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Natural Selection and Heredity

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The intimate connection between natural selection and heredity is indicated by Prof. Dobshansky's definition of evolution as essentially just a change in gene frequencies, for natural selection is the agency that causes gene frequencies to change. Just as mutations are the raw material of evolution, selection is the force that preserves good genes, eliminates bad genes, and produces the changes that lead to the formation of races, and eventually species.

The problem of the action of selection on gene frequencies can be treated, with suitable simplifying assumptions, mathematically, and many years ago Prof. J. B. S. Haldane published a series of papers on this subject (tab. I). The rate at which gene frequencies would change under the action of slow selection is shown in fig. 1. It will be seen that selection acts more slowly, at first, on recessive genes than on dominants, but in the long run the frequencies change from nearly zero to nearly one, or vice versa. Deleterious genes are often never completely eliminated, because they are continually recruited by recurring mutations.

That selection is effective in bringing about considerable changes in organisms is shown by the achievements of domestic plant and animal breeders. The results of selecting for long shanks in chickens are shown in fig. 2, and for a larger number of abdominal chaetae in fruit flies in fig. 3. Though it is not shown here, selection for a lower number of chaetae is also effective.

Another example of the action of selection, in this case acting to our own disadvantage, is the increased resistance that microorganisms often develop after exposure to antibiotics (tabb. II and III). I shall have another word to say about this phenomenon later.

The action of a gene is not quite independent of the particular chromosome, or the particular part of the chromosome, it finds itself on; consequently natural selection may favor certain chrosomal rearrangements over certain others. So long as a gene remains in the same chromosome and this chromosome does not exchange chromosomal material with other chro-

Tab. I. Change of Gene Frequency by Selection

$$kn = v_n - v_o + \log_e (v_n/v_o)$$

Were k = selection coefficient, n = number of generations of selection, v_o = ratio of frequency of dominant gene to frequency of recessive gene at start, v_n = ratio after n generations of selection, $\log_e$ = logarithm to the base e (natural logarithm).

from: Haldane J. B. S., 1924. Trans. Camb. Phil. Soc., 23, 19-41.

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Tab. II. Induced Resistance to Terramycin

Organism and strain	Made resistant to	Sensitivity in micrograms per milliliter			
		Terramycin	Aureomycin	Chloram-phenicol	Strepto-mycin
Escherichia coli 687	0	3.12	6.25	6.25	12.5
	Terramycin	100	50	100	6.25
Aerobacter aerogenes 1,155	0	3.12	3.12	6.25	6.25
	Terramycin	50	50	200	6.25
Streptococcus faecalis 2,323	0	1.56	0.78	12.5	50
	Terramycin	12.5	6.25	12.5	50
Escherichia coli 2,300	0	1.56	3.12	12.5	6.25
	Aureomycin	100	100	100	3.12
Aerobachter aerogenes 2,319	0	1.56	3.12	6.25	3.12
	Aureomycin	100	50	200	0.78
Escherichia coli 994	0	1.56	3.12	12.5	6.25
	Chloramphenicol	50	25	200	6.25
Aerobacter aerogenes 1,155	0	3.12	3.12	6.25	6.25
	Chloramphenicol	6.25	12.5	200	3.12
Escherichia coli 1,120	0	3.12	3.12	12.5	12.5
	Streptomycin	1.56	1.56	6.25	200
Aerobacter aerogenes 1,158	0	1.56	1.56	3.12	12.5
	Streptomycin	1.56	0.78	1.56	200

From Herrell et al., Anm. N. Y. Acad. Sciences 53, Art. 2 (1950), p. 449.

mosomes, selection acting to increase the frequency of one gene on this chromosome will also increase the frequency of the other genes on it. Normally, crossing over will soon abolish this correlation.

The action of natural selection to increase the frequency of genes producing effects that are favorable in a given environment an to reduce the frequency of genes producing unfavorable effects, causes the organism to become better adapted to its environment. Actually, since selection is probably faster, under ordinary conditions, than environmental change, we should say that the action of selection is to *keep* the organism adapted to its environment. This adaptation to local environments causes the formation of local races, of which an example which involves a visible difference is shown in fig. 4. Example of effects similarly visible are also found in man; the deepest skin pigmentation is correlated with areas of most intense ultraviolet radiation, as shown in 1845 by Fleure. The effects of adaptation are not always visible externally, as in the increased resistance to tuberculosis which the Jews seem to have acquired by long residence in cities under crowded and often unsanitary conditions (tab. IV).

In the above cases we could see what the advantage resulting in local adaptation consisted in, but in many cases we cannot. In the case of the insect whose local races were pictured ni fig. 4, we have no idea why any one of these races is better fitted to its particular environ-

Tab. III. Relative Sensitivity When Assayed with Penicillin after the Indicated Procedures

