sumably involves higher centers acting via the hypothalamus. A biological clock seems to control ovulation both in the immature rat induced to precocious puberty and in the adult. When the clock first appears in the immature rat it is already "set" to the same time as it is in the adult.

Preliminary experiments have revealed other aspects of this timing mechanism. Ovulation occurs in those animals blocked with barbital, but is a day later than in the controls. If a second injection of barbital is given 24 hours after the first, ovulation is again blocked and does not occur until 2 days after ovulation in the controls. Thus, there is a 24-hour periodicity in the release of ovulating hormone similar to that described by Everett and Sawyer in the adult rat (4).

It might be expected that the time of hormone release would follow the injection of the serum gonadotrophin by a constant time interval. However, when the serum gonadotrophin was given at various times within an 18-hour period the time of the critical period was the same. The setting of the timing mechanism may be determined by the lighting; when the beginning of the light period was shifted earlier or later, without change in length, the critical period shifted correspondingly.

The data in this report provide the basis for further study of the role of the hypothalamus and pituitary in controlling ovulation and for developing methods to test substances which either prevent or cause the release of pituitary ovulating hormone (9).

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References and Notes

- 1. "Ovulating hormone" is used to indicate what-"Ovulating hormone" is used to indicate whatever pituitary hormones are necessary for ovulation.
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 (1950) and C. H. Sawyer, *ibid.* 47, 198
- (1950)
- H. H. Cole, Am. J. Anat. 59, 299 (1936). Times are stated throughout as "colony time," using the convention of Everett and Sawyer wherein midnight, colony time, is the midpoint of the dark period. In our laboratory midnight, colony time, occurs at 1 A.M. Central Standard Time.
- Gonadogen" was supplied through the courtesy of the Upjohn Company. According to the Upjohn Company, "one Cartland-Nelson unit is equivalent to approximately 20 International Units.
- 8. C. E. McCormack and R. K. Meyer, Proc. Soc. Exptl. Biol. Med. 110, 343 (1962).
 9. This work was supported by grant A-804(C13) from the U.S. Public Health Service and by funds from the Wisconsin Alumni Research Foundation.

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Meiotic Drive

Matsunaga and Hiraizumi (1) have presented evidence suggesting that either meiotic drive or sperm competition may be responsible for an excess production of blood group O offspring from fathers heterozygous for the A and O or for the B and O alleles. As co-originator, with L. M. Sandler, of the phrase "meiotic drive," I am naturally favorably disposed toward any analysis which helps promote its usage; in this case, however, I feel that the approach is open to one criticism which may be of sufficient merit to warrant a more detailed analysis of the data.

In the method of Matsunaga and Hiraizumi it is necessary to calculate the probability that an A (or B) father will produce an O sperm. Since both homozygous AA and heterozygous AO genotypes are grouped as phenotypically of blood group A, the proportions of the two types of males are estimated by applying the Hardy-Weinberg formulation to the estimates of gene frequencies derived from observations on the Japanese population. After this is done, there appears to be an excess of progeny carrying the O alleles from that fraction of the males assumed to be heterozygous.

The pitfall in this procedure is similar to one pointed out earlier (2) in connection with an analysis of data from Drosophila populations. If there is some disturbance in a mating system such that the distribution of the genotypes in the progeny does not follow the Hardy-Weinberg expectations, then, if that disturbance is consistent, it should also have affected the frequencies of the genotypes in the preceding generation-that is, in the parents. It is not possible, therefore, to make a simple direct estimate of gene frequencies from the parental phenotypic frequencies because the Hardy-Weinberg distribution is being altered, by definition. Furthermore, if it is true, as Matsunaga and Hiraizumi point out, that postzygotic selection in the ABO blood groups also affects the genotypes differentially, then calculation of gene frequencies from the raw population data by the simple Hardy-Weinberg arithmetic and subsequent estimation of the genotypic frequencies from the gene frequencies becomes a somewhat hazardous enterprise.

