TABLE 1

Rat No.	Rat shaved	Wt of rat (g)	Length of immersion (hr)	D_2O in immersion liquid (mole %)	D_2O in blood (mole %)
1	yes	119	7	41.0	3.27
2	"	128	6½	40.6	0.72
3	no	118	6½	42.2	1.37
4	"	110	6½	40.9	1.42
5	"	118	6	40.1	0.70
6	yes	140	6	39.1	.80
7 (control)	no	152	6	0.0	.0
8 (")	"	170	5½	.0	.0
9 (")	"	198	6	.0	.0
10 (")	"	200	6	0.0	0.0

purified, and analyzed for deuterium content by the method of Keston, Rittenberg, and Schoenheimer (*9*). The results of these analyses are presented in Table 1.

It is evident from Table 1 that the deuterium oxide content of the blood of the test animals varied considerably even though they had been immersed in deuterium water for approximately the same period of time. The average deuterium oxide content of the blood of this group of animals was 1.38 mole %. The high deuterium oxide content of the blood of the test animals as compared with the controls is proof that the heavy water in which they were immersed penetrated through the skin and entered the systemic circulation.

It may be suggested that this D_2O entered the body in inspired air. This is not possible, for, if it is assumed that the air was 100% saturated with 40% deuterium oxide, and that all the deuterium oxide was retained by the lungs, rat No. 5 would have had to inhale about 840 liters air/min to reach a blood value of 0.70 mole % after 6 hr.

In three instances the fur from the trunk portion of the animal was removed by clipping and by an application of adhesive tape, two days before the immersion. This did not appear to influence the penetration of deuterium oxide, possibly because the hair did not interfere with the wetting of the skin of the immersed animal.

In a subsequent series of experiments (Table 2) rats were held so that only their tails were immersed in about 40% deuterium oxide. After the tails had been immersed for approximately 6 hr, the average content of deuterium oxide in the blood was 0.12 mole %. A rough calculation indicates that the area of the tail is approximately 1/10 the area of the whole body of these rats. It would seem, therefore, that on a square cm basis the rate of penetration of deuterium oxide through the skin of the body and the skin of the tail was the same.

TABLE 2

Rat No.	Tail length	Length of immersion	D_2O in blood (mole %)
11	—	6½ hr	0.08
13	7 in.	6 "	.18
13	6 13/16 "	6 " 10 min	.23
14	6 10/16 "	6 " 10 "	.08
15	6 8/16 "	5 " 45 "	.07
16	6 8/16 "	5 " 45 "	0.09

These experiments were not designed to determine whether a loss of water molecules through the skin had taken place. It cannot be stated dogmatically that there was a net uptake of water, a fact which all earlier investigators (*1, 2, 3, 5*) attempted to demonstrate. Indeed, it is possible that their results were indefinite because there was an exchange of water molecules.

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Social Fitness versus Reproductive Fitness

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It has been an axiom in genetics that if a mutant gene is to spread in a large population it must confer a selective advantage upon the individuals in which it occurs. In the broadest sense this axiom is true for man as well as for other organisms. One reason for a more detailed consideration of specific genes in man is that a deleterious gene that lowers social fitness could increase reproductive fitness.

Social fitness could be measured by an individual's contributions to civilization in the form of cultural heredity. Such gifts to the present and future might be either material or intellectual or both.

Reproductive fitness could be measured by an individual's contribution of his genes to future generations as demonstrated by the number of his descendants. The exact wording of these definitions may be ignored, but the ideas expressed are useful for an understanding of this paper. The "fitness" of a genotype has been defined in detail by Fisher (*1*), by Haldane (*2*), and by Penrose (*3*), and they use the term "fitness" as a measure of reproductive effectiveness. Consequently, the idea of reproductive fitness is well established in human genetics.

The presence of an inverse correlation between the

cultural and the biological contributions of the individuals of any particular generation has been demonstrated repeatedly. It is still impossible, however, to evaluate the effects of this inverse correlation upon the genetics of future generations. The difficulties involved in the genetic study of an important social character, such as intelligence, are many. It is possible, however, to study the relationship between social fitness and reproductive fitness when a clear-cut dominant gene such as that for Huntington's chorea is present.

