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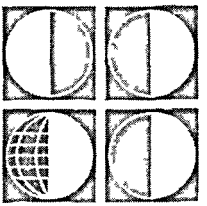
A Eugenic Effect of Medical Care



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ABSTRACT: When sophisticated medical attention substantially increases the life expectancy of individuals with a severe homozygous condition without significantly raising their reproductive success, an increase in parental investment should render a concomitant decrease in parental ability to reproductively compensate. This process will lower the expected number of heterozygous carriers produced by heterozygous parents and, in turn, will lower the equilibrium frequency of the gene.

In the absence of a heterozygote advantage, recessive genes that render a deleterious condition will naturally decrease in frequency, albeit slowly, until their existence depends on the mutation rate. For purposes of this paper, a *eugenic effect* is an effect that accelerates this rate of decrease and/or lowers the frequency at which equilibrium is attained. A *dysgenic effect* is one that decelerates that decrease and/or elevates the equilibrium frequency. That modern medical care can have an inadvertent eugenic effect on the frequency of genes that confer a lethal homozygous condition, though less obvious than its converse, proceeds in a straightforward manner when the following terms are related to each other as indicated: Medical Care↑→Homozygote Longevity↑→Heterozygote Parental Investment↑→Heterozygote Reproductive Compensation↓→Heterozygote Selective Disadvantage↑→Gene Frequency↓.

The key concepts in this paradigm are *parental investment* (PI) and *reproductive compensation*. Parental investment, as defined by R. L. Trivers (1972), is a reproductive cost function whose measurement is made "by reference to its negative effect on the parent's ability to invest in other offspring: a large parental investment is one that strongly decreases the parent's ability to produce other offspring" (p. 139). This definition rests on the assumption that a given set of parents possesses some finite amount of resources that can be expended on bearing and rearing offspring. Since there is no necessary relationship between the size of an investment and the return on that investment, a given individual offspring may consume more or less than the amount of PI required to rear an average offspring. Accordingly, a set of parents possessing the PI required by four normal offspring may have three or five offspring, depending on the amount of PI required by their particular children (cf. Hartung, 1977). The "expenses" incurred by childbearing and childrearing involve any limiting factor; they can be biological, emotional, temporal, material, etc. For example, during pregnancy, a woman's investment is very high for about eleven months, not so much as a result of her offspring's energy requirements, but because she can not be reimpregnated during this time.

Reproductive compensation simply refers to the fact that parents can almost completely "compensate," in terms of re-

productive success, for children who are nonreproductive *if* such children do not consume much PI. For example, a conceptus that is spontaneously (or therapeutically) aborted in the first trimester is not likely to have consumed an amount of PI that will significantly affect a parent's total reproductive success. The relationship between PI and reproductive compensation is inverse while the relationship between longevity and PI is direct (Figures 1 and 2).

The importance of this consideration lies in its effect on the fitness of a gene that is lethal in the homozygous state, but which does not directly affect the reproductive success of heterozygous carriers (does not reduce the size of the F_1 generation). In this situation, the longevity of the homozygote can affect the number of heterozygotes produced by carrier parents. That is, a long-lived high-PI-consuming homozygote will have a greater negative effect on his parent's reproductive success than will a short-lived low-PI-consuming homozygote.

If the prevailing medical environment greatly increases the life expectancy of a homozygote, it can be seen that such an environment will increase the disadvantage of the heterozygous parents. As a hypothetical example, consider two sets of parents (A and B) in which: (1) each parent carries the gene that is lethal in the homozygous state; (2) each couple has the PI resources required by four normal children; (3) the couples live under extremely disparate medical conditions; and (4) the

