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Lessons from a "Primitive" People

Do recent data concerning South American Indians have relevance to problems of highly civilized communities?

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The field of population genetics is in a state of exciting intellectual turmoil and flux. The biochemical techniques that are now so freely available have revealed a profusion of previously hidden genetic variability. The way in which this variability arose and is maintained in populations—to what extent by selection, past and present, and to what extent by simple mutation pressure—is currently a topic of intensive discussion and debate, and there is little agreement among investigators as to which are the most promising approaches to the questions [see (*1*)]. At the same time, it is becoming increasingly clear that the breeding structure of real populations—especially those that approximate the conditions under which man evolved—departs so very far from the structure subsumed by the classical formulations of population genetics that new formulations may be necessary before the significance of this variation can be appraised by mathematical means.

Some 8 years ago, as the new population genetics began to emerge, my co-workers and I began the formulation of a multidisciplinary study of some of the most primitive Indians of South America among whom it is possible to work (*2*). Scientists in the program ranged from the cultural anthropologist to the mathematical geneticist. The general thesis behind the program was that, on the assumption that these people represented the best approximation available to the conditions under which human variability arose, a systems type of analysis oriented toward a number of specific questions might provide valuable insights into problems of human evolution and variability. We recognize, of course, that the groups under study depart in many ways from the strict hunter-gatherer way of life that obtained during much of human evolution. Unfortunately, the remaining true hunter-gatherers are either all greatly disturbed or are so reduced in numbers and withdrawn to such inaccessible areas that it appears to be impossible to obtain the sample size necessary for tests of hypothesis. We assume that the groups under study are certainly much closer in their breeding structure to hunter-gatherers than to modern man; thus they permit cautious inferences about human breeding structure prior to large-scale and complex agriculture.

I will present here four of our findings to date and will consider briefly some possible implications of these findings for contemporary human affairs. You will appreciate that I am the spokesman for a group of more than a dozen investigators, whose individual contributions are recognized in the appropriate source papers. The article is tendered with no great sense of accomplishment—we the participants in the endeavor realize how far we are from the solid formulations we seek. On the other hand, some of the data are already clearly germane to contemporary human problems. Thus, it will be maintained on the basis of evidence to be presented that, within the context of his culture and resources, primitive man was characterized by a genetic structure incorporating somewhat more wisdom and prudence than our own. How he arrived at this structure—to what extent by conscious thought, to what extent through lack of technology and in unconscious response to instinct and environmental pressures—is outside the purview of this presentation.

The studies to be described have primarily been directed toward three tribes: the Xavante of the Brazilian Mato Grosso, the Makiritare of southern Venezuela, and the Yanomama of southern Venezuela and northern Brazil. At the time of our studies, these were among the least acculturated tribes of the requisite size (>1000) in South America (see *3–8*).

The four salient points about the Indian populations that we studied to be emphasized in this presentation are (i) microdifferentiation and the strategy of evolution, (ii) population control and population size, (iii) polygyny and the genetic significance of differential fertility, and (iv) the balance with disease (*9*).

Microdifferentiation and the Strategy of Evolution

The term "tribe" conjures to most an image of a more or less homogeneous population as the biological unit of primitive human organization. We have now typed blood specimens from some 37 Yanomama, 7 Makiritare, and 3 Xavante villages with respect to 27 different genetic systems for which serum proteins and erythrocytes can be classified. A remarkable degree of intratribal genetic differentiation between Indian villages emerges from these typings (*8*,

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10). One convenient way to express this differentiation in quantitative terms is to employ the distance function developed by Cavalli-Sforza and Edwards (*11*). On the basis of gene frequencies at the Rh, MNSs, Kidd, Duffy, Diego, and haptoglobin loci, the distances between seven of the central Yanomama villages and the distances between seven Makiritare villages are shown in Tables 1 and 2. The mean distance between the seven Yanomama villages is 0.330 unit, and between the Makiritare, 0.356 unit. Table 3 gives the distances between 12 Indian tribes of Central and South America, selected for consideration solely because 200 or more members have been studied for these same characteristics and the tribes were relatively free of non-Indian genes (admixture estimated at less than 5 percent) (*12, 13*). The mean distance is 0.385 unit. Thus the average distance between Indian villages is 85.7 (Yanomama) to 92.5 (Makiritare) percent of the distance between tribes. To some extent—an extent whose precise specification presents some difficult statistical problems—these distances result from stochastic events such as the founder effect of E. Mayr, sampling error, and genetic drift. But we have also begun to recognize structured factors in the origin of these differences. One is the "fission-fusion" pattern of village propagation, in consequence of which new villages are often formed by cleavages of established villages along lineal lines (fission), and migrants to established villages often consist of groups of related individuals (fusion) (*14*). A second such factor is a markedly nonisotropic (that is, a nonrandom and "unbalanced") pattern of intervillage migration (*8*). A third factor will be discussed below (see "Polygyny and genetic significance of differential fertility").

