where $(S_t/S_c) = 1 - M$, n is the mean number of common ancestors per consanguineous couple (in practice, n may be accepted as equal to 2), and F is the mean coefficient of inbreeding of the inbred sample.

The present method is very sensitive, since a difference of only a few per cent between P_c and P_t may lead to relatively high values of B. Therefore, it is not to be applied uncritically to all sorts of data from the literature. Among the best data to be used with our present approach are those of Marçallo, Freire-Maia, Azevedo, and Simoes (Inbreeding effect on mortality and morbidity in South Brazilian populations. *Ann. Hum. Genet.* 27: 203–218, 1964), where $P_c = 0.2049$ and $P_t = 0.2022$. The application of formulas (1) and (3) to these data led to an estimate of 0.25 lethons. These authors estimated 0.74 lethons in the form of abortions and miscarriages from about the second to the sixth month of pregnancy inclusive.

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A SEARCH FOR NATURAL SELECTION

Dear Sir:

Reed *et al.* (*Amer. J. Hum. Genet.* 16: 161–179, 1964) reported six of ninety tests of blood group selection to be significant at the .01 level and concluded "no simple explanation for these effects is apparent." I wish to suggest the simplest of all explanations, that the level of significance is incorrect.

In Table 4, they present an analysis of the Kell system in which the mean square for each effect is tested against an error variance that is based on the residual variation among families within mating types. This F test is above reproach. However, in the rest of the paper they use a χ^2 test based on a theoretical error variance which assumes that among families there is only binomial variation. This assumption is incorrect in two respects: (1) Means vary among families for both genetic and environmental reasons; (2) in some of the analyses, the family means were adjusted by regression analysis, which introduces a component of variance due to deviations of the independent variables from their sample mean. Had this residual variation among families within mating types been taken into account, it is likely that at least some of the reported effects would become nonsignificant.

The use of a χ^2 test which neglects nonbinomial variation is all too common. Lewis *et al.* (*Amer. J. Hum. Genet.* 15: 53–61, 1963) exaggerated the significance of segregation discrepancies by lumping together in a contingency

table families from carrier and noncarrier parents. Morton, Crow, and Muller (*Proc. Nat. Acad. Sci.* 42: 855–863, 1956) found evidence for a nonlinear inbreeding effect in Arner's study which probably would have been nonsignificant if residual variation among families within inbreeding levels had been taken into account. Undoubtedly much of the apparently significant variation among populations in estimates of genetic loads, if not due to confounding of social variables with inbreeding, is due to failure to estimate this error variance among families.

It is of course possible to eliminate the effects of nonbinomial variation by taking only one child per family, since the error for families of size s is $pq + (s-1)\sigma^2$ for a proportion p, and it is $821 + (s-1)\sigma^2$ for arc sine transformed p, where σ^2 is the nonbinomial variance. However, this throws the baby out with the bath water by discarding information about the way in which risks vary among families, a parameter of great genetic interest, especially to differentiate sporadic and high-risk mechanisms for complex traits.

Human biologists should worry more about the validity of the error variance in tests of hypotheses and interval estimation.

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REPLY TO DR. MORTON: MAGNITUDE OF NONBINOMIAL VARIATION IN FAMILY DATA

Dear Sir:

Dr. Morton makes two main points in the preceding letter: (1) that we (T. E. Reed, H. Gershowitz, H. Soni, and J. Napier, *Amer. J. Hum. Genet.* 16: 161–179, 1964) neglected sources of nonbinomial variation in calculating some of our error variances and (2) that the omitted variation is sufficiently large that had it been included some of our reported effects would become nonsignificant. The first observation is true. We followed the common practice of using a theoretical (binomial) error variance of 821 for our arc-sine transformed proportions. The second point, however, is Dr. Morton's assertion, offered without evidence. We would like to consider this point further.

We studied six indicators: (1) number of pregnancies, (2) proportion of couples who were sterile after at least ten years of marriage (wife married under 30 years of age), (3) proportion of pregnancies terminating in spontaneous abortions, (4) ditto in stillbirths, (5) ditto in fetal deaths, (6) proportions of liveborn children dying nonaccidentally under five years of age. As Dr. Morton illustrates for the Kell system, the analysis of (1) has its own estimate of within mating type variation and so is correct. Consequently, the two results which involve (1), wife's Kell group, and wife's joint ABO-Rh group are unaffected. Indicator (2), in addition, is correctly analyzed, even though there is a theoretical binomial error variance (821), because there is only one observation per couple (sterile or fertile) and so, as Dr. Morton notes, there