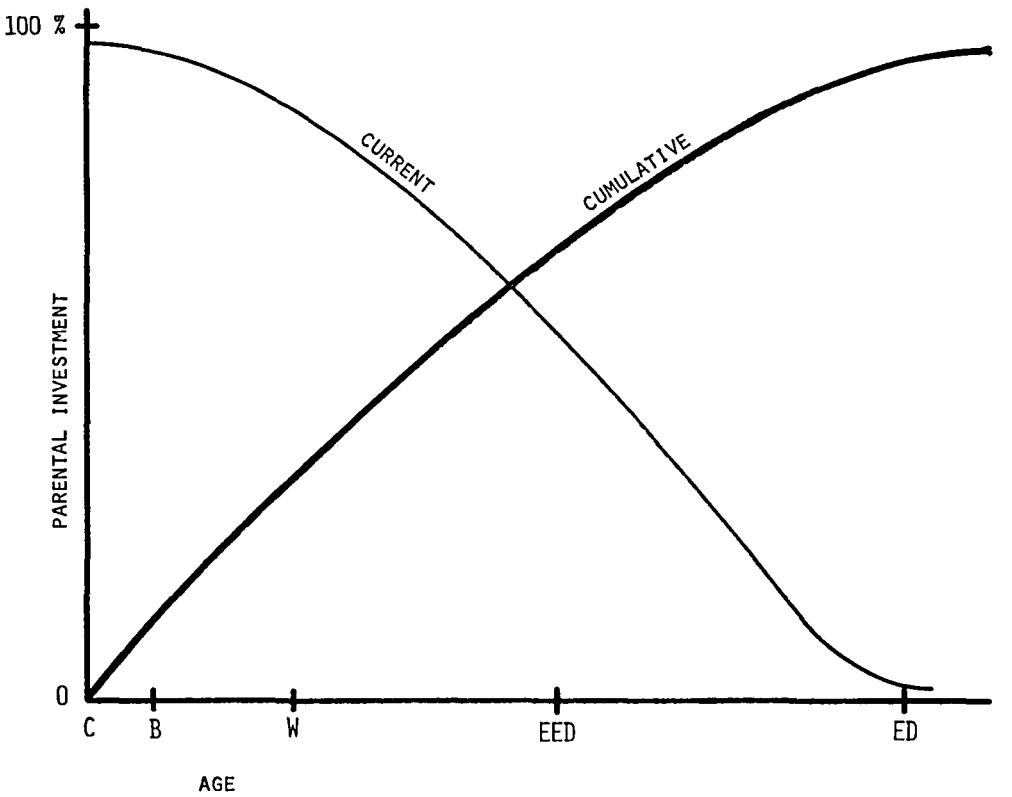

FIG. 1.—Consumption of parental investment (current and cumulative) as a function of age. C = conception, B = birth, W = weaning, EED = end of early dependency period, and ED = end of dependency.