An extensive study of Minnesota families containing the simple dominant gene for Huntington's chorea has just been completed by one of us (J. D. P.) and will be published in full elsewhere. We came upon the problem in this way. The state director of social welfare requested an opinion as to the advisability of placing a child for adoption whose grandmother had a "nervous disease." The family denied that any other relative had this same disease. The authors soon discovered that there were many close relatives with the disease, which was diagnosed as Huntington's chorea. The disease has been named by the members of the family after the original Minnesotan from whom they descended. It is feared and dreaded by all, and justly so, as it causes social damage to every member of the family, as well as the death of those who inherit the gene.

The original migrant to Minnesota was a man we shall call A. He was born in 1831 and came here accompanied by his brother, B, born in 1834. They adopted a new family name with the hope that their past would be left behind them. Unfortunately this was not to be the case. Their past was to be their future as well. The rich new lands of Minnesota offered great opportunities for those free from genetic defects—but A was not free. The two brothers each produced 10 children. As time passed, A and some of his descendants developed Huntington's chorea. The brother, B, and his descendants escaped the gene for the disease. They attempt to dissociate themselves from the affected branch of the family and have been partly successful in escaping the social consequences of the gene possessed by their relatives.

The effect of the gene for Huntington's chorea upon social and reproductive fitness is easily seen in the branches of this family. The onset of chorea lowers the economic standing of the family because the affected parent loses employability shortly after the onset of the disorder. Furthermore, a second member of the family must often give up employment in order to care for the choreic member. This loss tends to lower the social class of the family, and the stigma of the parent's disease will force the children to accept mates from a lower social stratum (if any) than their own. With the gradual drop in social class the reproductive rate may be expected to rise, and the deleterious gene must increase also in relation to its normal allele in higher social strata.

The continuing effect, as the generations pass, of the Huntington's chorea gene in depressing social fitness and stimulating reproductive fitness is easy to ascertain at the local scene and can be expressed quantitatively by tabulating the number of descendants of the two brothers.

There have been 787 descendants of A, of whom 716 are living. It will be recalled that B also produced 10 children, but he has only 186 descendants, of whom 167 are living. There are thus slightly fewer than 1/4 as many descendants of B as of the affected brother, A. It should be emphasized that great diligence has been exercised in checking the descendants of both brothers in order to be certain that every child born in each generation has been carefully accounted for regarding his own reproduction, both legitimate and illegitimate.

Although the descendants of A are 4 times as numerous as those of B, it should be evident that B has many more descendants than would be expected from a man of average social standing. An example of the opposite extreme, which appeared in the Minneapolis *Tribune,* comes from the genealogy of a former prominent citizen, Governor John S. Pillsbury, who was born in 1827 and came to Minnesota at the same time as the two brothers. There have been 19 descendants of the governor, of whom 15 are living. Of the 898 *living descendants* of these three contemporaries, 80% are from the choreic A, 18% from B, and 2% from the governor. This is a quantitatively established example of differential fecundity for the gene pair concerned with Huntington's chorea.

It would be useful to determine the rate of increase that might be expected among the descendants of an "average" man born in 1830. Unfortunately, such calculations would be difficult to make because of the effect of subsequent immigrants and their descendants upon the rate of increase. The increase in life expectancy would also confuse the issue. Consequently, we have had to content ourselves with comparing the number of descendants of the 3 men with the number just needed in a hypothetical stationary population to replace the original man and his wife and the unrelated persons who marry his descendants. In simplest terms there would have to be 2 children, 4 grandchildren, 8 great-grandchildren and 16 great-great-grandchildren, a total of 30 required descendants. Actually, the average man will have produced many more than this, inasmuch as the population has not been stationary. But the average man of 1830 failed dismally to equal the performance of A, who has 787 descendants credited to him. This is 26 times the stationary replacement figure. Even B, with 186 descendants, gives a value of 6 times the replacement figure. On the other hand, the 19 descendants of Governor Pillsbury account for only 6/10 the number required for replacement.