This situation, of subdivision of a population into genetically differentiated and competing demes, is one repeatedly visualized by Wright (*15*), beginning in 1931, as being most conducive to rapid evolution. Competition between these demes can only be termed intense (*4, 6*). On the basis of the genetic distance between these Indian tribes and an estimated arrival of the Indian in Central and South America some 15,000 years ago (*16*), we have with all due reservations calculated a *maximum* rate of gene substitution in the American Indian of 130,000 years per gene substitution per locus (*13*). This rate is approximately 100 times greater than an estimate of *average* rate based on amino acid substitutions in the polypeptides of a wide variety of animal species (*17*). For the present, we equate allele substitutions to amino acid substitutions on the assumption that the basic event in both cases is the partial or complete substitution of one codon for another. There is, of course, no logical discrepancy between these estimates, since one of them is a maximum estimate (*18*). On the other hand, part of the apparent difference may be valid. Thus, it seems a reasonable postulate that, all over the world in man's tribal days, the single most important step in the formation of a new tribe probably consisted of a village or a collection of related villages breaking away from its tribe and moving off into relative isolation. These villages, perhaps more than the breakaway units of other animal populations, tended to consist of related individuals, thus providing unusual scope in man for what we have termed the "lineal effect" in establishing subpopulations whose gene frequencies are quite different from those of the parent population (*19*).

There is a current tendency to regard much of evolution, as measured by gene substitution, as non-Darwinian—that is, not determined by systematic pressures (*17*). We have recently argued that no matter whether one assumes a predominantly deterministic or indeterministic stance, the above-mentioned aspect of the social structure of primitive man resulted in genetic experiments of a type conducive to rapid evolution (*18*). Conversely, the current expansion and amalgamation of human populations into vast interbreeding complexes must introduce a great deal of inertia into the system.

Population Control and Population Size

The total human population apparently increased very slowly up to 10,000 years ago (*20*). If we may extrapolate from our Indian experience, the slowness of this increase was probably not primarily due to high infant and childhood mortality rates from infectious and parasitic diseases (see "The balance with disease"). We find that relatively uncontacted primitive man under conditions of low population density enjoys "intermediate" infant mortality and relatively good health, although not the equal of ours today (*21–23*). However, most primitive populations practiced spacing of children. Our data on how this spacing was accomplished are best for the Yanomama, where intercourse taboos, prolonged lactation, abortion, and infanticide reduce the average *effective* live birth rate to approximately one child every 4 to 5 years during the childbearing period (*24, 25*). The infanticide is directed primarily at infants whose older sibling is not thought ready for weaning, which usually occurs at about 3 years of age (*25*). Deformed infants and those thought to result from extramarital relationships are also especially liable to infanticide. Female infants are killed more often than male infants, which results in a sex ratio of 128 during the age interval 0 to 14 years (*24*). An accurate estimate of the frequency of infanticide still eludes us, but, from the sex-ratio imbalance plus other fragmentary information, we calculate that it involves perhaps 15 to 20 percent of all live births.

There have been numerous attempts to define the development in human evolution that clearly separated man from the prehominids. The phenomena of speech and of toolmaking have had strong proponents, whose advocacy has faltered in the face of growing evidence of the complexity of signaling and the ingenuity in utilizing materials that are manifested by higher primates. Population control may be such a key development. Among 309 skeletons of (adult) fossil man classified as to sex by H. V. Vallois, 172 were thought to be males and 137 were classified as females, which gives a sex ratio of 125.6 (*26*). These finds were made over a wide area, and they extend in time depth from Pithecanthropus to Mesolithic man. I am aware of the controversy that surrounds the sexing of fossil skeletons, as well as the question of whether both sexes were equally subject to burial. Nevertheless, one interpretation is that preferential female infanticide is an old practice. In contrast to man, it appears that most higher primates must utilize their natural fecundity rather fully to maintain population numbers. I conclude, as has been suggested elsewhere (*25*), that perhaps the most significant of the many milestones in the transition from higher primate to man—on a par with speech and toolmaking—occurred when human social organization and parental care permitted the survival of a higher proportion of infants than the culture

Table 1. Matrices of genetic distances between paired villages of the Makiritare Indians (seven villages, six loci) [after (*18*)].

