FROM THE EDITOR

The Science of Race

BY PAUL HOFFMAN

Paul Hoffman, "The Science of Race," Discover, Volume 15, November 1994, p. 4.
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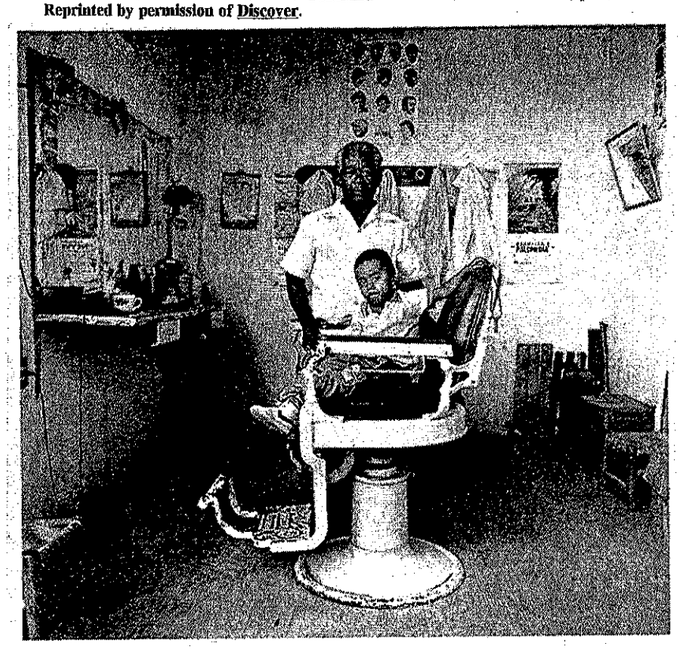

Barber Shop, 1990, from *Tengo Casi 500 Años: Africa's Legacy in Mexico: Photographs by Tony Gleaton*

MOST DISCOVER READERS, I presume, would like to live in a color-blind world, where the color of one's skin has no more bearing on human relations than, say, the color of one's shirt. That world, alas, is not in sight. You cannot open a daily paper without finding stories with racial overtones, and all too often those stories make the front page.

Riffling through random newspapers on my desk, story upon story leaps out: Polls show that blacks and whites are divided about O. J. Simpson's guilt, and his lawyers charge that a racist police officer manufactured evidence by planting a bloody glove in his yard. Anguished reflections on the incidence of black-on-black violence are occasioned by the mugging of civil rights legend Rosa Parks. A commentator wonders if the United States would have invaded Haiti months ago if the downtrodden there had white faces. The principal of an Alabama high school that was destroyed by arson after he tried to ban interracial couples from a prom is still in the hot seat for calling a biracial student a "mistake." A poll shows that one in five white Americans thinks interracial marriage should be outlawed. Medical researchers report that the veins of blacks are less elastic than those of whites, a finding that may explain why blacks are disproportionately affected by heart disease. Black golfer Tiger Woods fights his way into the record books in a sport dominated by white men.

Our society is obsessed with race and confused by it. Human beings are visual animals, so we notice each other's skin color. But do skin color and race matter in any fundamental, scientific way? That's the theme of this special issue, "The Science of Race," which starts on page 56.

This issue tackles a host of highly charged questions that are important to the way we view the people with whom we share the planet. Is skin color linked to other physiological characteristics? Are certain races predisposed toward certain diseases, and is that predisposition the result of genetics or of a shared environment? And what are we to make of the trendy "reverse racist" claim that the melanin that darkens skin also makes the brain run better, so that the darker your skin, the smarter you are? Why is the most common racial group in the Western world, Caucasian, named for a Russian and Georgian mountain range? Is it reasonable—or racist—to study the role biology and genetics might play in violent human behavior?

Scientists are divided on many of these questions, and we've tried in this issue to capture that diversity of opinion. In certain respects scientists are as confused as the rest of us about how race matters. Some researchers even go so far as to deny that races exist.

What is clear is that the genetic differences between the so-called races are minute. On average there's .2 percent difference in genetic material between any two randomly chosen people on Earth. Of that diversity, 85 percent will be found within any local group of people—say, between you and your neighbor. More than half (9 percent) of the remaining 15 percent will be represented by differences between ethnic and linguistic groups within a given race (for example, between Italians and French). Only 6 percent represents differences between races (for example, between Europeans and Asians). And remember—that's 6 percent of .2 percent. In other words, race accounts for only a minuscule .012 percent difference in our genetic material.

Skin color may only be skin deep. Surgeons, thankfully, understand this: in organ transplants a black donor can be a better match for a white patient than another white person might be. Would that the rest of us understood this, too. It is my hope that this special issue of DISCOVER will contribute to such an understanding.

☐ Black ☐ White ☑ Other

Racial categories are cultural constructs masquerading as biology

by Jonathan Marks

Jonathan Marks, "Black, White, Other", Natural History, Dec. 1994, pg.32-35
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David Burnett: CPI

While reading the Sunday edition of the *New York Times* one morning last February, my attention was drawn by an editorial inconsistency. The article I was reading was written by attorney Lani Guinier. (Guinier, you may remember, had been President Clinton's nominee to head the civil rights division at the Department of Justice in 1993. Her name was hastily withdrawn amid a blast of criticism over her views on political representation of minorities.) What had distracted me from the main point of the story was a photo caption that described Guinier as being "half-black." In the text of the article, Guinier had described herself simply as "black."

How can a person be black and half black at the same time? In algebraic terms, this would seem to describe a situation where $x = {}^1/_2x$, to which the only solution is $x = 0$.

The inconsistency in the *Times* was trivial, but revealing. It encapsulated a longstanding problem in our use of racial categories—namely, a confusion between biological and cultural heredity. When Guinier is described as "half-black," that is a statement of biological ancestry, for one of her two parents is black. And when Guinier describes herself as black, she is using a cultural category, according to which one can either be black or white, but not both.

Race—as the term is commonly used—is inherited, although not in a strictly biological fashion. It is passed down according to a system of folk heredity, an all-or-nothing system that is different from the quantifiable heredity of biology. But the incompatibility of the two notions of race is sometimes starkly evident—as when the state decides that racial differences are so important that interracial marriages must be regulated or outlawed entirely. Miscegenation laws in this country (which stayed on the books in many states through the 1960s) obliged the legal system to define who belonged in what category. The resulting formula stated that anyone with one-eighth or more black ancestry was a "negro." (A similar formula, defining Jews, was promulgated by the Germans in the Nuremberg Laws of the 1930s.)

Applying such formulas led to the biological absurdity that having one black great-grandparent was sufficient to define a person as black, but having seven white great-grandparents was insufficient to define a person as white. Here, race and biology are demonstrably at odds. And the problem is not semantic but conceptual, for race is presented as a category of nature.