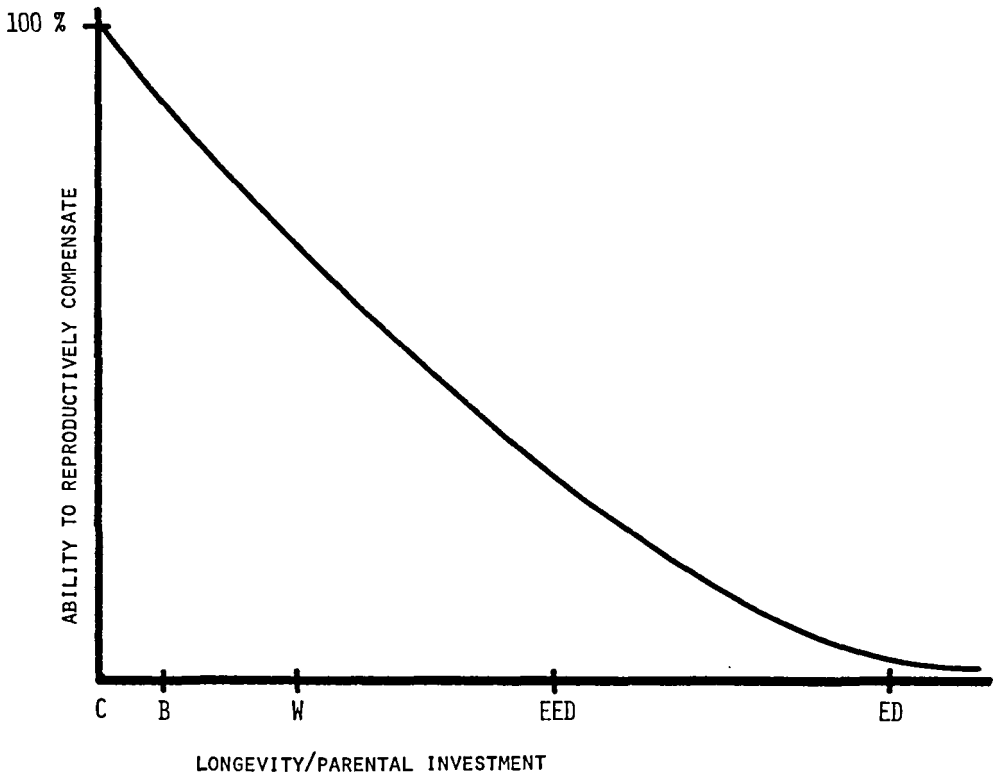

FIG. 2.—As longevity and parental investment increase, parental ability to reproductively compensate diminishes. Horizontal axis designations are as in Figure 1.

life expectancy of the homozygote depends on medical care. If couple A lives in a medically unsophisticated environment such that their homozygous offspring (p = 0.25) will not survive long enough to reduce their ability to reproductively compensate, they will have four offspring. None will be homozygous recessive, but each will have a 0.66 probability of being a carrier (expected number of heterozygotes $\simeq$ 2.7). If couple B's medical situation allows their homozygous offspring to survive long enough to consume the amount of PI normally required by one offspring, couple B will also produce four offspring (expected: 2 carriers, 1 homozygote, 1 noncarrier). Assuming conditions to be constant for A's and B's children, couple A will have 16 grandchildren with an expected number of carriers $\simeq$5.33 if such grandchildren are not conceived by cross with an exogenous carrier (the expected number of heterozygotes will increase according to the frequency of the gene and the resultant probability that one of A's children will mate with a carrier). Couple B, with a continuous medical advantage, will have only 12 grandchildren, and the expected number of carriers will be 4. This effect does *not* require that the homozygote consume more PI than a normal offspring, though such children often drain parents of more resources, especially emotional and material, than do their healthy siblings. Reproductive compensation can be categorized as *complete* (one for one replacement of lost homozygous offspring), *over* (replacement by more than one additional offspring), or *partial* (replacement by less than one additional off-

spring). The hypothesized eugenic effect occurs whenever the degree of compensation is reduced, especially when it is reduced to *negative compensation,* i.e., "replacement" of homozygous offspring by less than zero additional offspring (when the homozygote consumes more than normal PI). Of course, the possibility of negative compensation is greatly enhanced by the availability of effective contraception.

THE MODEL

The hypothesized selective disadvantage is not strictly "heterozygote disadvantage" in the common use of the term. That is, it does not represent a reduction in the viability or fertility of all heterozygotes, but refers only to the production of reproductive offspring by heterozygote-heterozygote crosses.

Consider a random mating situation with initial genotype frequencies:

$$AA = x,$$
$$Aa = y,$$
$$aa = z.$$

Heterozygote-heterozygote crosses would normally occur with frequency y^2, producing offspring in a 1:2:1 ratio. If, however, the recessive a is lethal and parents are able to completely compensate for homozygous recessive offspring, two heterozygous parents will produce offspring in numbers proportional to their mating frequency, but in a 1:2 ratio, AA:Aa. Genotype frequencies in the next generation would be:

$$AA' = \frac{x^2 + xy + y^2/3}{(x + y)^2}$$

and

$$Aa' = \frac{xy + 2y^2/3}{(x + y)^2}.$$

If homozygous recessive offspring survived to consume a normal amount of PI, but did not reproduce, genotype frequencies in the next generation would be:

$$AA' = \frac{x^2 + xy + \tfrac{1}{4}y^2}{(x + y)^2},$$

$$Aa' = \frac{xy + \tfrac{1}{2}y^2}{(x + y)^2},$$

and

$$aa' = \frac{\tfrac{1}{4}y^2}{(x + y)^2}.$$

(Consumption of less than a normal amount of PI represents an intermediate case, but is more difficult to express mathematically.) If homozygous recessives consumed more than a normal amount of PI, and thereby reduced their parents' offspring production by a fraction s, the genotype frequencies in the next generation would be:

$$AA' = \frac{x^2 + xy + \tfrac{1}{4}(1 - s)y^2}{x^2 + 2xy + (1 - s)y^2},$$

$$Aa' = \frac{xy + \tfrac{1}{2}(1 - s)y^2}{x^2 + 2xy + (1 - s)y^2},$$

and

$$aa' = \frac{\tfrac{1}{4}(1 - s)y^2}{x^2 + 2xy + (1 - s)y^2}.$$

Numerical examples of these cases are presented in Tables 1–4 and Figure 3, illustrating the eugenic effect of medical

TABLE 1

CHANGE IN GENTOYPE AND GENE FREQUENCIES UNDER CONDITIONS OF COMPLETE REPRODUCTIVE COMPENSATION FOR HOMOZYGOUS RECESSIVES, STARTING FROM HYPOTHETICAL INITIAL FREQUENCIES

Generation	*AA*	*Aa*	*aa*	*q**
0	0.81	0.18	0.01	0.1
5	0.86229	0.13771	0	0.06886
10	0.88890	0.11110	0	0.05555
15	0.90678	0.09322	0	0.04661
20	0.91965	0.08035	0	0.04018
25	0.92936	0.07064	0	0.03532

* q = frequency of recessive gene a.

TABLE 2

CHANGE IN GENOTYPE AND GENE FREQUENCIES WHEN HOMOZYGOUS RECESSIVE CONSUMES NORMAL AMOUNT OF PI BUT DOES NOT REPRODUCE, STARTING FROM SAME INITIAL FREQUENCIES AS IN TABLE 1

Generation	*AA*	*Aa*	*aa*	*q**
0.....	0.81	0.18	0.01	0.1
5.....	0.87092	0.12462	0.00446	0.06677
10.....	0.90238	0.09512	0.00250	0.05006
15.....	0.92130	0.07709	0.00161	0.04016
20.....	0.93424	0.06463	0.00112	0.03345
25.....	0.94352	0.05556	0.00082	0.02860

* q = frequency of recessive gene *a*.

TABLE 3

CHANGES IN GENOTYPE AND GENE FREQUENCIES WHEN HOMOZYGOUS RECESSIVE CONSUMES ENOUGH PI TO REDUCE THE OFFSPRING PRODUCTION OF ITS PARENTS BY AN AMOUNT $s = 0.1$, STARTING FROM THE SAME INITIAL FREQUENCIES AS IN TABLE 1

Generation	*AA*	*Aa*	*aa*	*q**
0.....	0.81	0.18	0.01	0.1
5.....	0.87515	0.12103	0.00382	0.06434
10.....	0.90694	0.09098	0.00207	0.04756
15.....	0.92585	0.07285	0.00130	0.03773
20.....	0.93838	0.06073	0.00089	0.03126
25.....	0.94730	0.05205	0.00065	0.02668

* q = frequency of recessive gene *a*.

TABLE 4

CHANGES IN GENOTYPE AND GENE FREQUENCIES WHEN HOMOZYGOUS RECESSIVE CONSUMES ENOUGH PI TO REDUCE THE OFFSPRING PRODUCTION OF ITS PARENTS BY AN AMOUNT $s = 0.3$, STARTING FROM THE SAME INITIAL FREQUENCIES AS IN TABLE 1

Generation	*AA*	*Aa*	*aa*	*q**
0.....	0.81	0.18	0.01	0.1
5.....	0.88274	0.11456	0.00270	0.05998
10.....	0.91489	0.08373	0.00138	0.04325
15.....	0.93323	0.06593	0.00083	0.03380
20.....	0.94508	0.05436	0.00056	0.02774
25.....	0.95336	0.04624	0.00040	0.02352

* q = frequency of recessive gene *a*.

care relative to a situation of reproductive compensation.