Village	Distance matrices					
	BD	C	E	F	G	HI
A	.362	.558	.353	.345	.268	.336
BD		.250	.221	.432	.314	.296
C			.393	.588	.485	.444
E				.379	.249	.273
F					.394	.383
G						.158

Table 2. Matrices of genetic distances between paired villages of the Yanomama Indians (seven villages, six loci) [after (*18*)].

Village	Distance matrices					
	B	C	D	E	H	I
A	.227	.228	.385	.157	.416	.243
B		.367	.506	.144	.537	.360
C			.298	.295	.346	.297
D				.464	.154	.364
E					.486	.296
H						.350

and economy could absorb in each generation and when population control, including abortion and infanticide, was therefore adopted as the only practical recourse available.

The deliberate killing of a grossly defective child (who cannot hope for a full participation in the society he has just entered) or of the child who follows too soon the birth of an older sibling (and thereby endangers the latter's nutritional status) is morally repugnant to us. I am clearly not obliquely endorsing a return to this or a comparable practice. However, I am suggesting that we see ourselves in proper perspective. The relationship between rapid reproduction and high infant mortality has been apparent for centuries. During this time we have condoned in ourselves a reproductive pattern which (through weanling diarrhea and malnutrition) has contributed, for large numbers of children, to a much more agonizing "natural" demise than that resulting from infanticide. Moreover, this reproductive pattern has condemned many of the surviving children to a marginal diet inconsistent with full physical and mental development.

We obviously cannot countenance infanticide. However, accepting the general harshness of the milieu in which primitive man functioned, I find it increasingly difficult to see in the recent reproductive history of the civilized world a greater respect for the quality of human existence than was manifested by our remote "primitive" ancestors. Firth (*27*), in protesting the disturbance in population balance in the Pacific island of Tikopia when Christianity was substituted for ancient mores, expressed it thus:

> It might be thought that the so-called sanctity of human life is not an end in itself, but the means to an end, to the preservation of society. And just as in a civilized community in time of war, civil disturbance or action against crime, life is taken to preserve life, so in Tikopia infants just born might be allowed to have their faces turned down [see (*28*)], and to be debarred from the world they have merely glimpsed, in order that the economic equilibrium might be preserved, and the society maintain its balanced existence.

Polygyny and Genetic Significance of Differential Fertility

The three Indian tribes among whom we have worked are polygynous (*4, 5, 21*), the reward in these nonmaterial cultures for male achievement (however judged) and longevity being additional wives. This pattern is found in many primitive cultures. As brought out in the preceding section, women seem to be committed to a pattern of child spacing, which in the Yanomama results, for women living to the age of 40 years, in a lower variance in number of reported live births than in the contemporary United States (*24*). By contrast with our culture, then, the mores of these primitive societies tend to minimize the variance of number of live births per female but maximize the variance of number of children per male.

One of our objectives is to understand the genetic consequences of polygyny. The translation of generalizations such as the above into the kind of hard data that can be employed in either deterministic formulations or stochastic procedures based on population simulation designed to explore the genetic consequences of polygyny has proved quite difficult. A single example will suffice. We have earlier directed attention toward the unusual reproductive performance of certain headmen among the Xavante (*21*), and N. A. Chagnon has similar unpublished data for the Yanomama. During the past 2 years, J. MacCluer, in collaboration with Chagnon and myself, has been trying to develop a computer model that simulates the genetic and demographic structure of the Yanomama. The basic input has consisted of Chagnon's detailed demographic data from four villages. One of the several objectives of this simulation is to derive a better estimate of the amount of inbreeding than is possible from pedigree information in which the genealogical depth is so shallow, with particular reference to the complications introduced by polygyny. For some time there were great difficulties in reconciling certain aspects of the inbreeding results after 150 simulated years with the results of the first 20 simulated years (during which the real, input population dominated the findings), even though in many other respects—age at marriage, mean

Table 3. Matrix of pair-wise genetic distances for 12 South American tribes [after (*18*)].