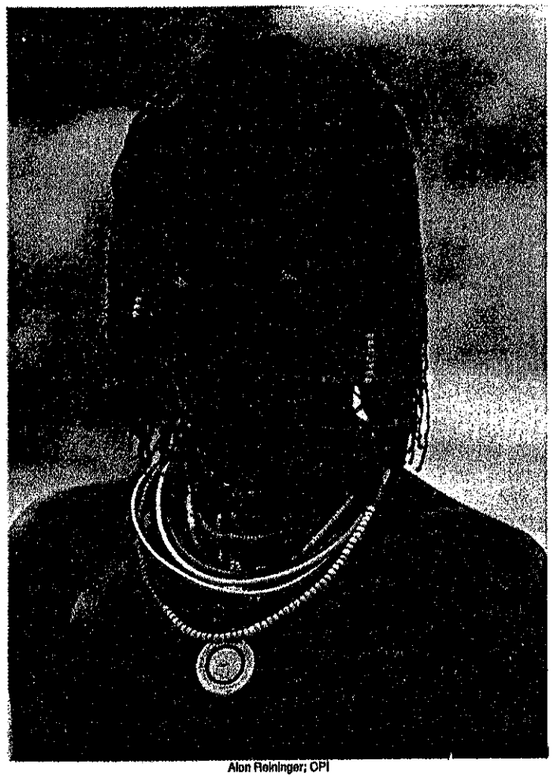
Human beings come in a wide variety of sizes, shapes, colors, and forms—or, because we are visually oriented primates, it certainly seems that way. We also come in larger packages called populations; and we are said to belong to even larger and more confusing units, which have long been known as races. The history of the study of human variation is to a large extent the pursuit of those human races—the attempt to identify the small number of fundamentally distinct kinds of people on earth.

This scientific goal stretches back two centuries, to Linnaeus, the father of biological systematics, who radically established *Homo sapiens* as one species within a group of animals he called Primates. Linnaeus's system of naming groups within groups logically implied further breakdown. He consequently sought to establish a number of subspecies within *Homo sapiens*. He identified five: four geographical species (from Europe, Asia, Africa, and America) and one grab-bag subspecies called *monstrosus*. This category was dropped by subsequent researchers (as was Linnaeus's use of criteria such as personality and dress to define his subspecies).

While Linnaeus was not the first to divide humans on the basis of the continents on which they lived, he had given the division a scientific stamp. But in attempting to determine the proper

number of subspecies, the heirs of Linnaeus always seemed to find different answers, depending upon the criteria they applied. By the mid-twentieth century, scores of anthropologists—led by Harvard's Earnest Hooton—had expended enormous energy on the problem. But these scholars could not convince one another about the precise nature of the fundamental divisions of our species.

Part of the problem—as with the *Times*'s identification of Lani Guinier—was that we humans have two constantly intersecting ways of thinking about the divisions among us. On the one hand, we like to think of "race"—as Linnaeus did—as an objective, biological category. In this sense, being a member of a race is supposed to be the equivalent of being a member of a species or of a phylum—except that race, on the analogy of subspecies, is an even narrower (and presumably more exclusive and precise) biological category.



Alon Reininger; OPI

The other kind of category into which we humans allocate ourselves—when we say "Serb" or "Hutu" or "Jew" or "Chicano" or "Republican" or "Red Sox fan"—is cultural. The label refers to little or nothing in the natural attributes of its members. These members may not live in the same region and may not even know many others like themselves. What they share is neither strictly nature nor strictly community. The groupings are constructions of human social history.

Membership in these *un*biological groupings may mean the difference between life and death, for they are the categories that allow us to be identified (and accepted or vilified) socially. While membership in (or allegiance to) these categories may be assigned or adopted from birth, the differentia that mark members from nonmembers are symbolic and abstract; they serve to distinguish people who cannot be readily distinguished by nature. So important are these symbolic distinctions that some of the strongest animosities are often expressed between very similar-looking peoples. Obvious examples are Bosnian Serbs and Muslims, Irish and English, Huron and Iroquois.

Obvious natural variation is rarely so important as cultural difference. One simply does not hear of a slaughter of the short people at the hands of the tall, the glabrous at the hands of the hairy, the red-haired at the hands of the brown-haired. When we do encounter genocidal violence between different-looking peoples, the two groups are invariably socially or culturally distinct as well. Indeed, the tragic frequency of hatred and genocidal violence between biologically indistinguishable peoples implies that biological differences such as skin color are not motivations but, rather, excuses. They allow nature to be invoked to reinforce group identities and antagonisms that would exist without these physical distinctions. But are there any truly "racial" biological distinctions to be found in our species?

Obviously, if you compare two people from different parts of the world (or whose ancestors came from different parts of the world), they will differ physically, but one cannot therefore define three or four or five basically different kinds of people, as a biological notion of race would imply. The anatomical properties that distinguish people—such as pigmentation, eye form, body build—are not clumped in discrete groups, but distributed along geographical gradients, as are nearly all the genetically determined variants detectable in the human gene pool.

These gradients are produced by three forces. Natural selection adapts populations to local circumstances (like climate) and thereby differentiates them from other populations. Genetic drift (random fluctuations in a gene pool) also differentiates populations from one another, but in non-adaptive ways. And gene flow (via intermarriage and other child-producing unions) acts to homogenize neighboring populations.

In practice, the operations of these forces are difficult to discern. A few features, such as body build and the graduated distribution of the sickle cell anemia gene in populations from western Africa, southern Asia, and the Mediterranean can be plausibly related to the effects of selection. Others, such as the graduated distribution of a small deletion in the mitochondrial DNA of some East Asian, Oceanic, and Native American peoples, or the degree of flatness of the face, seem unlikely to be the result of selection and are probably the results of random biohistorical factors. The cause of the distribution of most features, from nose breadth to blood group, is simply unclear.

☐ Black ☐ White ☐ Other

Leong Ka Tai; Material World

The overall result of these forces is evident, however. As Johann Friedrich Blumenbach noted in 1775, "you see that all do so run into one another, and that one variety of mankind does so sensibly pass into the other, that you cannot mark out the limits between them." (Posturing as an heir to Linnaeus, he nonetheless attempted to do so.) But from humanity's gradations in appearance, no defined groupings resembling races readily emerge. The racial categories with which we have become so familiar are the result of our imposing arbitrary cultural boundaries in order to partition gradual biological variation.

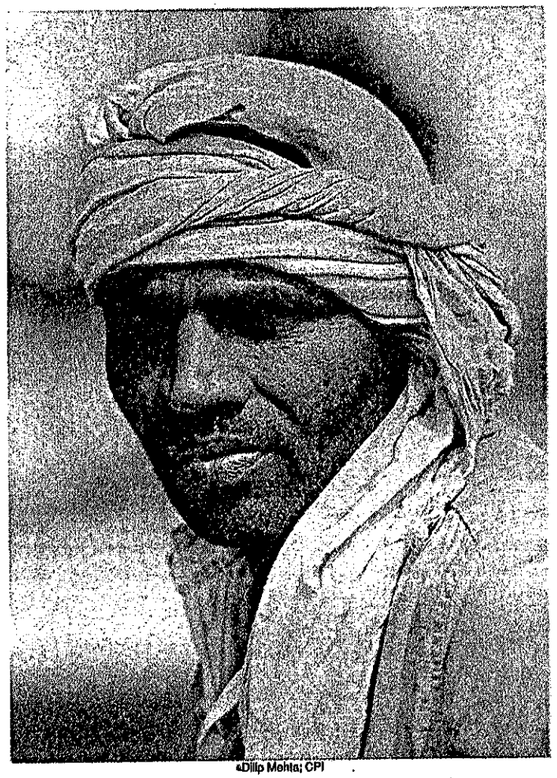
Unlike graduated biological distinctions, culturally constructed categories are ultrasharp. One can be French or German, but not both; Tutsi or Hutu, but not both; Jew or Catholic, but not both; Bosnian Muslim or Serb, but not both; black or white, but not both. Traditionally, people of "mixed race" have been obliged to choose one and thereby identify themselves unambiguously to census takers and administrative bookkeepers—a practice that is now being widely called into question.