If medical care not only extends the longevity of homozygous recessives, but also gives them a chance to reproduce, the hypothesized effect is quickly lost. The outcome would be dysgenic relative to the situation of total reproductive compensation. If homozygous recessives lived to produce a proportion r of the normally expected number of offspring, the genotype frequencies in the next generation would be:

$$AA' = \frac{x^2 + xy + \tfrac{1}{4}(1 - s)y^2}{t},$$

$$Aa' = \frac{xy + \tfrac{1}{2}(1 - s)y^2 + ryz + 2rxz}{t},$$

and

$$aa' = \frac{\tfrac{1}{4}(1 - s)y^2 + ryz + rz^2}{t},$$

where

$$t = x^2 + 2xy + (1 - s)y^2 + 2rxz + 2ryz + rz^2.$$

The value of r at which the situation becomes dysgenic depends on the associated value of s (Figure 4).

EXAMPLE

Cystic fibrosis is an important example ($\simeq$1 in 20 Caucasians is a carrier) of a recessive allele whose heterozygous fitness could be negatively affected by medical care. In 1938 the expected survival of homozygotes at 10 years of age was 1 per cent (Warwick and Poque, 1969), with an expected mean longevity of less than 1 year (Bowman, 1976). Today the expected survival at 12 years is 72 per cent (Holzel, 1975) in the United States, and 45 per cent at 20 years in Great Britain (Mearns, 1974), with a mean survival of 16 years (Bowman, 1976). While cystic fibrosis homozygotes have gained considerable longevity, their fertility remains negligible for purposes of significantly affecting the gene frequency (Taussig et al., 1972; Denning et al., 1968; Kaplan et al., 1968; Feigelson et al., 1969; Bumbalo, 1969; Rule et al., 1970; Holsclaw et al., 1971; Grand et al., 1966; Rosenow and Lee, 1968; Oppenheimer and Esterly, 1970). In