Strain of Organism	Initial M.I.C. of Penicillin mcg./ml.	Antibiotic Used for Transfers																				
		Penicillin					Aureomycin				Chloramphenicol				Terramycin				Streptomycin			
		Ratio of Final to Initial Sensitivity																				
		P5*	P10	B10	B20	B30	A10	B10	B20	B30	C10	B10	B20	B30	T10	B10	B20	B30	S10	B10	B20	B30
Staph. aureus (C)	0.06	2	4	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Staph. aureus (M)	0.06	4	8	4	2	1	1/2	1/2	1/2	1	1	1	1	1	1/2	1/2	1/2	1	1	1	1	1
Staph. aureus (V)	31.25	4	8	4	2	—	1/2	1/2	1	—	1/2	1	1	—	1/8	3/4	1/2	—	1/16	1/8	3/8	—
Str. β hem. A (B)	0.008	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Str. fecalis D (Gr)	1.95	2	4	4	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1/2	1/2	1	1
Str. fecalis D (K)	3.9	4	16	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1/2	1/2	1	1
E. coli Communior (W)	31.25	—	—	—	—	—	1	1	1	1	1	1	1	1	1/2	1	1	1	1/2	1	1	1
E. coli Communion (Pr)	<1,000	—	—	—	—	—	1*	1*	1*	1*	1*	1*	1*	1*	1*	1*	1*	1*	1*	1*	1*	1*
A. aerogenes (S)	<4,000	—	—	—	—	—	1/32	1/16	1/16	1/8	1/16	1/4	1	1	1/64	1/16	1/8	1/4	1/8	1/2	1	1
K. pneumoniae A (Th)	15.6	—	—	—	—	—	1/2	1	1	1	1/2	1	1	1	1/2	1	1	1	1/2	1/2	1/2	1/2
K. pneumoniae B (Gag)	<1,000	—	—	—	—	—	1/4	1/2	1/2	1	1/16	1/2	1	1	1/8	1/4	1/2	1/2	1/8	1/4	1	1
S. typhi Mutium (Pull)	15.6	—	—	—	—	—	1	1	1	1	1	1	1	1	1	1	1	1	1/2	1/2	1/2	

+ P5 Five transfers in penicillin containing medium, P10, A10, C10, T10, S10: ten transfers in penicillin, aureomycin, chloramphenicol, terramycin, streptomycin-containing media—B10, B20, B30: 10, 20, 30 subsequent transfers in drug-free medium.

* No inhibition by 1000 mcg./ml. of penicillin.

From Monnier and Schoenbach, Antibiotics and Chemotherapy, 1, 742 (1951).

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ment than another race would be. If it is true that the American Indians once possessed blood group B gene, but lost it, this would provide another example of a local adaptation conferring an advantage that is inapparent to us in the present state of our knowledge.

It is certainly true that pure blood American Indians do not possess blood group B gene

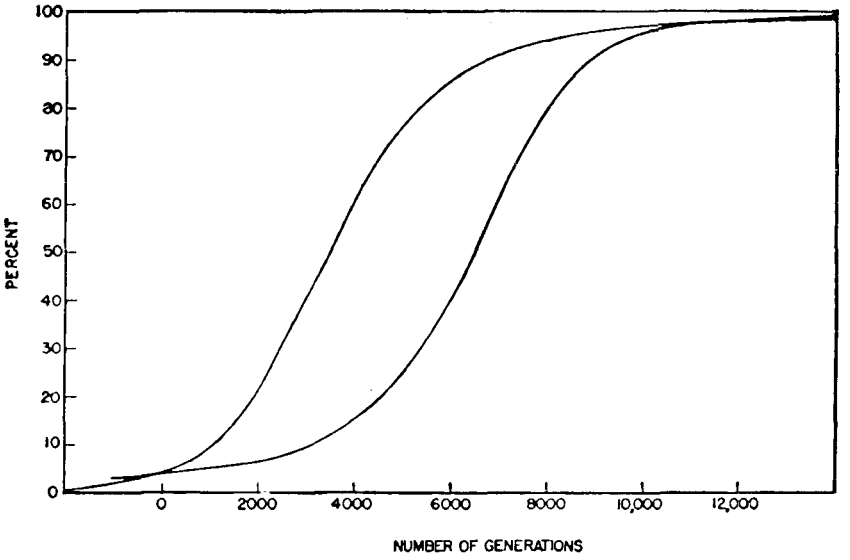

Fig. 1. From Boyd, W. C., Genetics and the races of man. Little, Brown, Boston, 1950

Tab. IV. Tuberculosis in Jews and Non-Jews

In Wien betrug in den Jahren 1901—1903 die Sterblichkeit an Lungentuberkulose

	auf 1000	im Verhältnis
bei den Juden	1,81	100
bei den Protestanten	3,28	179
bei den Katholiken	4,96	274

In Budapest waren die entsprechenden Zahlen 1901—1905:

	auf 1000	im Verhältnis
bei den Juden	2,06	100
bei den Katholiken	5,42	263
bei and. Nichtjuden	3,93	191

In Petersburg (Leningrad) starben auf 1000 Einwohner an Lungentuberkulose

	1900—1904	1905—1909	1910—1914	1915—1917	1918—1920
Juden	1,86	1,89	1,47	1,59	2,30
Nichtjuden	3,89	3,81	3,43	3,61	4,27

From Baur E., Fischer E., and Lenz F., Menschliche Erblichkeitslehre und Rassenhygiene. J. F. Lehmanns Verlag, München, 1931.