A scientific definition of race would require considerable homogeneity within each group, and reasonably discrete differences between groups, but three kinds of data militate against this view: First, the groups traditionally described as races are not at all homogeneous. Africans and Europeans, for instance, are each a collection of biologically diverse populations. Anthropologists of the 1920s widely recognized *three* European races: Nordic, Alpine, and Mediterranean. This implied that races could exist within races. American anthropologist Carleton Coon identified *ten* European races in 1939. With such protean use, the term race came to have little value in describing actual biological entities within *Homo sapiens*. The scholars were not only grappling with a broad north–south gradient in human appearance across Europe, they were trying to bring the data into line with their belief in profound and fundamental constitutional differences between groups of people.

But there simply isn't one European race to contrast with an African race, nor three, nor ten: the question (as scientists long posed it) fails to recognize the actual patterning of diversity in the human species. Fieldwork revealed, and genetics later quantified, the existence of far more biological diversity within any group than between groups. Fatter and thinner people exist everywhere, as do people with type O and type A blood. What generally varies from one population to the next is the *proportion* of people in these groups expressing the trait or gene. Hair color varies strikingly among Europeans and native Australians, but little among other peoples. To focus on discovering differences between presumptive races, when the vast majority of detectable variants do not help differentiate them, was thus to define a very narrow—if not largely illusory—problem in human biology. (The fact that Africans are biologically more diverse than Europeans, but have rarely been split into so many races, attests to the cultural basis of these categorizations.)

Second, differences between human groups are only evident when contrasting geographical extremes. Noting these extremes, biologists of an earlier era sought to identify representatives

of "pure," primordial races,—presumably located in Norway, Senegal, and Thailand. At no time, however, was our species composed of a few populations within which everyone looked pretty much the same. Ever since some of our ancestors left Africa to spread out through the Old World, we humans have always lived in the "in-between" places. And human populations have also always been in genetic contact with one another. Indeed, for tens of thousands of years, humans have had trade networks; and where goods flow, so do genes. Consequently, we have no basis for considering *extreme* human forms the most pure, or most representative, of some ancient primordial populations. Instead, they represent populations adapted to the most disparate environments.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And third, between each presumptive "major" race are unclassifiable populations and people. Some populations of India, for example, are darkly pigmented (or "black"), have Europeanlike ("Caucasoid") facial features, but inhabit the continent of Asia (which should make them "Asian"). Americans might tend to ignore these "exceptions" to the racial categories, since immigrants to the United States from West Africa, Southeast Asia, and northwest Europe far outnumber those from India. The very existence of unclassifiable peoples undermines the idea that there are just three human biological groups in the Old World. Yet acknowledging the biological distinctiveness of such groups leads to a rapid proliferation of categories. What about Australians? Polynesians? The Ainu of Japan?

Categorizing people is important to any society. It is, at some basic psychological level, probably necessary to have group identity about who and what you are, in contrast to who and what you are not. The concept of race, however, specifically involves the recruitment of biology to validate those categories of self-identity.

Mice don't have to worry about that the way humans do. Consequently, classifying them into subspecies entails less of a responsibility for a scientist than classifying humans into subspecies does. And by the 1960s, most anthropologists realized they could not defend any classification of *Homo sapiens* into biological subspecies or races that could be considered reasonably objective. They therefore stopped doing it, and stopped identifying the endeavor as a central goal of the field. It was a biologically intractable problem—the old square-peg-in-a-round-hole enterprise; and people's lives, or welfares, could well depend on the ostensibly scientific pronouncement. Reflecting on the social history of the twentieth century, that was a burden anthropologists would no longer bear.

This conceptual divorce in anthropology—of cultural from biological phenomena—was one of the most fundamental scientific revolutions of our time. And since it affected assumptions so rooted in our everyday experience, and resulted in conclusions so counterintuitive—like the idea that the earth goes around the sun, and not vice-versa—it has been widely underappreciated.

Kurt Vonnegut, in *Slaughterhouse Five*, describes what he remembered being taught about human variation: "At that time, they were teaching that there was absolutely no difference between anybody. They may be teaching that still." Of course there are biological differences between people, and between populations. The question is: How are those differences patterned? And the answer seems to be: Not racially. Populations are the only readily identifiable units of humans, and even they are fairly fluid, biologically similar to populations nearby, and biologically different from populations far away.

In other words, the message of contemporary anthropology is: You may group humans into a small number of races if you want to, but you are denied biology as a support for it. □

VIII A Biological View of Race

PAUL R. EHRLICH AND RICHARD W. HOLM

From Ashley Montagu, The Concept of Race Copyright 1964 by Collier Books, London, pp. 154-179. Reprinted by permission of the publisher.

Most of the problems clouding the study and description of human variation can be traced to the taxonomic premise that *Homo sapiens* is divided into a series of races which are significant biological entities. We shall attempt to deal with this premise in the context of current biological thinking about the taxonomic structure of nature.

The historical development of taxonomy follows closely the changing prejudices and philosophies of other sciences and of the humanities and arts as well. At any period taxonomy more or less reflects the prevailing world view of a somewhat earlier historical period. Thus it is understandable that the first formal taxonomy should have been an outgrowth of herbals and bestiaries. The Linnaean system developed in the 18th century along with the pervasive compulsion to order nature into mechanically logical systems. The taxonomic framework of the recent past is the result of the 19th century's propelling need to think in terms of linear progression. Today, however, in many areas of creative activity, there is a growing interest in problems of portrayal, description, and quantification of complex nonlinear relationships. It is not surprising that the impact of these approaches and of the devices necessary to sustain them is now beginning to be felt in taxonomy.

The New Systematics

In recent years, following the lead of the physical sciences and mathematicians, biologists have begun to examine some of and basic tenets and assumptions of their discipline. Taxonomy, often thought of as the least dynamic of the biological sciences, has assumed a position of leadership in this reevaluation of methods and principles. Taxonomy has experienced what might be regarded as two revolutions (see Kuhn, 1962) in the last 25 years. The first led to the establishment of the "new systematics" and derived primarily from the introduction of ideas from genetics and cytology into a largely museum-oriented field. Awareness of the principles of Mendelian genetics and the analysis of large population samples of organisms resulted in a greater interest in infraspecific categories. Thus the concepts of subspecies and geographic races, championed by Rensch, Mayr, Dobzhansky, and others, increased in importance. The commonly acccepted definition of subspecies was well-expressed by Mayr (1942, p. 106):

> The subspecies, or geographic race, is a geographically localized subdivision of the species, which differs genetically and taxonomically from other subdivisions of the species.

The new systematics shifted interest away from static species concepts, established by Linnaeus and reinforced, in a sense, by Darwin's emphasis on the term species. Differentiation of populations became the new point of focus and greater understanding was gained of the cytogenetic processes involved. However the problem of the taxonomic expression of the complex interrelationships discovered was largely ignored or attempts were made to solve the problem with the existing taxonomic framework. The new systematics, in introducing

dynamics into taxonomy, laid the groundwork for its own replacement. Extensive investigations of organisms in nature and of forms with widely divergent genetic systems (inbreeding, haplodiploidy, asexual reproduction, etc.), together with studies of multivariate patterns of geographic variation, made it apparent that the classical species-subspecies taxonomic structure (partially retained by the "new systematics") was inadequate for the expression of evolutionary relationships.

Perhaps the first signs of aging of the new systematics came in the early 1950's with the wide realization that the entities placed in the category "subspecies" were not necessarily evolutionary units. The subjective nature of the category had long been recognized (Mayr 1942). The dangers of its use were made clear by the controversy following a paper by Wilson and Brown (1953), who pointed out the arbitrary nature of the category and recommended that it no longer be used.