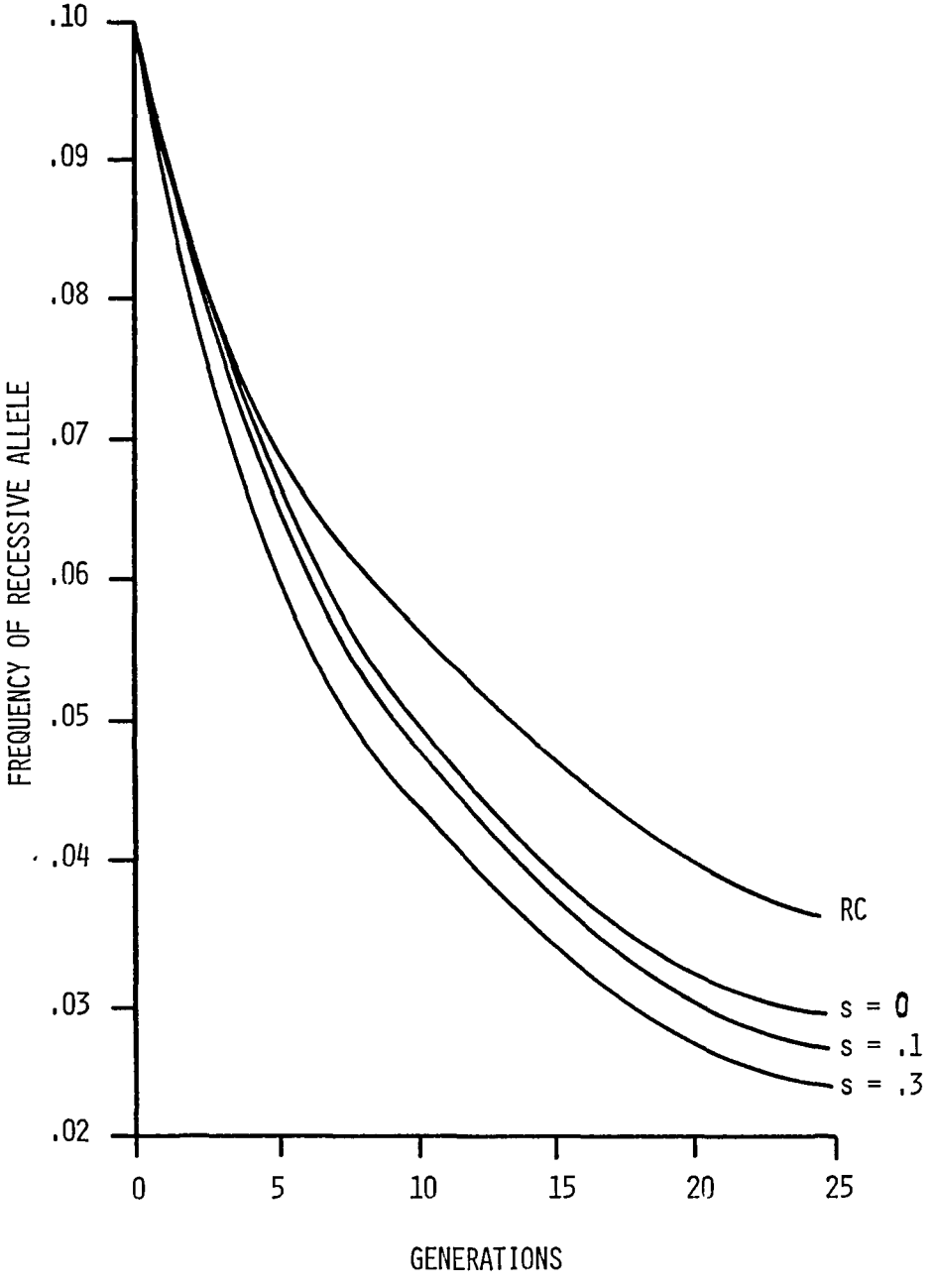

FIG. 3.—Change in gene frequency under conditions of total reproductive compensation (RC), normal PI consumption by homozygote recessive ($s = 0$), and excessive PI consumption ($s = 0.1$, $s = 0.3$).

a study of 31 couples, each with a CF child, Begleiter et al. (1976) found that 24 couples (77.4 per cent) had no further children after the birth of the affected child.

The sickle cell anemias provide examples of alleles whose frequencies are both negatively and positively affected by the medical environment. Classic sickle cell

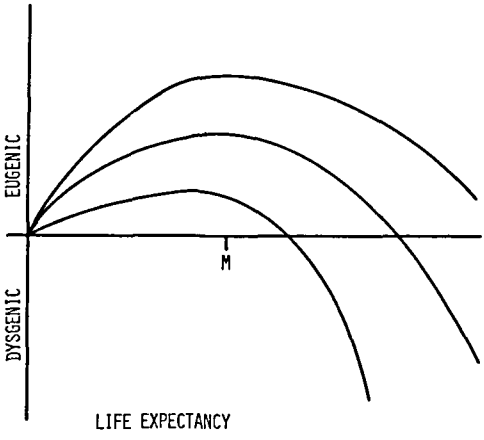

FIG. 4.—As medical care extends the life of homozygous recessives, the amount of PI they consume increases and the resultant eugenic effect is enhanced. However, as life expectancy extends beyond reproductive maturity (M) and homozygotes reproduce, the trend is reversed. Whether and when the effect becomes dysgenic depends on the amount of PI consumed by the homozygous recessive in attaining reproductive maturity.

anemia (HbS) homozygotes probably have sufficient reproductive success to counter any negative effect on their heterozygous parents (Billina and Bickers, 1974; Karayalcin et al., 1975; Powars, 1975; Anderson, 1971; Gima and Lee, 1975). In contrast to the HbS homozygote, whose fertility depends largely on medical care, HbC homozygotes have probably always had a sufficient probability of normal reproduction (Powars, 1975; Anderson, 1971; Gima and Lee, 1975; River et al., 1961). Like HbS homozygotes, information on HbC homozygotes has often been based on hospital populations, and the severity of the condition has been overestimated accordingly (Billina and Bickers, 1974; Powars, 1975; Gima and Lee, 1975; River et al., 1961; Attah et al., 1975). In contrast to both HbS and HbSC, severe homozygous β-thalassemia (thalassemia major, Cooley's anemia), especially in the form common to non-Black populations, exemplifies a condition for which extensive medical care greatly increases longevity without rendering significant reproductive success (Houston, 1974; Pearson and O'Brien, 1975; Necheles et al., 1974; Piomelli et al., 1974; Sloman, 1974; Canale et al., 1974). Carter et al. (1971) and Sultz et al. (1972) report data for the sickle hemopathies and cystic fibrosis which indicate an absence of reproductive compensation (Sultz et al., 1972) or even *negative compensation* (Carter et al., 1971).

