GENETIC AND SOCIAL SIGNIFICANCE OF DIFFERENTIAL FERTILITY

II. A STATEMENT OF GENERAL PRINCIPLES AND CONCEPTS OF POPULATION GENETICS

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THE first half of the present century has witnessed the extensive development of the principles of genetics. The formulation of these principles was brought about largely through careful laboratory analyses. Only recently has careful attention been given to the study of human genetics. As that study has progressed, it has become apparent that there are important differences between the genetic analysis of human populations and the genetic analysis of laboratory animals.

The laboratory study is *experimental;* that is to say, the matings are controlled in a uniform environment and made according to a definite plan in the mind of the experimenter: a plan designed to test the genetic nature of a trait by specifying the mating so that observable Mendelian ratios may result. Through examination of these ratios, the genetic basis for a trait may be estimated.

Human matings, on the other hand, occur largely at random as far as most gene pairs are concerned, and the number of offspring in a single family is small. It is thus difficult to specify the *genotype* of each individual. Collections of families must therefore be classified largely by *phenotypic* characters. The result is that even the best classified data will contain mixtures of different types of mating.

All the types of mating which the geneticist needs to analyze a trait are probably present in any considerable population of people, but they are largely incapable of being accurately sorted out. Under such circumstances, involving large populations

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breeding more or less at random, it becomes necessary to invoke certain concepts which need not ordinarily be considered in laboratory analyses. These concepts are the proportions in the population of a gene and its alleles (alternative conditions), and the proportions of the genotypes formed by a gene and its alleles. Thus the genetic analysis must be made, not on the basis of Mendelian ratios, but on the basis of population ratios. In other words, the study of human genetics is largely a study of population genetics.

The concepts of population genetics may be formulated as principles. Some of these principles are germane to this round-table discussion.

1. Classical Mendelian ratios are not to be expected in random samples from a free-breeding population, nor even necessarily among the offspring of a group of families classified together because the parents in any one family are phenotypically identical with the parents in any other family. Classical Mendelian ratios are to be looked for only among the offspring of a large family, or within a collection of families where the parents in any one family are *genotypically* identical with the parents in any other family.

2. Although classical Mendelian ratios are not to be expected among the offspring in a collection of families where the parents are of variable genotypes, even though of identical phenotypes, nevertheless predictable ratios do occur under such situations. These ratios are *population ratios,* in contrast to Mendelian ratios. They are expressed in terms of the proportions in the population of the genes concerned, and they vary as these proportions vary. Thus, where a common Mendelian ratio is, for example, $\frac{3}{4}:\frac{1}{4}$, an equally common and analogous population ratio is $\frac{1+2q}{(1+q)^2}:\frac{q^2}{(1+q)^2}$, where q is the proportion of the recessive gene in the population.

3. A demonstrated correlation between the occurrence of two traits in a randomly breeding population does not necessarily indicate linkage between the genes for these two traits.

4. In a large population, with the effects of mutation, selec-

tion and migration negligible or balancing each other, the proportions of the alleles of any set will remain constant from generation to generation. Furthermore, under a system of random mating, the proportions of the genotypes will likewise remain constant. This means that in a large human population, with no appreciable effects of mutation, selection, or migration, the frequency of a hereditary trait will remain constant from generation to generation.

5. The respective proportions of the alleles of a set may, however, be changed by any one of the above phenomena (mutation, selection, and migration), and, particularly in small populations, by still another process, random drift of gene proportions. Under selection would be included differential fertility.

6. Differential fertility will change the respective proportions of the alleles of any set, and thus presumably the proportions of the traits determined by these genes, provided that

a. The groups having differential fertility differ one from the other in regard to the occurrence of the trait, and

b. The trait concerned is dependent, at least to some appreciable extent, upon genetic factors.

7. Assortative mating in regard to the trait will increase the rate of the effect of differential fertility.

8. Dominant genes can readily be eliminated by complete selection against them, or partially eliminated in proportion to the degree that selection is used (for example, the degree of differential fertility).

9. Recessive genes can never be completely eliminated by differential fertility, even if selection against them is complete. The proportions of such genes can, however, be reduced by differential fertility.

10. Selection against *common* recessive traits is markedly effective at first, less and less so as the genes for the trait become rarer. This effect may be exactly specified. If, under a system of random mating, a recessive trait occurs in 17.2 per cent or more of the population, the trait can be cut to one half of its former frequency or less in a single generation of complete selection against it. Expressed in another way, the half life, under complete adverse selection, of a recessive trait occurring in 17.2

Table 1. A table to show the reduction in frequency of a recessive trait in a large population if complete selection against the trait occurs.