These problems were not unique to the subspecies category. Intensive studies of species, particularly in plants, have shown that the species itself is not necessarily a self-contained evolutionary unit (Epling and Catlin 1950). Attempts to create a rigorous and objective definition of species based on genetic criteria have failed because it is not possible to make them operational. A return to the original definition of species as "kind" has been recommended (Ehrlich and Holm 1962).

The major triumph of the "new systematics" was to introduce evolutionary thinking into taxonomy, and this led to the inevitable failure of the new systematics at the descriptive level. The inclusion of evolutionary hypotheses and assumptions into the word-symbols of taxonomy greatly reduces their usefulness for objective descriptions of patterns of relationships among organisms. If the process of evolution is to be inferred from the classifications of taxonomists, then the classifications cannot be based upon evolutionary hypotheses.

Numerical Taxonomy

The second post-Linnaean revolution in taxonomy began in the late 1950's and its effects are just beginning to be felt by the practicing taxonomist. The proximal cause of this revolution was the growing access to high-speed data-processing equipment. Although for many years taxonomists had recognized the usefulness of taxonomic systems based on multiple character comparisons (see, for instance, Anderson 1949), systems using large numbers of characters could not easily be analysed without the aid of digital computers. As availability of such equipment increased, people in many parts of the world began investigating phenetic relationships (relationships defined as degree of over-all similarity) among organisms. Developments in this field are largely outside the scope of this discussion; they are discussed concisely by Sneath and Sokal (1962) and in detail by Sokal and Sneath (1963). The broader implications of this approach, which perhaps are more concealed than revealed by the commonly used name, numerical taxonomy, are considered by Ehrlich and Holm (1962).

In brief, numerical taxonomy consists of the quantifying of large numbers of characteristics (usually 75 or more) which vary in the group of organisms to be studied. This is followed by the computation of some kind of coefficient of similarity among the units studied, based upon these characteristics. These coefficients may then be used as the basis for a taxonomic system by clustering the most similar entities. A simplified example is given in Figure 1.

The table (upper left) lists three entities, *A*, *B*, *C*. These entities may be individuals, species, genera, or any other units which are to be compared. In this example, only seven characters are evaluated for *A*, *B*, and C. A character, in the idiom

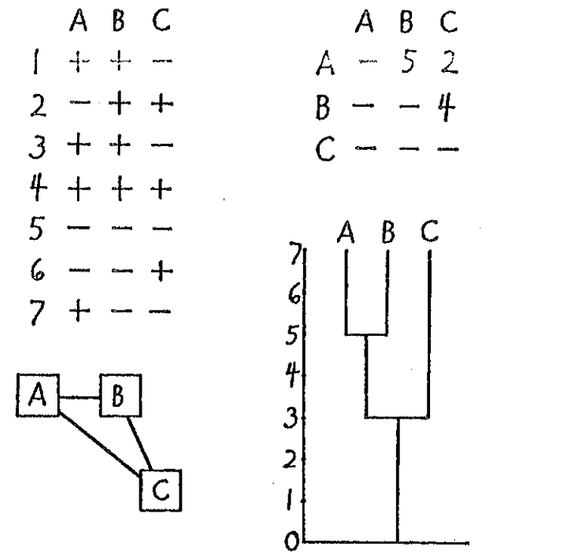


Figure 1. An example of numerical taxonomy. (Explanation in text.)

of the numerical taxonomist, is any characteristic which varies in the group under consideration. In our example, characters which have been coded into two states, plus or minus, have been listed. Certain characters in human beings, such as Rh positive or Rh negative blood types, could easily be coded in this fashion. Coding a character such as height in this manner results in considerable loss of information.

In order to obtain a measure of the degree of resemblance among *A*, *B*, and *C*, a very simple coefficient of association is obtained by counting the number of characters which are the same for each pair of entities. This coefficient may take values from a maximum of 7 (two entities the same in all characters)

to a minimum of 0 (two entities different in all characters). Values for all combinations are shown in the table in the upper right. This array of coefficients of similarity among entities is known as a Q-matrix. It can be seen that, with respect to the characters measured, *A* and *B* are more similar than *A* and *C*, *C* is more similar to *B* than to *A*, and *B* is more similar to *A* than to *C*.

Since only three entities are being compared here, it is possible to diagram these relationships in two dimensions as has been done in the lower left. The higher the coefficient of similarity, the shorter the line connecting any two entities. However, Q-matrices containing coefficients among more than three entities cannot be diagrammed in two dimensions. Nor is it easy by inspection to visualize the multi-dimensional relationships inherent in larger matrices. A matrix showing all of the possible comparisons among, say, 100 species of a genus would contain 4,950 different coefficients regardless of the number of characters employed in the comparisons. In order to obtain some grasp of the relationships in such an array, various methods of searching for and diagramming structure in the matrix have been devised.

The dendrogram (lower right) illustrates one method of structuring applied to our small sample matrix. The ordinate is the scale of values of the similarity coefficient. Since each entity has complete similarity with itself, each is placed at the top of the diagram with a value of 7. The highest coefficient in the Q-matrix is 5, between *A* and *B*, therefore the lines are joined at that level. The *A-B* stem is joined to the *C* stem at the average value of the coefficients of *C* with *A* and *C* with *B* (3). The diagram gives a more readily grasped picture of relationships, but only at the cost of the loss of some information present in the Q-matrix. For instance, from looking at the diagram one could not know that *C* is not equally similar to *A* and *B*.

The "taxonomy" of these entities could be viewed as one

taxon comprising two entities (or subordinate taxa) and another taxon comprising one. Various methods of applying nomenclature to dendrograms have been employed but their details need not concern us. The decision of how distinctive a group of entities must be before it should be distinguished (with a number or a name) as a "kind" or "species" is a decision which can only be made in the context of a particular investigation. It is important to realize that clusters derived by such analysis are based solely upon resemblances in the characteristics evaluated and are not based upon genetic or phylogenetic hypotheses. They comprise, however, the basic data set upon which such hypotheses may be constructed.

As might have been expected, such procedures have been decried by many taxonomists as being anti-evolutionary or typological. The first criticism is clearly not valid since the system is not concerned with the possible interpretations of the computed similarities. The second is partially true, although, as several authors (Daly 1961, Sokal 1962) have pointed out, there are fewer objectionable typological aspects to numerical taxonomy than there are to so-called phylogenetic taxonomy. A certain amount of the opposition to numerical taxonomy seems to be based on emotional reactions to the growing use of computers. There are dangers from the misuse of computers as with any mechanism extending human capabilities. Such misuse, if it occurs, is the result of a human decision. Emotional reactions to numerical taxonomy can be found even in the anthropological literature. For example (Coon 1962, p. 13):

> The determination of species cannot be made by feeding figures into a computer. It is in a sense an art, practiced by men of experience who know, first of all, how species are formed.

It is true that the so-called art or intuition of practicing taxonomists has resulted in classifications of practical and scientific use. These intuitive classifications, however, also

have led to some unfortunate misconceptions as will be discussed below. The rigorous and highly specified procedures of numerical taxonomy largely avoid such problems by limiting greatly the opportunity for personal bias to enter undetected at the stage of gathering data and making comparisons. Coon's statement also illustrates the confusion of data with hypotheses mentioned above.