There is an interesting additional effect of the gene for Huntington's chorea, an effect acting directly upon the fecundity of the affected person. The effect apparently occurs well before the onset of the disease. The

number of children ever born from affected persons was compared with the number ever born to their unaffected sibs, for all Huntington's chorea pedigrees worked out by us. The average number of children from affected individuals was 6.07 ± 0.9, and from unaffected sibs 3.33 ± 0.5. The difference between these means is 2.74 ± 1.03 and is statistically significant. A similar difference was also present in the entire material from the literature. It was present, consistently, when the sexes of the affected and unaffected persons were treated separately, when surviving children were compared with those ever born, both for the Dight Institute material and the literature. Eight different comparisons all gave excesses for the affected. (Our explanation for these differences is not well enough established to include here.)

Let us return to the effect of social class upon the spread of a medically deleterious, but reproductively advantageous, gene such as Huntington's chorea. Brother A and 18 of his descendants have already had the disease in extreme stages, usually accompanied by commitment to a state institution. A number of others are in early and moderate stages of the disease. It is a simple matter to calculate the number of expected descendants of A, now living, who will eventually develop the disease, which has a late onset in this family. In addition to the 19 obvious cases, we expect 101 additional cases if those persons with the gene reach their age of onset. This would make a total of 120 cases, a remarkable rate of increase for the gene introduced by this one man. These patients will cause great trouble and expense before their deaths, which are usually the result of exhaustion. It is practically impossible to care for them at home during the last few years of the disease; consequently, the state assumes the burden.

Patterson, Bagchi, and Test (*4*) have indicated that it is possible to detect a potential case of Huntington's chorea before the reproductive age, by means of the electroencephalograph. The descendants of A offer excellent material for testing the usefulness of the electroencephalogram in detecting Huntington's chorea early enough so that a voluntary eugenics program could be undertaken. Even partial success would be of value, although the psychological approach to the potential victims of the disease would have to be skillful.

An extensive program of testing the descendants of A with the electroencephalograph has been begun. They are also submitting most graciously to the Wechsler-Bellevue intelligence test and to the Rorschach and the Minnesota Multiphasic Personality tests. It is hoped that these latter tests may give some hint as to personality differences that would account for the greater fecundity of persons who will later acquire the disease.

This study demonstrates the way in which the dominant gene for Huntington's chorea has spread, not only because it increases the fecundity of the affected person compared with unaffected sibs, but also because the social stigmata connected with the disease confine the close relatives to the lower social strata. Persons with little education (and usually lower social fitness) have higher than average reproductive fitness, as shown by the U. S. census. This situation favors the spread of the gene for Huntington's chorea.

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A Rich Source of γ-Carotene[1]

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In 1940, Emerson and Fox (*1*) reported the occurrence of a high concentration of γ-carotene in the male gametangia of the Phycomycete water-mold *Allomyces*. These workers concluded that the synthesis and storage of carotenoids are usually associated with the processes involved in the metabolism of reproduction. Later, Smits and Peterson (*2*) showed that the orange color of the expanded telial galls of the rust fungus (*Gymnosporangium juniperi-virginianae* Lk.) was due in part to carotenoids, of which 36% was the rare γ-isomer.

The heteroecious rust fungus (*Gymnosporangium juniperi-virginianae* Lk.) produces telial galls on the common juniper (*Juniperis virginiana* L.) and pycnia and aecia on the leaves, young twigs, and fruit of apple species and related genera. The telial spores produced by the telial galls in the spring infect the apple and produce two types of injury on the leaves, the epiphyllous pycnidial lesions and the hypophyllous aecia (Stevens, *3*).

An investigation of the carotenoid pigments of the pycnidial lesions of crab apple leaves caused by this rust fungus was undertaken in the spring of 1950. Owing to the unusual distribution of rainfall, there was an abundance of leaves that had reached full maturity before they had become infected. The leaves used in this work were harvested June 10, 1950, at the first appearance of a deterioration of the pigments as indicated by the darkening of the pycnia. Approximately 80% of the leaf surface was covered with these lesions. The leaves were placed in pint fruit jars, tightly sealed, and held at –17.4° C until analyzed June 17, 1950.

The pigments were extracted by blending 2 g of leaves in a Waring blendor for 5 min in a mixture of 60 ml ethanol and 150 ml of a mixture of petroleum hydrocarbons[2] consisting principally of hexane (bp 60°–70°) according to the Wall-Kelley (*4*) method. It was obvious from examination that the extraction

[1] Contribution No. 420, Department of Chemistry.
[2] Skellysolve B, Skelly Oil Co., Lyman, Okla.