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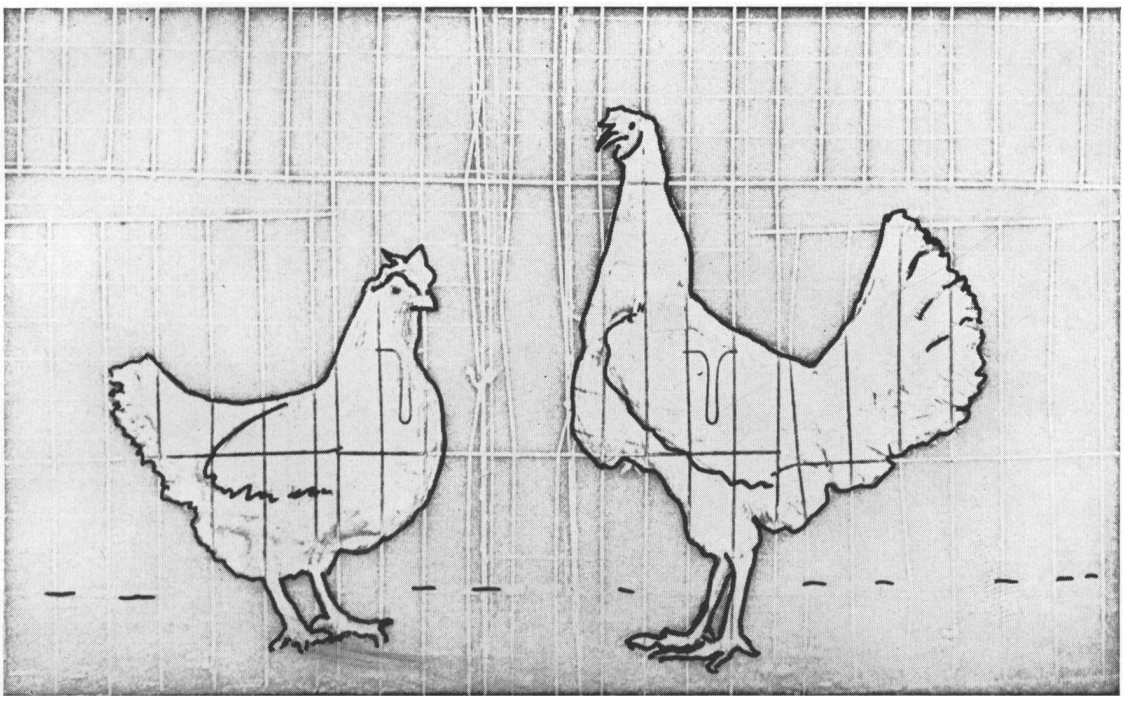

Fig. 2. From Lerner, I. M. Genetic Homeostasis. Oliver and Boyd, Edinburgh, 1954

Tab. V. Preliminary Report on Blood Grouping Tests of Coahuila Mummified Materia[1]

Group O	Group A	Group B	In process
C 59b–B1	Coyoto Cave 22776	C 68 –B18	C 68 –B19
C 68 –B3		C 596–B1	C 59c–B1
C 24 –B13			
C 79 –B1			
C 24 –B-H			
C 74 –B1			
Cojote Cave " Mummy "			
UNS Macc 9462			
Cat. 45581			

From Taylor W. W., and Boyd W. C., Am. Phil. Soc. Papers on Research 1940-1943, p. 179.

today (fig. 5). That they may have possessed this gene at one time is suggested by tests on American Indian mummies, known by carbon 14 dating to be over 8,000 years old, in which antigen B was apparently found (tab. V).

However, though we do not know what the special characteristics of the American envi-

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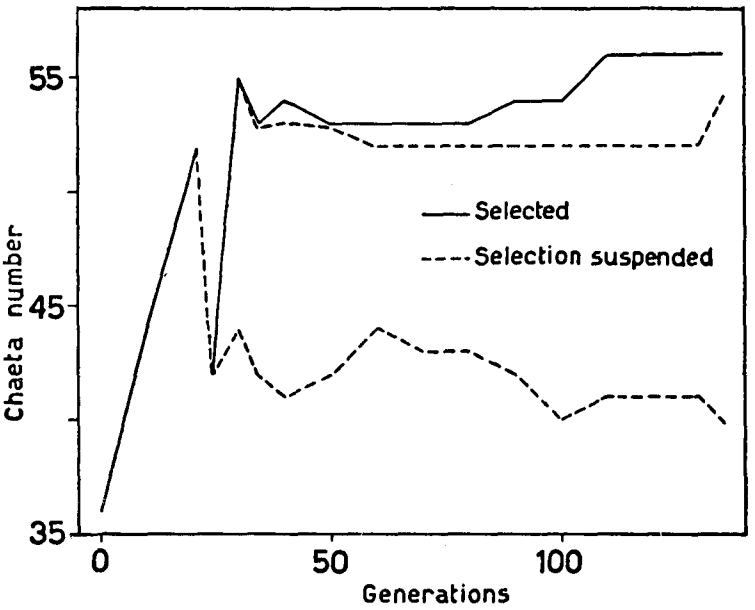

Fig. 3. From Lerner I. M., Genetic Homeostasis.
Oliver and Boyd, Edinburgh, 1954

ronment are (or were) which led to the elimination of B (assuming that the mummy tests are reliable), we do know that the blood group genes, contrary to what used to be believed, are not selectively neutral. A number of years ago Dr. Alice Brues, in a paper that is a tribute to the powers of pure thought, suggested that there must be selective forces acting on the ABO blood group gene frequencies, since only part of the available range of variability is occupied by actual