In some instances, the results of numerical taxonomy have been remarkably congruent with those produced by classical taxonomy. The numerical study retains the advantage, however, of having been done in clearly specified and repeatable steps. The classical taxonomist must depend for the evaluation of a taxonomic work largely upon his personal opinion of its author. Numerical taxonomists may check each other's work by repeating any or all steps. Other advantages of numerical taxonomy, such as precision in estimating relationships and ability to specify questions of character sampling and interrelationships of characters, cannot be discussed here. Most importantly perhaps, numerical taxonomy has retrieved the problem of what is meant by biological relationship from the cloudy realm of art and intuition.

It has long been assumed that satisfactory general classifications of organisms could be based on virtually any sample of the characteristics of individuals. In the past, the majority of these samples consisted of a small number of external characteristics of adult organisms. A few taxonomists have been concerned about the validity of this assumption in holometabolous insects and in plants with alternation of generations. This concern is understandable since larvae and adults or gametophytes and sporophytes may live in quite different environments and may seem strikingly different. Recently, numerical taxonomists have begun to investigate this question. Preliminary results indicate that congruence of taxonomies based on different stages in the life history may not be the

rule. For instance, Rohlf (1963) compared the classifications of larval and adult mosquitos using numerical taxonomic techniques. He found significant (but not large) correlations between larval and adult relationships. The sets of relationships were, however, not congruent. He concluded (p. 116):

> . . . while there is general agreement between the larval and adult interrelationships, there are also many distinct differences between the classifications. It was recommended that characters should be taken from all life-history stages, if possible, in order to form the most general classification.

Similar difficulties may be found when characteristics of different sexes or different parts of the adult are used in establishing phenetic relationships. Michener and Sokal (1963), for example, have found incomplete congruence in comparing the patterns based on males and females and on head and body characteristics of bees. The taxonomist assumes that the phenotypes he studies are representative of genotypes. The fact that more than one representation of the same genotype may be constructed by studying different stages in the life cycle or different sets of characters from the same stage clearly shows how biased our picture of the genotype may be and how poor is our understanding of the genotype-phenotype relationship.

The magnitude of this problem cannot be judged from the data in hand because so few detailed studies have been made. The data which are available give us little reason to feel sanguine about the precision of inferences about relationships estimated on the basis of small samples of characteristics. When it is remembered that paleontology deals with small samples of characteristics of small samples of organisms, the importance of this problem is easily seen. Little credence can be put in attempts to reconstruct phylogenies at the infraspecific level from paleontological data (as has been

attempted by Coon, 1962, in the case of human races). Indeed, the arbitrary subspecific units recognized by Coon almost certainly have no phylogeny to reconstruct. It is difficult enough to trace even major lineages when relatively abundant material is available, as for instance, in the history of horses summarized by Simpson (1951).

A general problem in biology is how to deal with continuous but ever changing phenomena. This problem is especially important for the taxonomist because one of the more unfortunate aspects of the hierarchy inherited from Linnaeus is its requirement for discrete taxa. Therefore continua in space and time must be fragmented by the taxonomist. The patterns created by hybridization, reticulate evolution, apomixis, etc., cannot be adequately expressed by the classical taxonomic structure. Quantified similarities in a Q-matrix are free of this problem, although any *classification* based upon a Q-matrix will inevitably lose some information (but in a predetermined pattern dependent upon the clustering procedure used). Very recently C. D. Michener (1963) has begun to explore ways of making taxonomic classifications more realistic biologically by allowing overlapping taxa. The phylogenetic taxonomist often feels, and always hopes, that his groups represent "real" entities. The numerical taxonomist is always aware of the real source of his groups.

The Subspecies Problem

When one looks at the systems of classification which have been employed by anthropologists, he cannot help but be struck by the diversity of these systems and their tendency to overemphasize differences. Nowhere is this more apparent than in the classification of human subspecies or "races."

The ancient observation that men from different areas may differ in superficial characteristics unfortunately has led to the assumption that man could be divided into some number of biological entities known as races. Beginning as a simple folk taxonomy, the idea of distinct or largely distinct races appears throughout the literature of anthropology. As anthropologists became aware of the new systematics, they naturally attempted to interpret their classifications in the genetic and phylogenetic terms appropriate to this approach.

The genetic definition of taxa seemed particularly suitable since modern *Homo sapiens* is perhaps the only widespread species which has been demonstrated to fit the "biological" species definition. In all probability every significant test of interbreeding within the species has been made under natural conditions and there is no known instance of successful interbreeding with a sympatric species. Indeed, the cytogenetic systems and behavioral mechanisms of the hominoids would seem to preclude the latter. Thus it is convenient to describe man in aggregate as the species *Homo sapiens*. Species is here used to connote *kind* and not to imply some sort of biological equivalence with other species of plants, animals, or microorganisms. We can be certain that *Homo sapiens* is quite a different sort of entity from the coast redwood, the common fruit fly, or *Paramecium aurelia*.

While *Homo sapiens* may qualify (perhaps uniquely) as a biological species, treatment of infraspecific variation in man under the rules of the "new systematics" has not proved so simple. As mentioned above, the arbitrary nature of the subspecies has long been recognized. Two general problems have plagued those who wish to circumscribe infraspecific units in plants and animals. The first is the selection of the characters on whose variation the units will be defined. The second is the decision as to the amount of difference which will be recognized as amounting to subspecific differentiation. This de-

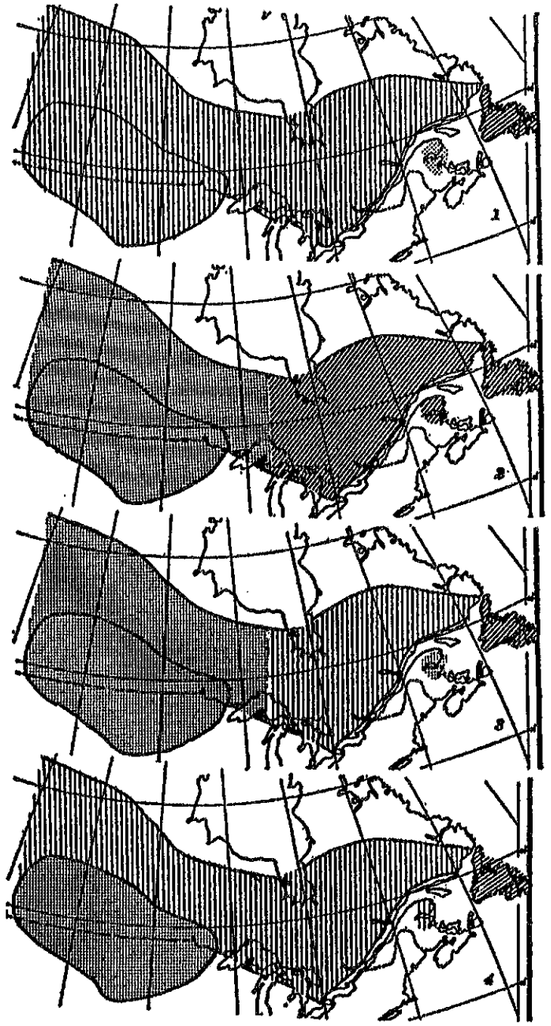
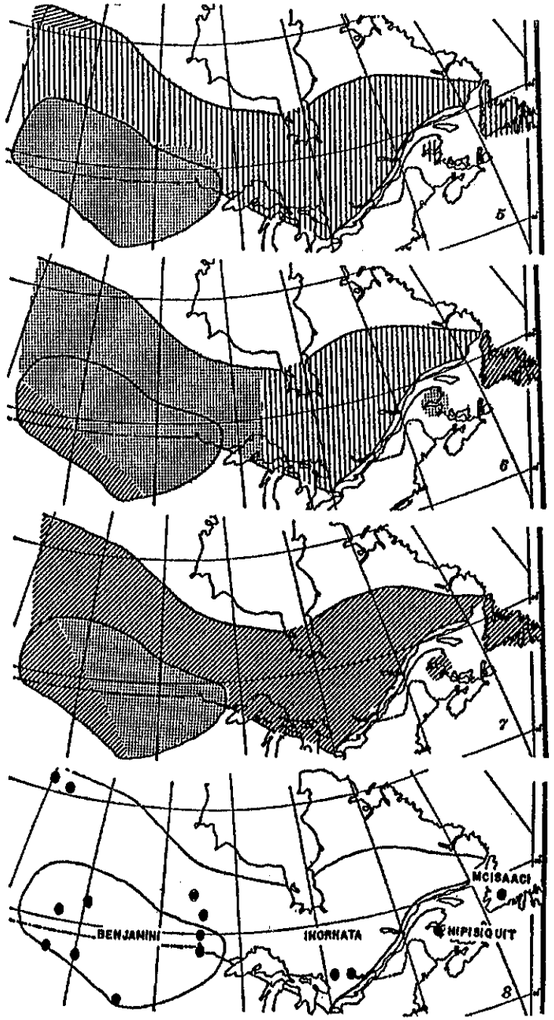