Tribe	Cakchiquel	Cayapa	Cuna	Guayami	Jivaro	Pemon	Quechua	Shipibo	Xavante	Yanomama	Yupa
Aymara	.260	.301	.355	.485	.370	.381	.288	.393	.374	.514	.450
Cakchiquel		.297	.224	.364	.342	.302	.278	.363	.250	.439	.326
Cayapa			.283	.446	.289	.346	.224	.486	.343	.473	.328
Cuna				.327	.381	.283	.331	.466	.227	.479	.239
Guayami					.444	.469	.398	.645	.410	.437	.433
Jivaro						.402	.270	.521	.375	.536	.433
Pemon							.319	.460	.371	.510	.354
Quechua								.433	.336	.479	.392
Shipibo									.335	.660	.479
Xavante										.549	.249
Yanomama											.452

number of children, and distribution of polygyny—there was a good accord with the facts. During the first 20 simulated years, the members of the (real) population were, on the average, more closely related to each other than those in the simulated population at 150 years, so that, even when the model specified the maximum opportunity for consanguineous marriages consistent with field data, the level of inbreeding declined with time.

The reason finally became clear when the distribution of number of grandchildren per male was considered. Table 4 contrasts the actual distribution in the input data with that predicted by the simulation program after 150 years on the assumption of no correlation in fertility between successive generations. It is clear that the assumption is incorrect. Note the disproportionate number of grandchildren born to some few males, a situation that greatly increases the possibilities for marriages between first cousins or half-first cousins. Added genetic significance is lent to this phenomenon by the fact that the four males whose living grandchildren outnumber those of any male in the computer population represent two father-son combinations. One reason for this "familial" fertility seems to be that, if because of the polygyny of his father a young man possesses many sisters or half-sisters (who can be "traded"), that young man has an advantage in forming alliances and obtaining extra wives; thus, polygyny begets polygyny. The phenomenon does not appear to be primarily genetic. Clearly here is the explanation of why, when MacCluer programmed for the maximum rate of marriage between relatives (but did not incorporate in the model this aspect of fertility), there was an apparent decline in consanguinity as the real world of input was replaced by the simulated world. To be sure, we might have recognized this aspect of polygyny in Indian culture before we programmed the model, but I prefer to view the development as an example of how simulation forces one to look at the real population more carefully. This degree of differential fertility must be another factor in the marked genetic microdifferentiation between villages. Since the number of wives a man obtains and holds also depends on personal attributes, unquestionably determined genetically to some extent, here is an example of an interaction between the genetic system and the social system. Such interactions occur at all cultural levels, but it was unexpected to find this one emerging so strongly in these circumstances.

Table 4. The number of grandchildren (who reach adult life) per male, for all males with at least one grandchild, in the input (real) population and the artificial population after 150 years of simulation. The simulation is based on the assumption of no correlation in fertility between generations.

No. of grand-children per male	Initial population	Artificial population after 150 years
1	28	17
2	11	9
3	11	10
4	7	7
5	10	9
6	9	6
7	5	9
8	5	5
9	1	5
10	7	5
11	3	5
12	2	3
13		7
14		5
15	1	2
16	2	3
17		3
18		1
19	1	1
20	2	
21	1	2
22	1	2
23		1
24	1	2
25	1	
26		
27		
28	1	
29		
30		1
31		
32		
33		
34		
35		
36		
37		
38		1
39		
40		
41	1	
42	1	
43		
44		
45		
46	1	
.	.	.
.	.	.
.	.	.
62	1	
Total	114	121

The *possible* genetic implications of polygyny are clear, but some of the facts necessary to a meaningful treatment are still lacking. Thus, one of our projected future investigations is an attempt to contrast certain mental attributes of polygynous with nonpolygynous males. In many respects, Indian culture is much more egalitarian than our own. The children of a village have the same diet and, by our standards, a remarkably similar environment. There are minimal occupational differences, and we do not find the differentiation into fishing villages, mining villages, or farming communities encountered in many cultures. Even with allowance for the happy accident of a large sibship, the open competition for leadership in an Indian community probably results in leadership being based far less on accidents of birth and far more on innate characteristics than in our culture. Our field impression is that the polygynous Indians, especially the headmen, tend to be more intelligent than the nonpolygynous. They also tend to have more surviving offspring. Polygyny in these tribes thus appears to provide an effective device for certain types of natural selection. Would that we had quantitative results to support that statement!