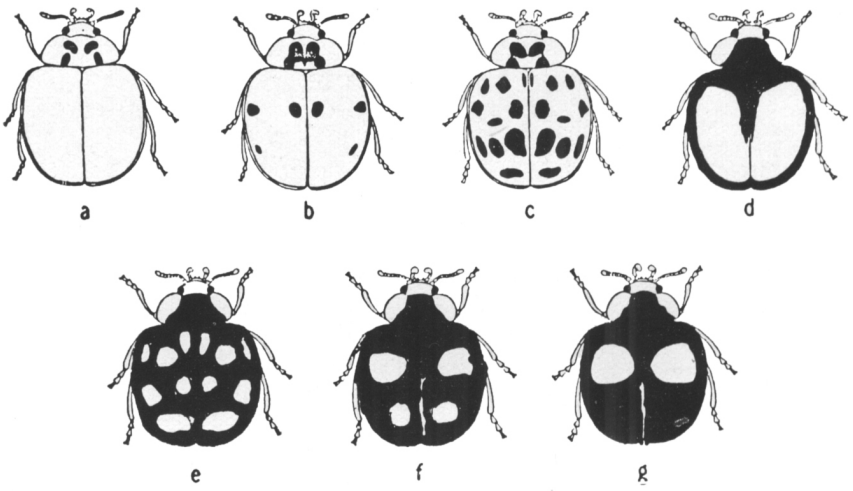

Fig. 4. From Dobzhansky T., Genetics and the Origin of Species.
Columbia Univ. Press., N. Y., 1941

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populations (fig. 6). Dr. Brues did not of course know what this selective force was. We still do not know that, but we do know that there are selective forces acting on the blood group gene frequencies. For example, various diseases have been found to be correlated with certain of the ABO blood groups (tab. VI). More recently we have found in my labora-

Tab. VI. Diseases Showing Strong Associations with the ABO Blood Groups (Roberts 1957)

Disease	Relative Susceptibility
Duodenal ulcer	O/(A + B + AB) = 1.38
Gastric ulcer	O/(A + B + AB) = 1.19
Cancer of the stomach	A/O = A/B = 1.19
Pernicious anemia	A/O = 1.26
Diabetes mellitus	A/O = 1.16

From Roberts, Fraser J. A., J. Prev. Soc. Med., 11, 107, (1957).

tory that one disease, at least, is correlated with the Rh blood groups (tab. VII). This latter example is of interest because it may provide part of the explanation why the selection pressure against the Rh negative gene due to the occurrence of erythroblastosis has not resulted in the elimination of this gene from our population.

The correlations of blood groups with disease, however, are mainly interesting because they demonstrate to a onetime skeptical world that selection can act on the blood groups. The correlations we know at present, however, would not explain any rapid change in gene frequencies, for the diseases do not kill enough people before they have completed their reproductive task (tab. VIII).

In spite of the undoubted effectiveness of natural selection in changing gene frequencies and reducing the frequency of deleterious genes, it has not succeeded in eliminating all deleterious genes, and this at first sight may require some explanation. For example, genes undoubtedly exist, in most human populations, making for susceptibility to various diseases. Tab. IX shows evidence that genetic factors are concerned in resistance to tuberculosis, for example, since susceptibility to this disease is seen to be much more similar in the genetically identical twins than in fraternal twins or other sibs, but nevertheless greater in sibs than in the marriage partner who might be thought to be more exposed to the risk of infection.

There are probably several reasons why these deleterious genes are not completely eliminated by natural selection. The first, and probably the most important, is based on the phenomenon of " balanced polymorphism ", demonstrated mathematically by Fisher in 1930 (tab. X). This depends upon the fact that if the three phenotypes of a pair of alleles, which appear in the population with frequencies $p^2 : 2pq : q^2$, where p is the frequency of one allele and q that of the other, have different selective advantages relative to one another, say in the ratios a:b:c, such that the advantage of the heterozygote b, is greater than that of either of the homozygotes, then there will be established an equilibrium such that the ratio of the frequencies of the two genes at this locus, p/q, will equal (b - c) / (b - a). This mechanism is capable