Such complications can be approached by the use of appropriate programs for high-speed computers. In collaboration

with Ray D. Owen we have in this way analyzed several independently collected (and self-inconsistent) sets of data on mother-child ABO blood group combinations. A test for meiotic drive of the type described was a constant feature of the program, but a drive of this type was not found to be a consistent factor in the data. Unfortunately, the data of Matsunaga and Hiraizumi (1) did not include either the phenotypes of the fathers (which had therefore to be assumed to be in the same distribution as those of the mothers) or specific information on family size. The possibility remains that the more detailed data that were available to us still provide evidence for some phenomenon such as meiotic drive when analyzed in a more sophisticated fashion.

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E. Novitski and E. R. Dempster, Genetics 43, 470 (1958). 1. E. 2. E.

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We agree that the frequencies of alleles and of genotypes, as well as of other coefficients, are best estimated by the maximum-likelihood method, but unfortunately a high-speed computer is not available in our Institute. For computing our "family size equivalent" values, the frequencies of alleles and genotypes were estimated by applying the simple Hardy-Weinberg formulation. Usually the observed phenotypic frequencies of the four blood types agree quite well with those expected from the Hardy-Weinberg law. But, of course, this agreement does not always imply that the distribution of each genotype takes place according to the Hardy-Weinberg expectation. For example, an excess in the frequency of AO but a deficiency in the frequency of AA may still give a good agreement of the observed frequency of blood type A with the Hardy-Weinberg expectation, and in that case \circ O \times δ A matings will give more O children than expected. However, this complication disappears if we compare the family size equivalent value for O children of $P A \times \delta O$ with the value for O children of \circ O \times & A, and we can check this by taking the respective equivalent values presented in Table 1 of our earlier report (1).

This matter, however, requires more

Table 1. Frequency distribution of children in reciprocal mating $A \times O$.

Number	Observed number of families		
of children	$\begin{array}{c} \mathbf{P} \mathbf{A} \times \mathbf{P} \mathbf{O} \\ \mathbf{mating} \end{array}$	$\begin{array}{c} \mathbf{P} \mathbf{O} \times \mathbf{P} \mathbf{A} \\ \mathbf{mating} \end{array}$	
0	No record	No record	
1	82	95	
2	48	48	
3	32	29	
4	14	15	
5	8	8	
6	2	3	
7	3	2	
8	1	1	
Total	190	201	

critical studies in order to eliminate the possibility of differential fertility in A and O mothers, and of reproductive compensation concurrent with the effect of incompatibility. From the data of Matsunaga and Itoh (2) and of Haga (3), the following values are derived for the average number of children of the O \times O, A \times δ O, and Q \times δ A matings (abbreviated C_{00} , C_{A0} , and C_{0A} , respectively); the average number of pregnancies (P_{00} , P_{A0} , and P_{0A}); and the proportions of prenatal deaths per pregnancy (PP_{oo} , PP_{Ao} , and PP_{oA}): C_{00} , 2.5388 \pm 0.1151; C_{A0} , 2.5070 \pm 0.1055; C_{0A} , 2.2958 \pm 0.1136; P_{00} , $3.1187 \pm 0.1443; P_{AO}, 3.0775 \pm$ 0.1320; P_{oA} , 3.2667 \pm 0.1501; PP_{oo} , $0.0761 \pm 0.0101; PP_{AO}, 0.0778 \pm$ 0.0091; and PP_{0A} , 0.1314 \pm 0.0121.

The values of C, P, and PP are nearly the same in O \times O and $\ensuremath{\,\widehat{}}\xspace$ A \times $\ensuremath{\,\widehat{}}\xspace$ O matings, indicating that there is no difference in the fertility of A and O mothers. The reduction in fertility of the incompatible $\circ \mathbf{O} \times \circ \mathbf{A}$ matings as compared with the $P A \times \delta O$ matings is apparent, and there is in fact some indication of reproductive compensation, since $P_{0A} > P_{AO}$, although the difference is not statistically significant. However, in view of the fact that the prenatal deaths due to ABO incompatibility often begin with the first

Table 2.	Frequency	distribut	ion of O	children
in recipro	ocal mating	$s A \times C$) for fam	ilies hav-
ing at lea	st three chi	ldren.		