Figure 2. Geographic variation of seven different characters in the butterfly *Coenonympha inornata.* Junctions between different kinds of shading indicate that adjacent populations are significantly different from one another in the particular character



mapped. The heavy black lines indicate the approximate ranges of two of the currently recognized continental subspecies, *inornata* and *benjamini. Mcisaaci* and *nipisiquit* are disjunct "subspecies." (After Gillham.)

cision is a matter of taxonomic judgment and the discussion over percent rules and other guidelines for making decisions need not concern us here.

Concordance and Discordance

The question of character selection is of greater moment. If characters are largely concordant (that is, if they tend to vary together), then the study of the variation in any one character, or a few characters, would reveal the patterns in which population differentiation has occurred. If, on the other hand, variation is mostly discordant (characters are largely independent), then population differentiation must be studied with respect to one variable at a time. With discordance predominating subspecies recognized on the basis of one or a few convenient characters would not be evolutionary units. They would be simply units of convenience for filing specimens. Our zeal for discovering evolutionary units is predicated upon the belief, of course, that such units will have greater information content and hence greater predictive value than units recognized on other bases. Units of convenience for filing would not necessarily have these attributes and are not commonly thought of as useful in this way.

Too few studies have been made to permit a clear statement as to whether concordance or discordance in variation prevails in plants and animals. Subspecies in plants often seem to show concordant variation. In those zoological situations which have been analyzed, however, discordance seems to be the rule. For example, Gillham (1956) has analyzed a series of studies of geographic variation in butterflies in which both continental and insular subspecies have been recognized.

His survey revealed widespread discordance, as exemplified by Figure 2. As Gillham puts it (p. 120):

> In view of the prevailing discordance of geographical patterns followed by different variates, racial partition of butterfly species is not only arbitrary, but it must also necessarily weight some variates and ignore others, without regard for the biological significance of any of them. The best that can be hoped for now is an analysis of variation by individual characters, avoiding arbitrary subdivision of the species. Such analysis will eventually yield a less distorted picture of species formation than that to which the artificial subspecies now inevitably leads.

It seems fair to state that, as a tool for understanding biological processes, the subspecies has deservedly lost favor. In the past ten years, only a very few papers in the journal *Evolution* have dealt primarily with the subspecies concept.

The Situation in Homo Sapiens

Is man an exception to this trend of discordance in animals? The problem of taxonomic structure within the species *Homo sapiens* is very complex. Certain statements, however, seem almost beyond dispute:

1. There is geographic variation in numerous human phenotypic traits.
2. This geographic variation has a largely genetic basis.
3. Variation in many instances cuts across cultural lines.

Furthermore, there is reason to believe that differences among populations are largely the result of the action of selective agents. An inspection of a series of maps of the geographic distribution of human traits shows that the observed variation

patterns are quite discordant. The problem is not solved even if recent migrations are discounted and only so-called aboriginal populations considered. It is obvious that the choice of a characteristic for the primary division will determine in large measure what races will be recognized. The vast majority of classifications which have been proposed thus far, both folk and scientific, have been based primarily on skin color. Had blood groups, hair type, or body build been the primary standard, the lines would certainly have been drawn differently.

Doubtless there are many internal structural and physiological characteristics which are not immediately obvious, but which show geographic variation. Only a few of these have been studied, especially those relating to metabolism and temperature tolerance. As W. L. Brown has aptly put it (p. 152):

> Applied to the wealth of data on the variation of modern *Homo sapiens*, the "no race" idea seems worth considering on this basis [discordance of characters], even though the value of the race concept in studies of man has already been challenged widely on other grounds by anthropologists themselves. In the face of such obvious discordance as, for instance, human skin pigmentation with blood type factors, or hair form with cephalic index (taken on a world basis), the wildly varying opinions of anthropological schools on the racial classification of our species show up as irrelevant and unnecessary.

Psychological characteristics, such as intelligence, drive, and disposition, certainly have a genetic basis (Erlenmeyer-Kimling and Jarvik, 1963). Although there can be no doubt that these psychological attributes are in part determined by the genetic information, the problem of estimating the genetic component of the variation in ability to reason abstractly, for example, is difficult in the extreme. In other words, the hereditary endowment of an individual and his environment interact to produce the psychological phenotype. It is virtually

impossible to separate the two components completely. While most mental characteristics are highly subject to environmental (particularly cultural) modification, it is clear that the range of possible responses is genetically set. One would expect, therefore, the frequency of the genes concerned to vary geographically. Psychological characteristics undoubtedly show basically the same sort of geographical variation as physical characteristics, even though their environmental component may, in many cases, be greater.

It seems very unlikely that satisfactory tests will be devised in the near future which will permit accurate evaluation of the genetic range of psychological characteristics, even within rather close-knit cultural groups, let alone among diverse cultures. One might expect variation in the genetic range of abstract reasoning ability from culture to culture, perhaps based on weak selection for or against individuals showing a high capacity for abstraction. One might hypothesize that, say, a Chinese population would have a slightly higher or lower average genetic ability for abstraction than one from the United States. It is difficult, however, to conceive of any practical way of testing this hypothesis in the face of overriding cultural influences.

It is generally accepted that attributes like intelligence are composite in nature. There would seem to be *a priori* no reason to expect concordant variation in the frequencies of genes controlling these various components (if they could be estimated), any more than in those controlling so-called physical characters. It also seems quite clear that geographic variation in genetic components of intellectual traits must be relatively insignificant in comparison with the variation induced by social and cultural environments.