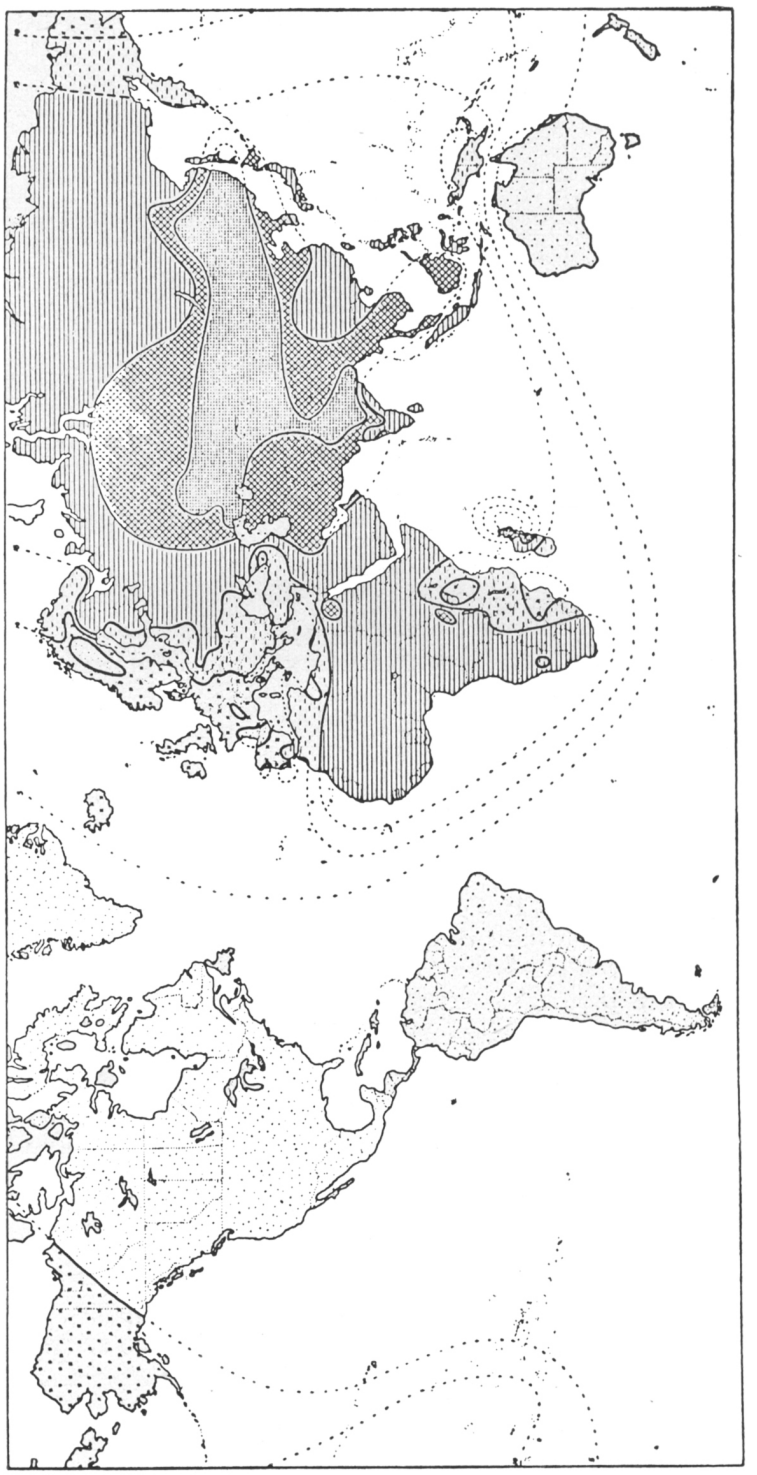

Fig. 5. From Mourant A. E., The distribution of the human blood groups: C. C Thomas, Springfield 1954

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of maintaining surprisingly high frequencies of even a lethal gene in the population, depending on the relative advantage of the heterozygote (fig. 7).

It seems that an example of this has been demonstrated in man. The sickle cell gene, which produces in either single or double dose red blood cells that, deprived of oxygen, shrink into

Tab. VII. Correlation between Ulcerative Colitis and Rh Blood Groups

	Rhesus type			Total
	CC	Cc	cc	
Patients with colectomy	51	97	37	185
Normals	209	502	360	1,071

From these figures a value of chi-square with two degrees of freedom of 15.214 was calculated; this value is very definitely significant (P about 5×10^{-4}). So far as we could judge, the group of patients we tested did not differ in ethnic composition in any notable way from our controls. There is, however, evidence of heterogeneity in our test material ($\chi^2_{(10)} = 19.115$, $0.05 < P < 0.02$). No correlation was found with ABO, MN, or secretor status.

William C. Boyd, Mary Heisler, Egon Orowan: Nature, Vol. 190, No. 4781, pp. 1123-1124, June 17, 1961.

Tab. VIII. Proportion of the White American Population Dying Under Age 45 Years from Certain Diseases in 1955 (U. S. Vital Statistics)

Disease	Number dying		Proportion dying < 45 years
	< 45 years	Total	
Cancer of the stomach	689	19,815	0.0348
Gastric ulcer	348	4,352	0.0800
Duodenal ulcer	450	4,630	0.0972
Diabetes mellitus	379	22,956	0.0165
Pernicious anemia and hyperchromic anemia	27	1,039	0.0260
Total	1,893	52,792	0.0359

Total deaths from all causes: 1,350,869
Living U. S. population:
Total 146.54×10^6
< 45 yrs. 102.94×10^6

$$\frac{\text{Total deaths} < 45 \text{ years for above disease}}{\text{Living population} < 45 \text{ eyars}} = \frac{1893}{102.94 \times 10^6} = 1.84 \times 10^{-5}$$

From Reed T. E., Polymorphism and Natural Selection in Blood Groups, In Proc. Conf. on Genetic Polymorphisms and Geog. Variations in Disease. Ed. B. S. Blumberg. U. S. Dept. of Health, Educ. and Welfare, Bethesda, 1960.

abnormal shapes somewhat reminiscent of sickles (fig. 8), causes the production of an abnormal hemoglobin in the person carrying the gene (tab. XI). In homozygous dose it also causes a profound anemia usually resulting in death before puberty, so the gene is prac-