FREQUENCY OF A RECESSIVE TRAIT IN THE POPULATION

	.005	.010	.020	.030	.040	.050	.100	.200	.300	.400	.500	.600	.700	.800	.900	.990
Original Frequency	.005	.010	.020	.030	.040	.050	.100	.200	.300	.400	.500	.600	.700	.800	.900	.990
After 1 Generation	.004	.008	.015	.021	.028	.033	.057	.095	.125	.150	.172	.191	.208	.223	.237	.249
After 2 Generations	.003	.007	.012	.016	.019	.024	.037	.055	.068	.078	.086	.093	.098	.103	.107	.111
After 3 Generations	.002	.006	.009	.013	.015	.018	.026	.036	.043	.047	.051	.055	.057	.059	.061	.063
After 4 Generations	.001	.005	.008	.011	.012	.014	.019	.025	.029	.032	.034	.036	.037	.038	.039	.040
After 5 Generations		.004	.007	.009	.010	.011	.015	.018	.021	.023	.024	.025	.026	.027	.027	.028
After 6 Generations		.003	.006	.008	.008	.009	.012	.014	.016	.017	.018	.019	.019	.020	.020	.021
After 7 Generations		.002	.005	.007	.007	.008	.010	.011	.013	.013	.014	.015	.015	.015	.015	.016
After 8 Generations		.001	.004	.006	.006	.007	.008	.009	.010	.010	.011	.012	.012	.012	.012	.013
After 9 Generations			.003	.005	.005	.006	.007	.008	.008	.008	.009	.010	.010	.010	.010	.011
After 10 Generations			.002	.004	.004	.005	.006	.007	.007	.007	.008	.008	.008	.008	.008	.009
After 11 Generations			.001	.003	.003	.004	.005	.006	.006	.006	.007	.007	.007	.007	.007	.008
After 12 Generations				.002	.002	.003	.004	.005	.005	.005	.006	.006	.006	.006	.006	.007
After 13 Generations				.001	.001	.002	.003	.004	.004	.004	.005	.005	.005	.005	.005	.006
After 14 Generations						.001	.002	.003	.003	.003	.004	.004	.004	.004	.004	.005
After 15 Generations							.001	.002	.002	.002	.003	.003	.003	.003	.003	.004
After 16 Generations								.001	.001	.001	.002	.002	.002	.002	.002	.003
After 17 Generations											.001	.001	.001	.001	.001	.002
After 18 Generations																.001

per cent of a randomly breeding population, is one generation. Under. similar circumstances, the half life of a recessive trait occurring in four per cent of the population is two generations; that of a recessive trait occurring in two per cent of the population is three generations; and that of a recessive trait occurring in but one per cent of the population is four generations.

As a trait due to a recessive gene becomes rarer, its half life becomes longer.

Differential fertility implies that adverse selection is not complete, hence the half life of a trait in such circumstances becomes correspondingly longer.

The essential things to be established in order to specify the genetic implications of differential fertility are, then, these:

1. Does differential fertility actually exist between certain groups? If so, what is the extent of the differential fertility?

2. Do these groups actually differ in regard to the proportions of a specific trait? If so, what are the respective proportions of the trait in the various groups?

3. Is the trait genetically determined? If so, what is the mode of transmission?

4. Does assortative mating occur in regard to the trait? If so, what is the nature and extent of the assortative mating?

Given the answers to these questions, the geneticist can specify the expected genetic results of differential fertility.

Assume a large population breeding at random, and being in equilibrium for a pair of alleles A and a, where p is the proportion of A and q is the proportion of a. The genotypes in the population will occur in the equilibrium ratio $p^2AA + 2pq\,Aa + q^2aa = 1$. Further assume the instituting of complete selection against the genotype aa. The proportion of aa individuals produced in the next generation will then be $q^2/(1 + q)^2$. These individuals will, of course, be produced entirely from matings of heterozygotes Aa (Snyder 1934).

Table 1 shows the effect of complete selection against the recessive phenotype starting with various proportions in the original generation.

Where selection against the recessive phenotype is not complete, such as in differential fertility, the calculation of the diminishing proportions of recessives is more complex. Haldane (1931) has presented a formula for these calculations as follows:

$$n = 1/k(u_n - u_o - \log_e u_n/u_o)$$

where

n = number of generations required to change the value of u from u_o to u_n;

u = ratio of the frequency of a given dominant gene to its recessive allele;

k = coefficient of selection against the recessive phenotype. If k, for example, is 0.01, the proportion of offspring from dominant and recessive parents, respectively, will be 1:0.99 instead of 1:1.

Haldane's formula may also be written in terms of the more usual gene proportions p and q, as follows (David, personal communication):

$$n = 1/k[1/q_n - 1/q_o + \log_e(p_n/q_n) - \log_e(p_o/q_o)]$$

Selection is extremely slow, but nevertheless effective, even with low values of k. The greater the initial proportion of the recessive phenotype, the more rapidly will selection reduce this proportion in the early generations. The rate of reduction becomes less as the proportion diminishes. With a selection coefficient of 0.01, it would require 1,090 generations to reduce an initial recessive phenotype proportion of 0.9999 to 0.25, but 1,020 generations to reduce it from 0.25 to 0.01.

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