Although the data presented here are admittedly meager, it would seem that the supernumerary chromosomes carry genes for pigment production which are similar to or the same as those on the normal chromosomes (*6*).

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Estimate of the Human Load of Mutations from Heterogeneous Consanguineous Samples

Abstract. A formula is presented for the calculation of the mean number of lethal and abnormal equivalents per person. It has been applied to Brazilian, French, and Japanese data.

A number of the methods for the estimation of the mutational load in man are based on procedures in which only one class of consanguineous marriages is used (see *1*). For samples containing marriages with different degrees of consanguinity, a more general formula may be developed as follows:

The probability that a zygote from a consanguineous marriage will be homozygous for any one of the alleles present at a specific locus in the common ancestors is given by the coefficient of inbreeding. Suppose that each one of the common ancestors, considered here to be average individuals, is a carrier of a rare deleterious recessive mutation. The probability that the zygote will be homozygous for derivatives of any one of the deleterious genes is given by $f/2$. If we suppose now that the average individual carries not one, as postulated above, but D deleterious recessive mutations, the probability of homozygosity for any one of the D deleterious genes turns out to be $Df/2$. This value can be obtained by analyzing the frequency, $\bar{x}$, of deleterious recessive homozygotes in the offspring of consanguineous marriages. Thus,

$$\bar{x} = Df/2 \quad \text{and} \quad D = 2\bar{x}/f \quad (1)$$

By a different reasoning Penrose (*2*) and Slatis *et al.* (*3*) came to the conclusion that in the special case of full first-cousin marriages ($f = 1/16$), $D = 32\bar{x}$.

Now, given the fraction of abortions, miscarriages, stillbirths, mortality from birth to the mean marriage age, and anomalies, due to homozygosity for recessive genes, we could obtain the mean number, per person, of lethal equivalents acting in the different stages of development, as well as the mean number of abnormal equivalents. The summation of all these values would give us the total mean number of deleterious equivalents per person:

$$D = \sum_k \frac{2\bar{x}}{f} \quad (2)$$

In samples containing not one but different types of consanguineous marriages, the frequency of homozygotes due to inbreeding is given by the mean coefficient of inbreeding:

$$\bar{f} = \sum_{j \neq 0} \frac{f_j n_j}{N} \quad (3)$$

where f_j is the jth coefficient of inbreeding, n_j is the number of pregnancies (for data on abortions and miscarriages) or children born (for stillbirths) or children born alive (for mortality from birth to the mean marriage age, and anomalies) associated with f_j, and N is $\sum_j n_j$. A rigorous analysis would score a monozygous twin pregnancy as one event and a dizygous twin pregnancy as two, but the use of any pregnancy—single or twin—as one event will introduce only a trivial error. Substituting for f in formula (2) the value $\bar{f}$, we obtain:

$$D = \sum_k \frac{2N\bar{x}}{\sum_{j \neq 0} f_j n_j} \quad (4)$$

In cases of mortality it is impossible to differentiate deaths caused by recessive genes from those caused by other factors. In such cases, as well as for anomalies in general, the frequency $\bar{x}$ of recessive homozygotes cannot be detected. It is possible, however, to obtain a rough estimate of $\bar{x}$ by subtracting the rates of mortality or anomalies in a suitable control sample (S_c) from those rates in the consanguineous (inbred) sample (S_i). Substituting (S_i-S_c) for $\bar{x}$ in formula (4), we get

$$D = \sum_k \frac{2N\,(S_i - S_c)}{\sum_{j \neq 0} f_j n_j} \quad (5)$$

that is, an estimate of the mean number of deleterious equivalents per individual. This formula does not correct for the error introduced into the data by those deaths where the individual was simultaneously homozygote for two or more lethals, or semilethals. Since the probability of this event is rather small, the error introduced would appear negligible.

When S_i is lower than S_c, D will take a negative value. This will not have genetic meaning with respect to deleterious equivalents and may be interpreted as an accident of sampling. If D is based on large samples, a negative value may be interpreted as indicating a very low mean number of deleterious equivalents per person.

Formula (5) has been applied to data on abortions plus miscarriages, stillbirths, and mortality from birth to the mean marriage age, from some Brazilian populations (*4*). The mean number of lethal equivalents per individual in the whole sample has been found to be 1.55. A large difference was found, however, between the two ethnic groups involved in the analysis; the mean number was −0.37 for Caucasians (almost all of Portuguese ancestry) and 9.12 for Negroes (*5*). The method of Morton, Crow, and Muller (*6*) has also been applied to these Caucasian and Negro data and lead to estimates close to those obtained according to formula (5): −0.24 for Caucasians and 10.46 for Negroes (*1*).

Formula (5) has been applied to Schull's (*7*) and Sutter and Tabah's (*8*) data and gave results similar to those obtained by the method of Morton *et al.* (*6*; *9*).

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