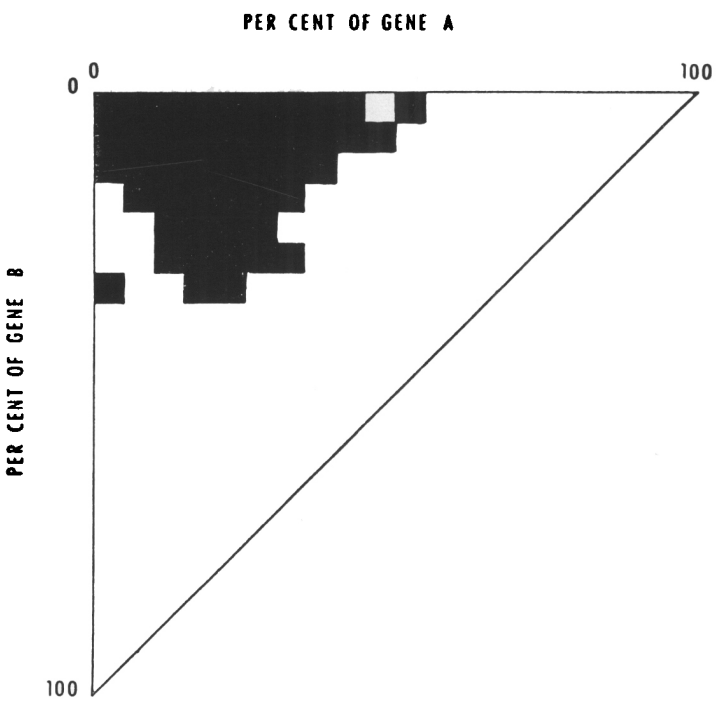

Fig. 6. From Brues A. M., Selection and polymorphism in the A-B-O blood groups. Am. J. Phys. Anthrop. 12, 559 (1954)

Tab. IX. Tuberculosis in Twins

Relation to index case	Percentage with tuberculosis
One-egg twin	87
Two-egg twin	25.6
Other brother or sister	25.5
Marriage partner	7

In addition to the 87 per cent correspondence in the fact of clinical infection, identical twins also showed a close resemblance in the type and progress of the disease.

From Burnet M., The natural History of Infectious Disease. Camb. Univ. Press, 1953.

tically a lethal in homozygous dose. Nevertheless, appreciable frequencies of it exist in some parts of the world, especially in Africa (tab. XII). The explanation was apparently found by Anthony Allison, who noticed that the areas with the highest frequency of the sickle cell

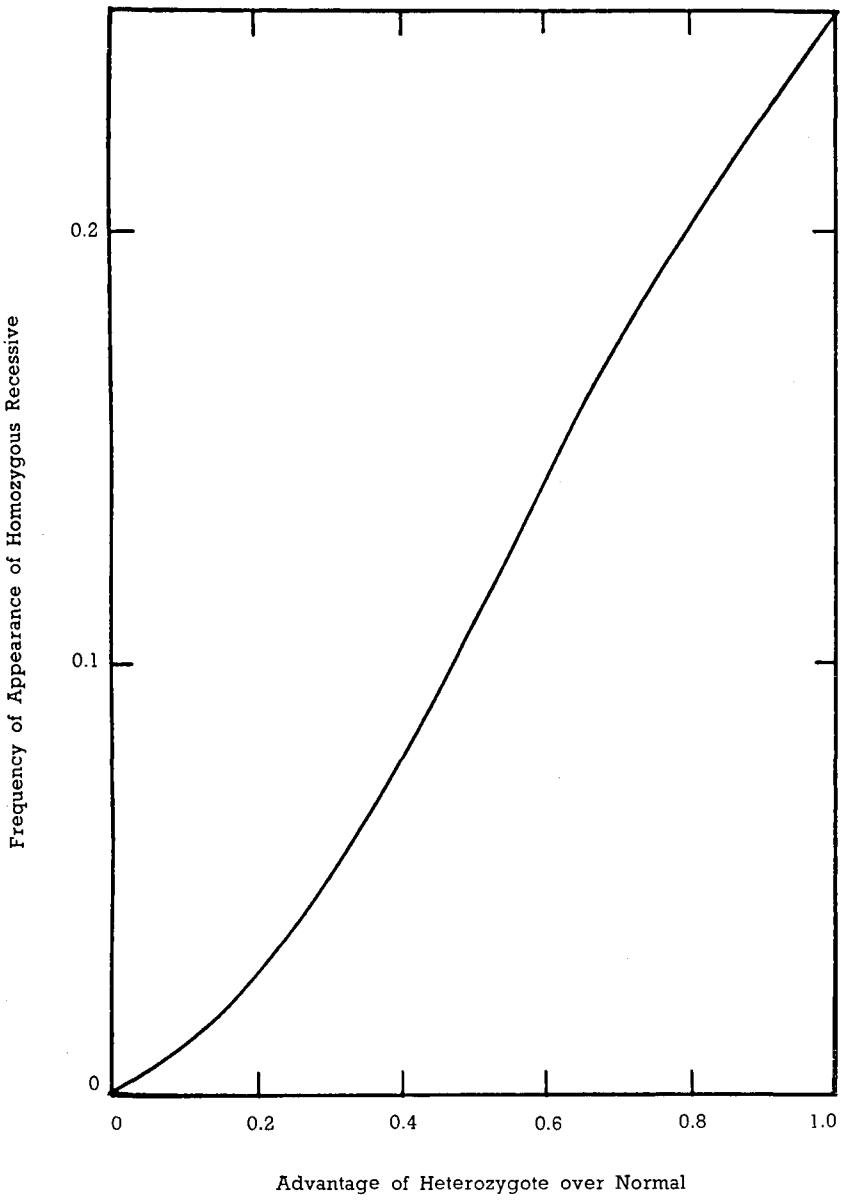

Fig. 7. Redrawn from Lerner I. M., The Genetic Basis of Selection, John Wiley and Sons, New York, 1958