The Balance with Disease

Inasmuch as viral, bacterial, and parasitic diseases are commonly regarded as among the important agents of natural selection, a particular effort has been directed toward assaying the health of primitive man and the characteristics of his interaction with these disease agents. We have reported that the Xavante are, in general, in excellent physical condition (*21, 22*), and we have similar unpublished data on the Yanomama and Makiritare. In terms of morbidity, perhaps the most important disease is falciparum malaria, which is probably a post-Columbian introduction (*29*). Fortunately for our view of the health of the pre-Columbian American Indian, we can find villages in which malaria does not seem to be a problem. Figure 1 presents our working concept of the Yanomama life expectancy curve, to be improved as more data become available (*23, 24*). Although infant and childhood mortality rates are high by the standards of a civilized country such as present-day Japan, they are low in comparison with India at the turn of the century, especially since there was probably gross underreporting in the data from India. Note the relatively high Yanomama death rate during the third, fourth, and fifth decades, a substantial fraction of which is due to warfare. One way to view the differences between these three curves is that the advent of civilization dealt a blow to man's health from which he is only now recovering.

Dunn (*30*) has properly emphasized the degree to which the ecological setting influenced disease patterns in primitive man and the difficulty in reaching generalizations. Even so, certain common denominators may be emerging. For instance, the pattern of acquisition of immunity to endemic diseases in the Indian and possibly other primitives can already be seen to differ in a number of respects from the pattern in most civilized communities (*23*). Among the Xavante and Yanomama, for example, we find gamma globulin levels approximately two times those in civilized areas (*31*). Newborn infants presumably possess a high measure of maternal antibody acquired transplacentally. From the first, these infants are in an intimate contact with their environment that would horrify a modern mother—or physician. They nurse at sticky breasts, at which the young mammalian pets of the village have also suckled, and soon are crawling on the feces-contaminated soil and chewing on an unbelievable variety of objects. Our thesis is that the high level of maternally derived antibody, early exposure to pathogens, the prolonged period of lactation, and the generally excellent nutritional status of the child make it possible for him to achieve a *relatively* smooth transition from passive to active immunity to many of the agents of disease to which he is exposed. The situation is well illustrated by the manner in which concomitantly administered gamma globulin reduces the impact of a rubeola vaccination while still permitting the development of effective immunity. To be sure, civilized tropical populations also have relatively high globulin levels [see references in (*21*)], so that there should be high placental transfer of passive immunity; however, because of the higher effective birth rate, the child of the civilizado is seldom nursed as long as the Indian child and thus falls prey to weanling diarrhea and malnutrition.

By his vaccination programs, then, modern man is developing a relatively painless immunity to his diseases, similar in some ways to the manner in which the Indian seems to have developed immunity to some of his diseases. A danger for both groups is the sudden appearance of a "new" disease. Burnet (*32*) has described some of the possible consequences for civilized societies in the appearance in the laboratory of strains of pathogens with new combinations of antigenic and virulence properties, and Lederberg (*33*) has labeled this threat as one of the hidden dangers in experiments related to biological warfare. At the other extreme, we have

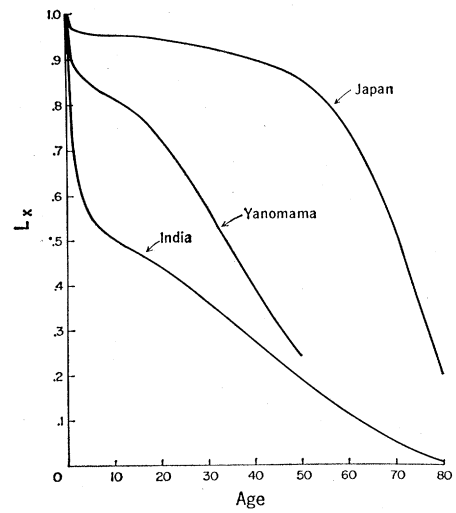

Fig. 1. "Life curves" for three types of populations: a highly urbanized and industrialized country (Japan in 1960); a densely populated, primarily agricultural country (India in 1901); and an unacculturated tribal population (the Yanomama) [after (*23*)]. Probability of survival is indicated by L_x.

recently witnessed at first hand the consequences of a measles epidemic among the Yanomama, known from antibody studies to be a "virgin-soil" population with respect to this virus (*34*). Although the symptomatic response of the Indian to the disease may be somewhat (but not markedly) greater than our own, much of the well-recognized enhanced morbidity and mortality in such epidemics is due to the secondary features of the epidemic—the collapse of village life when almost everyone is highly febrile, when mothers cannot nurse their infants, and when there is no one to provide for the needs of the community. After witnessing this spectacle, I find it unpleasant to contemplate its possible modern counterpart—when, in some densely populated area, a new pathogen, or an old one such as smallpox or malaria, appears and escapes control, and a serious breakdown of local services follows.