While medical treatment of some conditions has been so successful as to counter the hypothesized eugenic effect (e.g., HbS anemia and PKU deficiency) by sufficiently raising the expected fertility of homozygotes, other conditions are not yet sufficiently well treated to affect parental ability to reproductively compensate. Tay-Sachs disease exemplifies a condition which may soon move out of this category and into the category of a disease whose frequency will diminish as a by-product of more effective medical care and increased longevity.

Of course, the sword of the medical insignia is double-edged, and the eugenic effect hypothesized here, no matter how strongly it applies in reality, can not counter the potential dysgenic effect of amniocentesis; that is, if therapeutic abortions are elected only when the fetus is homozygous for a deleterious recessive, and not in the case of carrier fetuses, then the paradigm becomes: Therapeutic Abortion$\uparrow \rightarrow$Homozygote Longevity$\downarrow \rightarrow$ Heterozygote Parental Investment$\downarrow \rightarrow$ Heterozygote Reproductive Compensation$\uparrow \rightarrow$Heterozygote Selective Disadvantage$\downarrow \rightarrow$Gene Frequency$\uparrow$ (cf. Hagy and Kidwell, 1972; Fraser, 1972*a*, 1972*b*). Although complete reproductive compensation is likely to raise the equilibrium frequency of a recessive lethal, it is unlikely, as originally hypothesized by Lewontin (1953), to raise frequency levels to those generally attributed to balanced polymorphism (cf. Williams, 1959).

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REFERENCES

ANDERSON, M. F. 1971. The foetal risks in sickle cell anemia. West Indian Med. J. **20**:288–295.

ATTAH, E. B., C. PATH, and M. C. EKERE. 1975. Death patterns in sickle cell anemia. JAMA **233**:889–890.

BEGLEITER, M. L., V. F. BURRY, and D. J. HARRIS. 1976. Prevalence of divorce among parents of children with cystic fibrosis and other chronic diseases. Soc. Biol. **23**:260–264.

BILLINA, J. H., and J. N. BICKERS. 1974. Modern management of sickle cell disease in pregnancy. South. Med. J. **67**:426–429.

BOWMAN, B. H. 1976. Cystic fibrosis. New Engl. J. Med. **294**:937–938.

BUMBALO, T. S. 1969. Infertility in males with cystic fibrosis. Pediatrics **43**:468.

CANALE, V. C., P. STEINHERZ, M. NEW, and M. ERLANDSON. 1974. Endocrine function in thalassemia major. Ann. N.Y. Acad. Sci. **232**:333–345.

CARTER, C. O., E. A. EVANS, J. A. F. ROBERTS, and A. R. BUCK. 1971. Genetic clinic: A follow-up. Lancet **1**:281–285.

DENNING, C. R., S. C. SOMMERS, and H. J. QUIGLEY. 1968. Infertility in male patients with cystic fibrosis. Pediatrics **41**:7–17.

FRASER, G. R. 1972*a*. The implications of prevention and treatment of inherited disease for the genetic future of mankind. J. Génét. Hum. **20**:185–205.

———. 1972*b*. Selective abortion, gametic selection, and the X chromosome. Amer. J. Hum. Genet. **24**:359–370.

FEIGELSON, J., Y. PECAU, and H. SHWACHMAN. 1969. A propos d'une paternité chez un malade atteint de mucoviscidose: études des fonctions génitales et de la filiation. Arch. Fr. Pediat. **26**:937–944.

GIMA, A. S., and J. C. LEE. 1975. Prevalence of sickle cell anemia: an improved outlook. J. Natl. Med. Assoc. **67**:259–263.

GRAND, R. J., R. C. TALAMO, and P. A. DISANT AGNESE. 1966. Pregnancy in cystic fibrosis of the pancreas. JAMA **195**:993–1000.