Number	Observed number of families		
of children	$\begin{array}{c} \mathbf{P} \mathbf{A} \times \mathbf{\sigma}^{\mathbf{T}} \mathbf{O} \\ \text{mating} \end{array}$	♀ O × ♂A mating	
0	15	11	
1	19	10	
2	13	15	
3	10	15	
4	2	6	
5	0	1	
6	1	0	
Total	60	58	

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pregnancy, it is suspected that the differences in the values of C, P, and PP between the reciprocal matings would disappear if we chose families having, say, at least three children. Unfortunately, about half the original records of Matsunaga and Itoh have been lost; the remaining data, plus the data of Haga, are used in the following analysis. After the selection for family size has been made, values are obtained as follows: $C_{A0} = 4.0909 \pm 0.1538$ and $C_{0A} = 3.9565 \pm 0.1592; P_{AO} = 4.9487$ \pm 0.2226 and P_{0A} = 4.9130 \pm 0.2113; $PP_{A0} = 0.0415 \pm 0.0101$ and $PP_{0A} =$ 0.0531 ± 0.0122 . Thus, the two matings now give nearly the same values for C, P, and PP. This suggests that the reduction in viability of the incompatible AO children occurs mostly in small families and that the effect of incompatibility becomes smaller as family size increases. This also suggests that there is little chance for reproductive compensation in the families selected for having at least three children. We may expect, then, that the average number of O children in the two kinds of mating will be almost the same, unless the segregation ratio of the O allele from the AO fathers differs from 0.5.

Some of the data used in our earlier report did not provide a record for each family; therefore they are excluded from the analysis presented here. The distribution of the number of children in the reciprocal $O \times A$ matings is presented in Table 1.

The distributions in the two kinds of mating are nearly the same when we choose only families having at least three children. For such selected families, $C_{A0} = 3.8833 \pm 0.1596$ and C_{0A} = 3.9138 \pm 0.1580. The average number of O children in $P A \times \delta O$ matings is 1.4833 ± 0.1655 , while the average number in $\circ O \times \circ A$ matings is 1.9655 ± 0.1755 . The difference between the two values is statistically significant (the distribution of O children is presented in Table 2).

This result strongly suggests that prezygotic selection favoring the O allele is operating in the AO fathers. However, the data available for the present discussion are rather incomplete, and we hope for more complete data in order to obtain conclusive evidence of prezygotic selection.

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Individuality of Human Serum by Immunoelectrophoresis

Abstract. A method is described which implements the direct comparison of serum samples from different individuals by simultaneous electrophoresis followed by simultaneous diffusion and precipitation by anti-human horse serum. Results have been evaluated, with an arbitrary reference grid, by comparison of the numbers of precipitin bands present in the paired immunoelectrophoretograms. Graphic representation of these differences distinguishes serum samples of like from those of unlike origin.

In the search for the laws and generalizations which govern the physical world, the scientist's preoccupation with similarities has often led to the neglect of the opposite side of the coin-the individuality of objects and organisms. As applied to human beings, individuality is not significantly less important than similarity, inasmuch as it influences all aspects of life and is of direct interest in many fields, including medicine and criminalistics. Numerous studies have been made of the individuality of certain features of human blood, one of which is the subject of this report.

Both qualitative and quantitative differences in the distribution of serum protein fractions, as revealed in electrophoretic studies of one type or another, have been noted by a number of investigators (1). However, though electrophoresis has been a powerful tool in showing variations in the separated protein components of normal blood, the demonstrable differences have been less definitive than is required for discrimination among large numbers of individuals.

The development of highly refined techniques for immunoelectrophoresis (2) leads naturally to the application of this method to further differentiation among the serum proteins and the consequent establishment of individual differences in the blood of healthy persons. In this study a number of blood sera from healthy individuals of collegestudent age were subjected to direct comparison by immunoelectrophoresis. The technique employed is a modification of that described by Grunbaum and

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