gene were precisely the parts of Africa where falciparum malaria is most intensely endemic (tab. XII). Allison, as is now well known, tested this hypothesis by deliberate infection of normal and sickle cell volunteers, with strikingly confirmatory results (tab. XIII).

Other mechanisms also probably operate to prevent the complete elimination of an apparently deleterious gene. In some cases, no doubt, perhaps in many cases, the gene has some

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Tab. X. Proof of Balanced Polymorphism Equilibrium

A single factor may be in stable equilibrium under selection if the heterozygote has a selective advantage over both homozygotes. For if we suppose the three phases of the factor to appear in any generation in the ratio $p^2 : 2pq : q^2$, and that their relative selective advantages are respectively in the ratio $a : b : c$, then the three phase in this generation will reproduce in the ratio $ap^2 : 2bpq : cq^2$, where the absolute magnitudes of the quantities a, b, c are a matter of indifference, only their ratios being required. If equilibrium in the gene ratio is established this ratio will be the same in those which reproduce as it was in the preceding generation, and therefore,

$$\frac{p}{q} = \frac{ap^2 + bpq}{bpq + cq^2} ;$$

whence it appears that

$$ap + bq = bp + cq.$$

Subtracting each of these from $b\ (p + q)$ we obtain

$$p(b - a) = q(b - c),$$

or

$$\frac{p}{q} = \frac{b - c}{b - a} .$$

There is therefore always a real ratio of equilibrium if $b - a$ and $b - c$ are either both positive or both negative; that is, if the heterozygote is either better or worse adapted than both the homozygotes.

From FISHER R. A., The Genetical Theory of Natural Selection. Clarendon Press, Oxford, 1930.

Tab. XI

Haemoglobin A	—his—val—leu—leu—thr—pro—glu—glu—lys—
Haemoglobin S	—his—val—leu—leu—thr—pro—val—glu—lys—
Haemoglobin C	—his—val—leu—leu—thr—pro—lys—glu—lys—

Key: his = histidyl— val = valyl—
leu = leucyl— thr = threonyl—
pro = prolyl— glu = glutamyl—
lys = lysyl—

Aminoacid sequences in anomalous peptides from haemoglobin S and C compared with the equivalent peptide in haemoglobin A (After Hunt and Ingram).

From Harris H., Human Biochemical Genetics. Cambridge Univ. Press, 1959.

good effect that we do not know about that more than compensates for the bad effect we do know. Most genes, after all, are pleiomorphic.

Another factor, probably, is that too high a frequency of a good gene may begin to have a bad effect. Each organism is the result of the interaction of a large number of genes with the environment and with each other. A gene that produces a good effect in one environment may produce a bad effect in another. In tabb. II and III we saw that increasing the resi-

Tab. XII

Tribe	Linguistic or ethnic affinity	District or location where tested	Total number tested	Total S.C.T.	% S.C.T.	Malarial severity
1. Ganda	Bantu	Kampala	334	65	19.5	+
2. Amba	Bantu	Bundibugyo	220	86	39.1	+
3. Konjo	Bantu	Kichwamba, Kisomoro	124	12	9.7	—
4. Chiga	Bantu	Kabale	206	2	1.0	—
5. Hutu	Bantu	Kisoro	135	4	3.0	—
6. Twa	Bantu	Kisoro	33	0	0	—
7. Iru	Bantu pigmoid	Mbarara	127	7	5.5	—
8. Hima	Hamitic	W. Ankole	134	3	2.0	—
9. Teso	Hamitic	Kampala	81	12	14.8	+
10. Lugbara	Nilotic	Kampala	76	18	23.7	+
11. Madi	Nilotic	Kampala	62	14	22.6	+
12. Luo	Nilotic	Kisumu	288	74	25.7	+
13. Suba	Bantu	Rusinga Island	173	48	27.7	+
14. Kuria	Bantu	Musoma, Busigire	102	28	27.5	+
15. Kwaya	Bantu	Musoma	107	33	30.8	+
16. Simbiti	Bantu	Musoma, Kanesi	126	51	40.5	+
17. Jita	Bantu	Musoma, Ukerewe	124	36	29.0	+
18. Zanaki	Bantu	Musoma, Busegwe	104	37	35.6	+
19. Kizu	Bantu	Musoma, Ikizu	52	15	28.9	+
20. Sukuma	Bantu	Mwanza	175	47	26.9	+
21. Kerewe	Bantu	Ukerewe Island	92	29	31.5	+
22. Kara	Bantu	Ukerewe Island	52	15	28.8	+
23. Kisii	Bantu	Chemagal	160	7	4.8	—
24. Kikuyu	Bantu	Nairobi	227	1	0.4	—
25. Kamba	Bantu	Machakos	213	0	0	—
26. Chagga	Bantu	Old Moshi	130	0	0	—
27. Rusha	Bantu	Arusha	126	1	0.8	—
28. Pare	Bantu	Same	54	4	7.4	—
29. Sambaa	Bantu	Amani, Tanga	103	9	8.7	— (+)
30. Zigua	Bantu	Tanga	57	8	14.0	+ (—)
31. Digo	Bantu	Tanga	66	18	27.3	+
32. Bondei	Bantu	Tanga	81	23	28.4	+
33. Kipsigis	Hamitic	Letain	75	0	0	—
34. Masai	Hamitic	Magadi	104	0	0	—
35. Iraqw	Unique,3 semitic	Mbulu	102	2	2.0	—
		Total	4,605			