This relative balance with his endemic diseases is only one aspect of the generally harmonious relationship with his ecosystem that characterizes primitive man. There is an identification with and respect for the natural world, beautifully described by Radcliffe-Brown (*35*), Redfield (*36*), and Lévi-Strauss (*37*), among others, which we, who have walled it off so successfully while penetrating its secrets, find difficult to understand. In general, the religion of the tribes among whom we have worked is a pantheism in which both the heavens and the immediate environment are peopled by ubiquitous spirits, of human and nonhuman origin, whom it is vitally important to propitiate at every turn. To some extent their apparent respect for their ecosystem probably stems from ignorance and technical incompetence, but, in common with White (*38*), I believe that it also reflects the difference between a religion that regards man as a part of a system and one in which he is the divinely appointed master of the system.

A Program

In a world in which our heads are spinning under the impact of information overload, studies of primitive man provide, above everything else, perspective. Civilized man is a creature who each year is departing farther and farther from the population structure that obtained throughout most of human evolution and that was presumably of some importance to the evolutionary process. At the same time he is not only living far beyond a reasonable energy balance but is despoiling the resources for primary production so as to narrow increasingly the options available to redress the imbalances. The true dimensions of the dilemma that our present course has created are only now emerging [see especially (*39*)]. The intellectual arrogance created by our small scientific successes must be replaced by a profound humility based on the new knowledge of how complex is the system of which we are a part. To some of us, this realization carries with it the need for a philosophical readjustment which has the impact of a religious conversion.

We various members of the scientific community are all deeply engaged these days in speculating on the role that we will play in the next major cultural cycle. I find much of relevance to contemporary problems in my field, human genetics, in our studies of primitive man. It is clear that our primary objective—to understand the origin and significance of polymorphic variability—still eludes us. But there are other insights. In the light of our recent experiences among the Indian tribes, I shall now briefly consider some possible emphases in human genetics in the immediate future. In keeping with the new humility incumbent upon us all, it is not surprising that my suggestions are rather conservative; they are designed to preserve what we have rather than to promote unreal hopes of spectacular advances. They constitute in many respects an attempt to recreate, within limits, certain conditions that we have observed. These suggestions do not stem from any romanticism concerning the noble savage: Indian life is harsh and cruel, and it countenances an overt aggressiveness that is unthinkable today. Obviously the world should not return to a state of subdivision into demes of 50 to 200 persons constantly involved in a pattern of shifting loyalties and brutal conflict vis-à-vis neighboring demes. Nor are we likely to return to polygyny, with number of wives in part a function of one's "fierceness" —demonstrated by a series of duels with clubs or stylized bouts of chest poundings. Clearly we do not wish to abandon modern medical care to permit natural selection to have a better opportunity to work. But there are other, less disruptive aspects of primitive society for which there is a modern counterpart. These are enumerated below as a series of principles.

Stabilization of the Gene Pool

First principle: Stabilize the gene pool numerically. Throughout the world, primitive man seems to have curbed his intrinsic fertility to a greater extent than has the civilized world in recent centuries. Exactly how those curbs were relaxed with the advent of civilization is unclear, but the agricultural revolution undoubtedly played a part. Although it is currently fashionable to indict the great religions, on the basis of the Old Testament injunction to "be fruitful and multiply," their precise role (until recent times) is in my opinion unclear. The remaining pockets of dissent with the principle of population limitation are rapidly disappearing; the next 5 years will convince even the most reluctant. But by what precise formula should population limitation be accomplished? I have previously urged a simple quota system, set at three living children per couple on the thesis that failure to marry, infertility, and voluntary limitation to less than three would result in a realized average of approximately two children who reach the age of reproduction (*40*). I now wonder whether failure of contraception will not result in so many well-intentioned persons exceeding their quota that these guidelines are not sufficiently stringent; I would therefore amend the earlier suggestion to include provision for voluntary sterilization after the third child.

You will recognize that this proposal implies relative stabilization of the present gene pool, a move that will tend to conserve all our present bewildering diversity but hinder evolution. It makes no value judgments about any specific group. There would be less opportunity for changes in gene frequency than with present patterns of differential fertility.

Such a policy cannot succeed if some religions and governments simply continue their present half-hearted admonitions and leave the rest to science, while other religions and governments actually oppose effective population control. What has been signally lacking thus far is a clear statement at every possible level of responsibility of the implications of continuing the present rate of population increase. Also lacking has been an administrative framework within which all peoples move toward population control simultaneously, thus dispelling deep-rooted fears that some sectors are being subjected to a subtle form of genocide. Bills now pending in the U.S. Congress—S. 2108, S. 2701, S. 3219, S. 3502, H.R. 11550, H.R. 15165—carry the hope that the United States will shortly be facing these questions much more forthrightly than in the past.

