg number which have been drawn in this section are that the variance is proportional to the mean egg number after natural ovulation, and possibly also after superovulation when the dose is not varied; but when superovulation is induced by varying doses of PMS then the standard deviation is proportional to the mean egg number corresponding to each dose.

DISCUSSION

The essential requirement, in statistical terms, for any postulated physiological mechanism of ovulation to be consistent with the random (binomial) distribution of eggs between the two ovaries, is that the maturation of one follicle reduces the probability of the maturation of any other follicle, whether in the same ovary or in the other. This requirement can only be met if the maturation of any follicle changes the conditions influencing both ovaries. One obvious way of meeting this requirement is that the maturation of each follicle uses up some of the circulating hormone; less would then be available for the stimulation of other follicles to maturation, whether in the same ovary or in the other. Whatever the physiological basis it may well be common to most mammals. A random distribution of corpora lutea between the two ovaries exists in the common shrew (Brambell, 1935), the lesser shrew (Brambell & Hall, 1937) and the bank vole (Brambell & Rowlands, 1936). The negative correlation between ovaries reported in guinea-pigs (Eckstein & McKeown, 1955) and rabbits (Adams, 1959) also makes it probable that the same binomial distribution may occur in most mammals including women; in species ovulating one egg, a random ovulation would often give the impression of regular alternation (Brambell, 1956). Nevertheless, in several species of mammals the female has been reported to ovulate more frequently from one ovary, e.g. the mare, the wild mountain viscacha and some species of bats (Eckstein & Zuckerman, 1956).

The random distribution between sides, even in mice with the largest numbers of eggs, proves that if there is a limit to the number of follicles that can mature in one ovary at the same oestrus, this limit has not been reached even
with superovulation by the highest doses of PMS administered. This conclusion is supported by three other lines of evidence. Edwards & Fowler (1960) found that a second ovulation almost always resulted from a second treatment with PMS and HCG given between 1 and 3 days after the first treatment. Jones & Krohn (1961) showed, from detailed counts of the numbers of oocytes in the ovaries of inbred and hybrid mice of various ages between birth and senescence, that many hundreds of oocytes were available in all strains at ages comparable to those of the mice used in the present experiment. Lastly, after complete removal of one ovary and even the partial removal of the other, the remaining ovarian tissue hypertrophies and can shed approximately the same number of eggs at each oestrus as the two ovaries had done previously (e.g. Hollander & Strong, 1950). But the number of oocytes available in these ovarian fragments declines with an increasing interval after removal of the ovarian tissue (e.g. Lipschütz, 1928; Mandl, Zuckerman & Patterson, 1952). The largest number of eggs counted from one ovary in the present data was thirty-one, which occurred in three different mice.

Statistical analysis showed that the variation between the numbers of eggs counted from the two ovaries after natural ovulation was a little greater than the random amount, but the variation in corpora lutea between the two ovaries was less than the random amount. The following possible causes of increased or of reduced variation between sides may be suggested:

(i) Some mice might be slightly 'left-sided' and others slightly 'right-sided'. This would increase the variation both of egg counts and of corpora lutea counts. A difference of this sort between the two ovaries might result from a difference in the hormonal supply, perhaps through a difference in the blood supply to the two ovaries, or from the impairment of one ovary by disease in some mice.

(ii) The occurrence of follicles not represented by an egg in the Fallopian tube. Two processes leading to such an event are the formation of corpora lutea atretica, i.e. the luteinization of a follicle without the liberation of its oocyte, and intraovarian ovulation, in which the oocyte is liberated into the ovarian tissue. A first report of the latter process and measurements of the incidence of both processes in mice have been given by Jones & Krohn (1961). The loss of eggs, from any cause, would increase the variation between sides in egg counts, but not in corpora lutea counts. The occurrence of atretic corpora lutea would do the same, unless they require less hormone during their formation than do normal corpora lutea. Both processes would, however, reduce the variation between sides if they occurred relatively more frequently in ovaries that shed a large number of eggs. They would then tend to diminish high counts without altering the low counts.