From Allison A. C., Trans. Roy. Soc. Trop. Med. and Hyg. 48, 315 (1954).

stance of a microorganism to one antibiotic might decrease its resistance to another, an outcome having disadvantages for the microorganism. Also, though it was not shown in fig. 3, it was always found that when selection for more (or fewer) abdominal chaetae in the fruit fly was carried far enough, the experiment had to be discontinued, because the strain died out because of sterility. Evidently too much of the genes making

Tab. XIII

No.	Mode of Infection and Strain	Day after Infection																
		8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40
								Luo With No Sickle-cells										
1	M_2 B_1	0.03	—	0.07	5.0	5.0	2.5	5.0	1.2	0.4	0.02	0.01	—	—	0.1	0.01	0.01	ST
2	M_2 B_1	—	—	—	—	—	—	—	0.03	0.13	0.41	—	—	—	—	0.03	—	ST
3	M_2 B_1	—	—	—	—	—	—	—	0.1	0.02	0.20	5.0	2.5	1.25	1.67	0.2	5.0	2.0 S
4	M_2 B_1	—	—	—	—	0.02	0.02	0.5	0.83	0.12	0.2	0.2	1.0	0.83	0.25	0.17	—	ST
5	M_2 B_2	—	—	—	—	0.05	1.0	1.67	0.25	0.05	0.07	0.25	1.2	1.0	0.03	—	—	ST
6	B_1	0.02	5.0	10.0	10.0	1.0	1.0	0.01	ST	—	—	—	—	—	—	—	—	—
7	B_2	—	—	—	—	15.0	50.0	ST	—	—	—	—	—	—	—	—	—	—
8	B_2	—	—	0.13	5.0	1.67	0.33	—	—	ST	—	—	—	—	—	—	—	—
9	B_1	—	—	—	—	5.0	—	0.1	0.5	0.5	—	1.0	0.1	2.5	10.0	5.0	0.5	ST
10	B_2	—	—	—	—	—	—	0.05	0.05	—	—	0.67	—	0.1	0.05	5.0	5.0	ST
11	B_2	—	0.05	0.3	—	—	—	0.2	ST									
12	B_2	—	—	0.3	0.3	0.3	0.1	0.3	ST									
13	B_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
14	B_2	2.0	1.7	2.0	60.0	5.0	0.6	ST	—	—	—	—						
15	B_2	0.05	0.3	—	0.4	0.1	0.3	ST										
								Luo With Sickle-cell Trait										
1	M_1 B_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
2	M_1 B_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
3	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
4	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
5	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
6	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
7	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5.0	0.5	ST
8	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
9	M_1 B_1	0.7	—	—	—	—	—	—	—	—	—	0.03	0.1	0.03	0.03	—	—	ST
10	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
11	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
12	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
13	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
14	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
15	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST

Figures represent parasite counts in hundreds per mm.² of blood. ST = Stopped by chemotherapy.

From Allison A. C., Sickle-cell trait and malaria. Brit. Med. J. 1, 292 (1954).

for this apparently unimportant and harmless characteristic had a deleterious and very important effect, that of reducing fertility, though it is not understood how this effect is produced. It may very well be that in man selection to increase the resistance of the population to a certain disease acts to decrease the resistance to another disease, or to impair the fitness of the

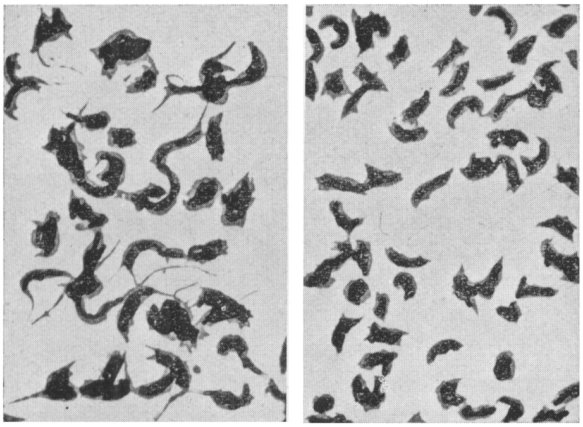

Fig. 8. From Sorsby, A., Clinical Genetics. Butterworth and Co., London, 1953

resulting progeny in some other way. Natural selection always results in an equilibrium, and evidently in any real population a number of genes having some effects we consider undesirable are present, and some such genes always will be present.

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