Protection of the Gene Pool

Second principle: Protect the gene against damage. If, as we have implied, polygyny among the Indian has eugenic overtones, there is no acceptable modern counterpart in view. However, we can at least protect the gene pool from obvious damage. The world of primitive man is remarkably uncontaminated. This fact, plus his lower mean age at reproduction, probably results in lower mutation rates than our own (*41*), but we have no direct evidence.

Until recently, the principal concomitant of civilization that appeared capable of damaging the gene pool was an increasing exposure to radiation. Now concern is shifting to the many potentially mutagenic chemicals being introduced into the environment as pesticides, industrial by-products, air contaminants, and so forth. The magnitude of this problem is currently undefined. About 6 percent of all newborn infants have been found to have defects partially or wholly of genetic origin (*42*). Let us assume that half of these defects (3 percent) result from recurrent mutation. Doubling the mutation rate would *eventually* double that 3 percent.

For all the work that has been done on the genetic effects of radiation, involving both man and experimental organisms, there still remain large areas of ambiguity, especially as regards the effects of low-level, intermittent, or chronic-type doses, such as characterize most human exposures. The current working estimate of the "doubling dose" of radiation of this type is 100 to 200 roentgens (*42*). In general, current man-made human exposures in the United States [probably less than 3 rem to the gonads in 30 years (*42*)] appear to be of the order of perhaps 1/30 to 1/60 of the "doubling dose," a price society thus far seems prepared to accept for the benefits of the medical uses of radiation and the development of nuclear sources of energy. It may be that genetically effective exposures to the chemical mutagens are as low or even lower, but we cannot be certain.

The technical advances of the past 20 years now render it possible and feasible to screen a representative 20 proteins in newborn infants for evidence of mutational damage [see (*43*)]; hence we need no longer rely, as in the studies at Hiroshima and Nagasaki, on the potential genetic effects of the atomic bombs, on such imprecise indicators of genetic damage as congenital malformations, survival rates, and sex ratio. A society that can afford to send man to the moon surely has the resources and the intelligence to monitor itself properly for increased mutation rates. If a significant increase is detected, however, the task of identifying the responsible agent or agents will, because of the many possibilities, be extremely difficult, and that agent, when identified, may be so relevant to the welfare of society that, as with radiation, the goal will be to minimize rather than to eliminate exposures. Despite these difficulties in detection and control, immediate steps to determine the facts are needed.

Genetic Counseling and Prenatal Diagnosis

Third principle: Improve the quality of life through parental choice based on genetic counseling and prenatal diagnosis. Both the pressures on the social system and its services and the increasing demands of society on the individual render it imperative that full advantage be taken of all morally acceptable developments that promise to minimize the number of unfortunate individuals incapable of full participation in this complex society. We will not return to infanticide, but there are ethical alternatives. Genetic counseling, which defines the high-risk family, represents one such development. In the past, once the identification had been made, the individuals who wished to limit the entry of defective children into the population had only two alternatives: to practice birth control or to apply for voluntary sterilization. Recently the possibilities inherent in prenatal diagnosis based on fetal cells obtained through amniocentesis during the first trimester of pregnancy have been receiving active attention (*44*). Where accurate diagnosis is possible and the presence of a defective fetus is established, the parents can be offered an abortion, usually with reasonable prospects of a normal child in the next pregnancy. Thus far the conditions that can be accurately diagnosed in the very early stages of pregnancy and the numerical impact of these entities are relatively small.

The moral issues that are involved cannot be evaded, and it is better in this time of reappraisal for society to face them forthrightly. At what point is the artificial termination of a pregnancy no longer ethical, even when the fetus concerned is incapable of marginal participation in society? Just what defects are of such gravity as to justify intervention? To what extent should persuasion be employed in implementing these new possibilities? In my opinion, once the principle of parental choice of a normal child is established, it seems probable that in large measure the parental desire for normal children can be relied on to result in the purely voluntary elimination of affected fetuses.

Realizing the Genetic Potential of the Individual

Fourth principle: Improve the phenotypic expression of the individual genotype. It is a sobering thought that the relatively egalitarian structure of most primitive societies, plus the absence of large individual differences in material wealth, seems to ensure that, within the culturally imposed boundaries, each individual in primitive society leads a life (and enjoys reproductive success) more in accord with his innate capabilities than in our present democracy. In the difficult times ahead, society clearly needs the fullest possible participation of all its members. In the past, a very major effort has gone into the provision of special services for the physically and mentally handicapped. A retreat from such compassion is unthinkable, but it is apparent that a similar effort directed toward realizing the genetic potential of the underprivileged or the gifted would have far more impact on the solution of our problems.