(iii) The occurrence of polyploidal follicles; i.e. the presence of more than one oocyte in a follicle. The incidence of polyploidal follicles in 6-week-old 'Swiss' mice has recently been estimated as about 10% (Kent, 1960), though it declined in older mice. An incidence as high as this in our material could have had some effect on the variation between the two ovaries, though it is not clear to what extent polyploidal follicles contribute to the eggs ovulated. Allen, Brambell & Mills (1947) showed that the incidence of eggs from these follicles
was unimportant (0·23%) in the wild rabbit. If a polyovular follicle requires the same amount of hormone for its maturation as a normal follicle, then the variation between sides in egg counts would be increased but that of corpora lutea counts would not. If the amount of hormone required is in proportion to the number of eggs maturing, then polyovular follicles would have no effect on the variation between sides in egg counts, but would reduce the variation in corpora lutea counts. Thus the occurrence of polyovular follicles could account for either the excess variation between sides in egg counts or the reduced variation in corpora lutea counts, but not for both. We have no means of discriminating between these two possibilities on the basis of the present data.

(iv) Miscounting of corpora lutea. Perhaps the most likely reason for the reduced variation between sides in corpora lutea counts is miscounting. Crowded corpora lutea in a mouse ovary are not easy to distinguish, and close contiguity may often lead to two corpora lutea being counted as one. This would tend to reduce the counts for ovaries that shed a large number of eggs, and so diminish the variation between sides. This explanation is supported by the observation that the variation between sides declined as the total number of corpora lutea went up, though the decline was not statistically significant. On the other hand, miscounting on a scale sufficient to affect the variation between sides would be expected also to affect the mean. But a comparison of the means of corpora lutea counts and egg counts made on the same strains gives no evidence of miscounting (see Table 3). Although counts of corpora lutea as estimates of the numbers of eggs shed have often been criticized, the close correspondence between the corpora lutea counts and the egg counts in our data show that they can be reasonably reliable. Similar agreement was also reported by Falconer & Roberts (1960).

It is possible that several of the foregoing causes of increased or reduced variation were operating to produce the variation actually observed. The most likely cause of the reduced variation between sides in corpora lutea counts was miscounting in crowded ovaries. The increased variation between sides in egg counts was probably due to a difference in the blood supply to the two ovaries. After superovulation, however, there was little or no excess variation between sides in egg counts, though the difference in this respect from natural ovulation was not statistically significant. If the reduced variation between sides after superovulation was real, it could have resulted from the techniques employed: for example, the PMS and HCG injected intraperitoneally might reach the follicles partly through the surface of the ovary. This might then reduce any effect of a difference in the blood supplies to the two ovaries.

The striking effect that the dose of PMS had on the variation of the total number of eggs shed is puzzling. With doses of $\frac{1}{4}$ and $\frac{1}{2}$ i.u., the mean was similar to that of natural ovulation but the variance was considerably greater. With higher doses the variance was very much greater than would be expected from the extrapolation of data from natural ovulation. Thus the induction of superovulation by PMS introduced an additional cause of variation not present in naturally ovulating mice. What this cause of variation might be can only be surmised. It might be related to the stage of the oestrous cycle at which the PMS was injected, though there was no evidence that this had any effect (Fowler...
& Edwards, unpublished). It might be due to the suppression of ovulation by excessive amounts of PMS in some mice through premature luteinization of follicles (Noble, Rowlands, Warwick & Williams, 1939; Fowler & Edwards, 1960). Or, it might depend on the rate of elimination of hormone from the circulation, though it would then have to be supposed that the differences between mice in their rates of elimination were more marked at high concentrations of PMS than at low.

One consequence of the greater variation after superovulation is that it produces a positive correlation between sides in place of the negative correlation found after natural ovulation. This change of sign need have no physiological implications other than those connected with the difference in variance. The correlations found are fully accounted for by the random distribution of eggs between the left and right ovaries together with the differences of the mean and variance of the total number of eggs shed.

ACKNOWLEDGMENTS

We are much indebted to Miss Mary Wheeler for carrying out the bulk of the statistical computations on which this work rests, and to Mr E. D. Roberts for drawing the figures.

REFERENCES


Numbers of eggs shed in mice


