

## A CHROMOSOME FREQUENCY TEST FOR LINKAGE OF THE RHESUS BLOOD FACTORS

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Two different hypotheses have been proposed to account for the inheritance of the Rhesus blood antigens. Wiener (3) explains their inheritance on the basis of a set of multiple alleles, while Fisher (2) accounts for it on the basis of three closely linked pairs of factors. At least six different genes are required for either explanation, as three different kinds of Rhesus antigen are known, each of which is dominant in its absence, but none of which show dominance to each other. If multiple alleles are responsible for the inheritance, it means that two genes ( $Rh^{oI}$  and  $Rh^{oII}$ ) each produce two different antigens. Linkage would mean that each gene would produce only one antigen. The genes and their products, both for multiple alleles and for linked genes are shown below, the three antigens being designated as antigen  $Rh^o$ , antigen  $Rh^I$ , and antigen  $Rh^{II}$ .

<i>Multiple alleles</i>	<i>Products</i>	<i>Linked genes</i>
$Rh^-$	no antigen	c, d, e
$Rh^o$	antigen <sup>o</sup>	D
$Rh^I$	antigen <sup>I</sup>	C
$Rh^{II}$	antigen <sup>II</sup>	E
$Rh^{oI}$	antigens <sup>oI</sup>	C, D
$Rh^{oII}$	antigens <sup>oII</sup>	D, E

Wiener (3) has tested the multiple allelic hypothesis with gene frequency analysis, and his results show close agreement between the expected and the actual frequencies. Fisher's hypothesis cannot be tested by the usual methods of gene frequency analysis. It is possible, however, to test the linkage hypothesis by *chromosome* frequency analysis, if we have data on the frequencies of the Rh types in a population in which mating has occurred at random. Within such populations, non-allelic genes should occur quite independently of each other. Even genes from sets of alleles too closely linked for any crossing over to occur should still show the same ratios of various combinations within chromosomes as expected on random assortment. That is to say, if alleles Aa and Bb are linked, regardless of how closely, and if the gene frequencies are  $A-.9$ ;  $a-.1$ ;  $B-.1$ ;  $b-.9$ ; we should expect the following chromosome ratios in the population:

A	B	.09
A	b	.81
a	B	.01
a	b	.09

The frequency of a chromosome carrying any combination of genes, then is the product of the frequencies of these genes.

This note is concerned with such a test for linkage of the Rh genes. Data on actual frequencies is based upon a population of 1,000 in New York City, tested by Wiener and Sonn (3). Gene frequencies are readily obtained from such data. For example, the frequency of gene *c* is the square root of the frequency of persons lacking antigen Rh<sup>i</sup>. It follows that  $C=1-c$ . In a similar manner the frequencies of genes *D*, *d*, *E*, and *e* may be readily ascertained.

$$\begin{array}{l} C - .466 \\ c - .534 \end{array}$$

$$\begin{array}{l} D - .625 \\ d - .375 \end{array}$$

$$\begin{array}{l} E - .161 \\ e - .839 \end{array}$$

The frequencies of the eight combinations of the Rhesus genes within chromosomes are easily computed and are shown below:

p	C	D	E	.047
q	C	D	e	.244
r	C	d	E	.028
s	c	D	E	.054
t	C	d	e	.147
u	c	d	E	.032
v	c	D	e	.280
w	c	d	e	.168

If *p*, *q*, *r*, *s*, *t*, *u*, *v*, and *w* represent the chromosome frequencies, the expected chromosome combinations within individuals are  $(p+q+r+s+t+u+v+w)^2$ . The frequencies of the expected Rh types within the population are as follows:

$$CDE = p^2 + 2pq + 2pr + 2ps + 2pt + 2pu + 2pv + 2pw + 2qr + 2qs + 2qu + 2rs + 2st + 2rv$$

$$CDe = q^2 + 2qt + 2qv + 2qw + 2tv$$

$$cDE = s^2 + 2su + 2sv + 2sw + 2uv$$

$$CdE = r^2 + 2rt + 2ru + 2rw + 2tu$$

$$Dde = t^2 + 2tw$$

$$cdE = u^2 + 2uw$$

$$cDe = v^2 + 2vw$$

$$cde = w^2$$

The calculated and observed frequencies are shown below:

<i>Classes</i>	<i>Observed</i>	<i>Calculated</i>
CDE	164	181.963
CDe	541	432.216
CdE	0	29.624
cDE	128	72.686
Cde	9	71.001
cdE	3	11.776
cDe	26	172.480
cde	129	28.224
Total	1000	999.970

Extreme deviations of the observed from the expected are readily apparent, and indicate that the genes responsible for the inheritance of the Rh antigens are not linked.

#### LITERATURE CITED

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- (2) **Fisher, R. A.** 1947. The Rhesus factor. *American Scientist* 35: 92-102, 113.
- (3) **Wiener, A. S., and E. B. Sonn.** 1946. *Annals of the New York Academy of Sciences* XLVI: 883-992.