Much of the thrust of the geneticist and those with allied interests has been directed toward the treatment of specific genetic diseases. Obviously these efforts need not only to be continued but to be greatly expanded. And equally obviously, the Indian contributes no insight into a program in this field of endeavor. Others are speaking eloquently to the needs and potentialities of this type of investigation.

But an even greater effort should be directed toward what I have elsewhere termed "culture engineering" (*45*), which merges at one extreme with the euphenics of Lederberg (*46*). There is presumably an environment (or group of environments) in which the still poorly understood potentialities of the human animal find the fullest and most harmonious expression. Although our present environment-culture reduces the impact of a number of previously important causes of mortality and morbidity, it creates a host of other "casualties of our times" (*47*). The challenge to culture engineering is, of course, greatest in the realm of the mind. It is not enough to think in terms of better schools and more attractive housing; the subtle and lasting influence of prenatal and early postnatal influences is becoming increasingly apparent [see (*48*)]. Experimental mammalian models are yielding fascinating evidence on the complexity of these interactions (*49*). It is doubtful whether our precipitous and helter-skelter attacks on our present world will yield an optimum environment. We cannot escape the consequences of the peculiar position in which we have placed ourselves; we must now cautiously and reverently accept the full responsibility for shaping our own world.

Summing Up

The foregoing principles constitute an extremely conservative program in human genetics, which advocates for the present a return to as many of the features of the population structure under which we evolved as is consistent with our present culture. The urgent need to understand the biomedical and social significance of human genetic variability as a basis for an eventual, more definitive program should be clear, and yet we seem to be retreating from support of the necessary research while we are squandering billions in pursuit of dubious military goals.

There has been no mention in this presentation of that brand of genetic engineering concerned with controlled changes in transmissible genetic material. This omission is not due to oversight or limitations of time. My thesis is clearly a plea for a profound respect for ourselves and the system in which we function. It would be inconsistent with that thesis to suggest that, with our present limited knowledge of the human genome, we should in the near future think of intervening to alter it in ways we cannot completely understand. Research along these lines with experimental organisms is inevitable and desirable—but I question the wisdom of attempting, in the foreseeable future, to apply the results of that research to man.

The past decade has witnessed spectacular triumphs in the "inner space" of the cell and the "outer space" of the cosmos. Perhaps this decade will in retrospect be seen as the first of many decades of spectacular advances in our understanding of *"intermediate* space" —the biosphere—the space defined as that narrow life-supporting zone wherein occur the interactions between intact humans and other organisms and their environment which by definition are an ecosystem. As we realize the full complexity of intermediate space, it seems very probable that the scientific challenge to produce new knowledge will be equaled by the challenge of integrating the applications of that new knowledge smoothly into the ecosystem. In the most sophisticated way we can summon, we must return to the awe, and even fear, in which primitive man held the mysterious world about him, and like him we must strive to live in harmony with the only biosphere that we can be certain will be occupied by our descendants.

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Sunlight Ultraviolet and Bacterial DNA Base Ratios

Natural exposure to ultraviolet may be an evolutionary pressure toward high guanine plus cytosine in DNA.

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The base composition of DNA is a constant characteristic of a given species. The percentage of guanine (G) plus cytosine (C) in the DNA (G + C content) varies widely among species and ranges from about 23 percent to 74 percent. Although about 1000 G + C contents have been measured, mostly in bacteria, no satisfactory explanation has been advanced for why a particular species has a high or low G + C content. We propose that bacterial species exposed to sunlight evolve high G + C contents to avoid thymine specific damage from the ultraviolet radiation in sunlight. Although there may be similar effects in some fungi (*1*) and higher algae, we restrict our discussion primarily to bacteria, because in higher organisms screening due to the larger cell size and cell mass appears to be a major factor. In addition, higher organisms are diploid or have multiple copies of the genetic material, and this complicates any analysis of ultraviolet sensitivity.

Environment and G + C Content

We have found a strong correlation between the amount of sunlight to which a bacterium is normally exposed and its G + C content. Because of uncertainties concerning many bacterial habitats we have restricted ourselves to those habitats which clearly receive a high ultraviolet exposure or a low ultraviolet exposure. Bacteria exposed to considerable sunlight (bacteria with aerial reproduction, aquatic bacteria, and carotenoid-containing bacteria) almost universally have high

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