This does not mean that the differences observed among men are some sort of mirage. Eskimos and Ubangis are obviously different in many respects. The crucial question is

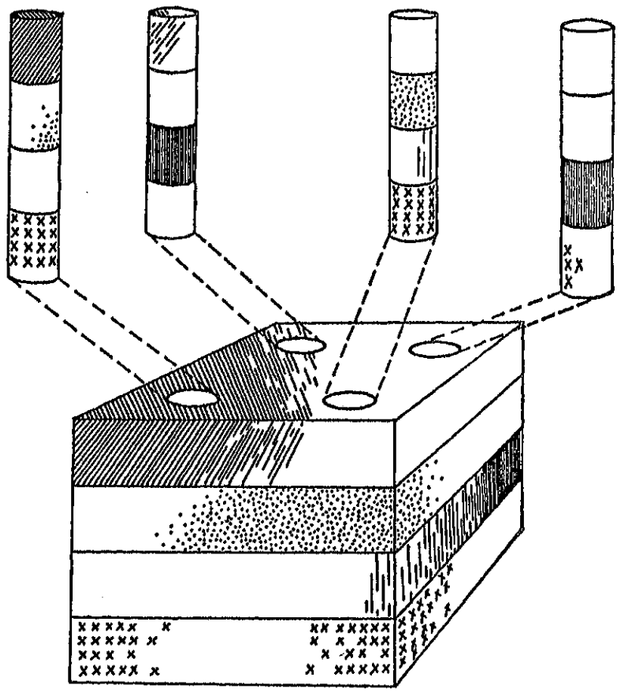


Figure 3. Diagram of discordant variation in four characters. (Explanation in text.)

whether or not one can classify human populations into discrete biological units (races or subspecies) one of which contains, say, the Eskimos and the other the Ubangis. This point is clarified in Figure 3. Each layer in the cube represents the geographic variation in a single hypothetical character. For example, if the top layer represented skin color, individuals in the near left-hand corner would have the darkest skin, those in the righthand half of the cube would have light skin, and so

forth. The cores extracted from the cube each represent a sample of individuals taken in that geographic area. Each sample is different; indeed, one might say that each represents a different "race." However, a set of four samples taken at any four places in the "character cube" would also produce four different "races." There is no "natural" racial division because the abundant geographic variation is in discordant characters.

The goal of any system of classification is, or should be, to abstract patterns of variation in such ways that they may be comprehended. Hiernaux (1963) has clearly expressed the crux of the matter (p. 199):

> Classification is not a goal in itself, but a tool, a very useful one indeed when it works. When it does not, discarding it will not withdraw any scrap of knowledge, but on the contrary force us to face the facts as they are, in their full complexity.

Present-day subspecific classifications of man do not satisfactorily abstract the patterns of infraspecific variation apparent in *Homo sapiens*. Numerical taxonomic techniques will permit the evaluation of phenetic relationships among different geographic samples of men. It seems unlikely, however, that such analysis would result in sets of relationships which could reasonably be structured into discrete subspecific entities. It would be interesting to determine if discrete clusters exist at any level and if any indication of hierarchical structure exists.

Thing-Concept Confusion

Why then, in the face of these difficulties, do many biologists still feel that "good species" and "good subspecies" must exist in nature and, that, given the time and tools, such entities will be discovered or delimited? The answer may be found

in what might be called the "thing-concept confusion." The average biologist, when he says bird, flower, or Negro, feels that he is referring to a real, clearly delimited, biological entity. Although certain items may be referred unambiguously to one or another of these concepts, even a cursory consideration of them reveals that their unity resides primarily in the mind. How are the penguin, the ostrich, and the sparrow related? The systematist would say that they belong to a unit, birds, because of recency of descent from a common ancestor. Unfortunately this answer ignores the question of when, in time, birdlike reptiles became reptilelike birds. The limits of the entity bird become indefinite when the paleontological dimension is considered. The question of how to determine recency of descent is also ignored. One might assert that a penguin's most important biological relationships are with other organisms in their ecological situation such as killer whales, seals, and Antarctic fishes. These relationships at least have the advantage of being amenable to a certain degree of definition. It is only by making value judgments that one can decide which of these sorts of relationship are more important. Many biologists feel that phylogenetic relationship is more important because they can conceive of the transfer of genetic information along lineages back through time. We would not care to make this judgment. The transfer of energy in ecosystems seems equally (or more) significant than transfer of genetic information. In addition little is known about the structure and evolution of ecosystems and the possibilities of exchange of genetic information across what are considered to be phylogenetic lines.

The word flower might be considered to refer unambiguously to a morphological unit. In some plants, however, it is difficult to delimit one flower from another because they are reduced and crowded together in the inflorescence. From the point of view of function, the situation is even more complex.

The familiar poinsettia is an example of a group of very specialized flowers arranged in an inflorescence with brightly colored leaves or bracts. Just as most of us think of a daisy as a single flower although it is a cluster of small florets, so could we regard an entire flowering branch of poinsettia as the ecological equivalent of a flower. Nearly all of the grasslike sedges are wind-pollinated and have inconspicuous flowers. The highly modified, small, and clustered flowers of the sedge, *Dichromena*, however, are surrounded by colored leaves and the whole complex resembles a single flower. This genus of sedge is insect-pollinated. As soon as one attempts to make an exclusive definition, he immediately perceives borderline situations which do not clearly fit within the limits he wishes to impose.

The concept Negro has much in common with the concepts bird and flower. Sociologically, Negro is defined differently in the United States and Brazil. In the southern United States anyone who is not "pure white" is a Negro. In Brazil, anyone who is not "pure black" is a caucasian. Biologically the concept Negro has even less unity. Heavy skin pigmentation may be associated with a wide variety of other characteristics.

It is all too easy to decide from one's mental patterns and prejudices or one's distorted percepts from nature that there is an actual structure out there waiting to be found. This is the phenomenon of reification of concepts, well-known to the historian of scientific thought. This concept-thing confusion may seem unimportant when dealing with, say, subspecies of butterflies. With *Homo sapiens* such confusion creates not only social problems in the present, but perhaps evolutionary problems in the future. The evolution of man is an interaction between classical "biological" evolution and psychosocial or cultural evolution (Ehrlich and Holm 1963, Montagu 1962). In the realm of psychosocial evolution, conflicting ideas may be analogous to alleles at a genetic locus, their relative frequency

fluctuating through chance effects and what might be termed cultural selection. In this context, one might view the waxing and waning of ideas concerning the significance of races and racism as a problem in population phrenetics.

The Consequences of the Classical Approach

It might be profitable to look more closely at the harm that is done by continuing to use the classical species-subspecies categories and the usual hierarchic structure. Intellectual damage is done at virtually every level of investigation in both theory and practice. It is difficult to specify the extent of "damage" when it involves misfiling of specimens of grosbeak study skins as pointed out by West (1962) or the arbitrary pigeonholing of butterfly populations as was done by Ehrlich (1955). It is even more difficult to determine the extent to which our understanding of the process of evolution has been distorted by the imposition of the rigid set of taxonomic categories. In a recent textbook on evolution, one finds the statement: "The very hierarchy of genera, families, orders, and so forth is in itself evidence for the correctness of the theory of evolution, for that is the pattern that evolution should cause to develop." Since evolutionary theory has almost always been dealt with in terms of this hierarchical structure it is hardly surprising that our present theory may be misconstrued as automatically leading to such a structure. The systems of relationship established by unbiased procedures lend little comfort to the view that the structure of nature is inherently hierarchic.

There is no question, however, about the harm which has resulted from the extension of this taxonomic approach to considerations of the nature of geographic variation in *Homo*

sapiens. It has, among other things, led to the mistaken assumption that arbitrary racial subdivisions of *Homo sapiens* can be considered as evolutionary units in space and time. As has been discussed above, there is no basis for assuming, without extensive genetic study, that any population or any taxonomic group is an evolutionary unit. Discussions of the biological origins and characteristics of subjectively determined races (e.g., Coon, 1963), based exclusively, as they must be, on evolutionary misconceptions, are useful only for strengthening culturally determined prejudices against groups which have reality only in a social, rather than a biological, sense.