HAGY, G. W., and J. F. KIDWELL. 1972. Effect of amniocentesis, selective abortion, and reproductive compensation on the incidence of autosomal recessive diseases. J. Hered. **63**:185–188.

HARTUNG, J. 1977. An implication about human mating systems. J. Theor. Biol. **66**:737–745.

HOLSCLAW, D. S., A. D. PERLMUTTER, and H. JOCKIN. 1971. Genital abnormalities in male patients with cystic fibrosis. J. Urol. **106**:568–574.

HOLZEL, A. 1975. Cystic fibrosis. The Practitioner **214**:776–785.

HOUSTON, R. G. 1974. Dietary nitriloside and sickle cell anemia in Africa. Amer. J. Clin. Nutr. **27**:766–778.

KAPLAN, E., H. SHWACHMAN, and A. D. PERLMUTTER. 1968. Reproductive failure in males with cystic fibrosis. New Engl. J. Med. **279**:65–69.

KARAYALCIN, G., F. ROSNER, K. Y. KIM, P. CHANDRA, and A. J. ABALLI. 1975. Sickle cell anemia—clinical manifestations in 100 patients and review of literature. Amer. J. Med. Sci. **269**:51–67.

LEWONTIN, R. C. 1953. The effect of compensation on populations subject to natural selection. Amer. Nat. **87**:375–381.

MEARNS, M. B. 1974. Cystic fibrosis. Brit. J. Hosp. Med. **12**:497–506.

NECHELES, T. F., S. CHUNG, R. SABBAH, and D. WHITTEN. 1974. Intensive transfusion therapy in thalassemia major: An eight-year follow-up. Ann. N.Y. Acad. Sci. **232**:179–185.

OPPENHEIMER, E. H., and J. R. ESTERLY. 1970. Observations on cystic fibrosis of the pancreas. VI. The uterine cervix. J. Pediat. **77**:991–995.

PEARSON, H. A., and R. T. O'BRIEN. 1975. The management of thalassemia major. Seminars in Hematology **12**:255–265.

PIOMELLI, S., M. H. KARPATKIN, M. ARZANIAN, M. ZAMANI, M. H. BECKER, N. GENEISER, S. J. DANOFF, and W. J. KUHNS. 1974. Hypertransfusion regimen in patients with Cooley's anemia. Ann. N.Y. Acad. Sci. **232**:186–192.

POWARS, D. R. 1975. Natural history of sickle cell disease—the first ten years. Seminars in Hematology **12**:267–285.

RIVER, G. L., A. B. ROBBINS, and S. D. SCHWARTZ. 1961. SC hemoglobin: A clinical study. Blood **18**:385–415.

ROSENOW, E. C., and R. A. LEE. 1968. Cystic fibrosis and pregnancy. JAMA **203**:227–230.

RULE, A. H., L. KOPITO, and H. SHWACHMAN. 1970. Chemical analysis of ejaculates from patients with cystic fibrosis. Fertil. Steril. **21**:515–520.

SLOMAN, M. J. 1974. Guide to thalassaemia. Nursing Times **70**:1968–1971.

SULTZ, H. A., E. R. SCHLESINGER, and J. FELDMAN. 1972. An epidemiologic justification for genetic counseling in family planning. Amer. J. Publ. Health **62**:1489–1492.

TAUSSIG, L. M., C. C. LOBECK, P. A. DISANT AGNESE, D. R. ACKERMAN, and J. KATTWINKEL. 1972. Fertility in males with cystic fibrosis. New Engl. J. Med. **287**:586–589.

TRIVERS, R. L. 1972. Parental investment and sexual selection, p. 136–179. *In* B. Campbell (ed.), Sexual selection and the descent of man. Aldine, Chicago.

WARWICK, W. J., and R. E. POGUE. 1969. Computer study of cystic fibrosis, p. 320–331. *In* Lawson (ed.), Proceedings of the Fifth International Cystic Fibrosis Conference, Cambridge. Cystic Fibrosis Trust, London.

WILLIAMS, G. C. 1959. The genetic effects of reproductive compensation. Hum. Biol. **31**:344–351.