One unfortunate aspect of persisting in considering races to be discrete biological entities is seen in discussions of the consequences of interbreeding between supposed races of *Homo sapiens*. Many of these discussions do not accurately represent what is known about the genetics of interfertile ("infraspecific") populations in other organisms. For example, much attention has been drawn to the problem of the supposedly deleterious effects of "racial intermixture." Zoologists and some botanists, by their use of a "biological" species concept, are constrained to regard exchange of genetic material between what they call species as somehow detrimental to the continued existence of the species. Such interchange in effect becomes an illicit process and the biologist may unconsciously regard it as "unnatural." In the minds of some, hybridization comes to be thought of as a process deleterious to further evolutionary differentiation and not as a part of the evolutionary repertoire of the populations involved.

Biologists do not take this point of view about genetic interchange among populations of the same species. Indeed, the presumed existence of such interchange of genes is critical to the so-called biological species concept. Anthropologists and others have sometimes proposed that the supposedly harmful effects of gene exchange at the species level in other organisms

occur at the racial level in man. The term hybridization with its psychologically based overtones, or the ugly word miscegenation, are then used to describe what is presumed to be happening.

There is evidence that some infraspecific crosses made in the laboratory between geographically distant populations produce offspring which are relatively inviable. This has been found in butterflies, moths, frogs, and some plants. Such evidence seems largely lacking for crosses within *Homo sapiens*, although it is possible to construct models involving such phenomena as Rh incompatibility in which crossing might prove deleterious to a population. However, there is also some reason to believe that progeny of parents drawn from two different human populations would be, on the average, more fit in the sense of the population geneticist than the offspring of individuals from the same population. There would appear to be no genetic support either for the encouragement or the repression of intergroup gene exchange in man. Indeed, the situation of partially differentiated populations with some gene exchange among them has been postulated to be the ideal state for further evolution.

It is not necessary here to dignify the George Report and similar tracts with a point-for-point refutation. The pertinent facts are well known to biologists and anthropologists and are widely available to the interested layman (Commoner, et al. 1963). It might be maintained by any scientist that it is his duty to publish facts in his discipline as he sees them. This presumably would include speculations based on these facts. While this is clearly so for the more abstruse ideas of basic science, it does not seem reasonable to absolve the scientist of all social responsibility for his views. The question would rarely arise in the domain of pure science, but it arises frequently wherever *Homo sapiens* is concerned. The situation with race finds an interesting parallel in the discussions of the

responsibility of nuclear physicists in designing and building nuclear weapons. Surely no one would wish to prescribe rules of conduct in such matters; one must depend upon the judgment and good faith of the scientist.

It seems little enough to ask, however, that the scientist working in areas where any results are of great social consequence should follow the behavioral pattern of scientists in general. His results should first be published in the scholarly literature. Potential social effects of the results should be considered thoroughly. This would be true whether the scientific results concern nuclear fission, cancer-related viruses, extrasensory perception, organic poisons of potential use as pesticides, or the evolution of *Homo sapiens*. Should the work be misinterpreted or be used to further causes which it does not support, it surely is the responsibility of the scientist immediately to make clear the misinterpretation and to disavow the misuse of his work. In the absence of such a disavowal, it may properly be assumed that the scientist supports such use of his work. Definition of the areas of a scientist's responsibility is an important and vexing question and deserves further discussion. It seems obvious, however, that certain types of behavior are to be avoided. A scientific idea of merit does not become part of the formal structure of science by its acceptance by the public at large. Rather, it must be weighed and reworked by the scientific community. It must not become the basis for social actions until it has passed this important test.

In conclusion it may be said that so-called subspecies or races in man, as in many other organisms, are not evolutionary units. They are arbitrarily created to describe certain variation patterns in one or a few characteristics. They have no common genetic pattern nor may their genetic future be predicted. It is an error to believe that human subspecies or races are *things* that may be discussed and compared or whose separate evolutionary development may be traced. Whereas in

other organisms use of the subspecies concept may do only intellectual damage by creating a distorted view of nature, in *Homo sapiens* the results are very different. Promulgation of views of races and their supposed properties may have serious and far-reaching consequences both for man's present behavior and for his future psychosocial evolution. In 1768 the botanist von Haller said:

> Natura in reticulum sua genera connexit, non in catenam: homines non possint nisi catenam sequi, cum non plura simul sermone exponere.[1]

His words have even greater cogency today when we know so much more about man's evolutionary background, his behavior and culture, and at least some of the possible consequences of his activities.

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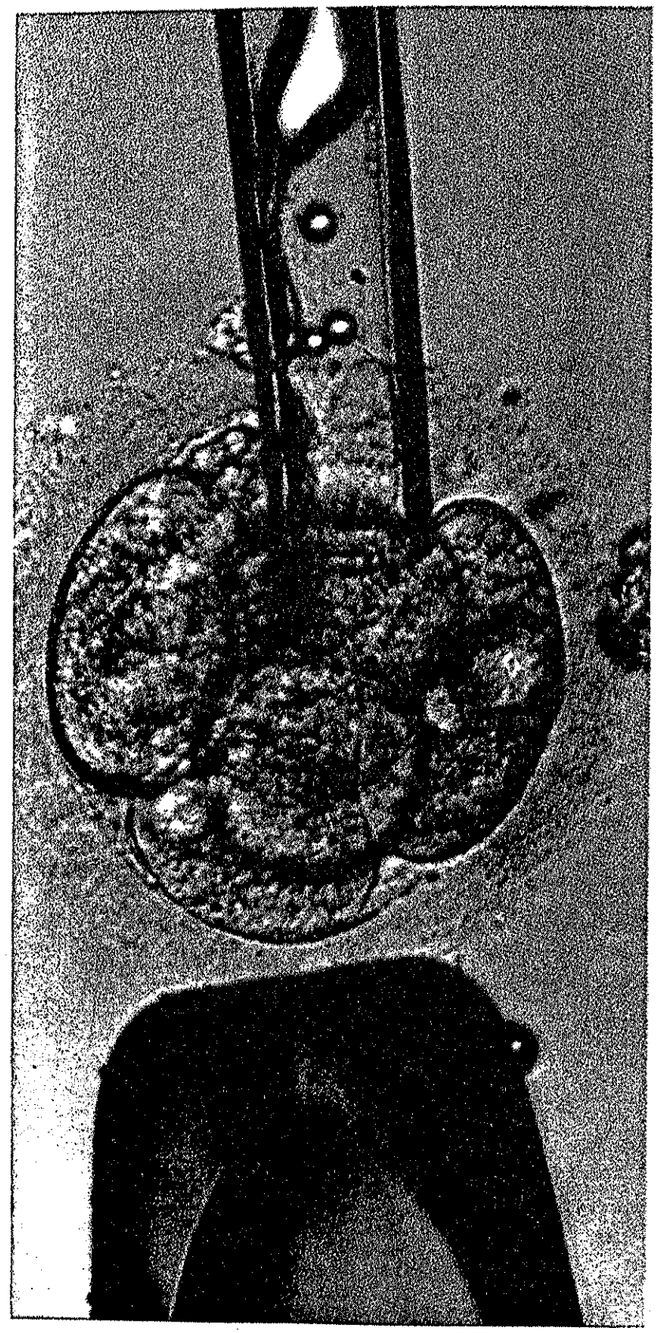
Grading the Gene Tests

From just a snippet of DNA, geneticists can sometimes forecast a patient's health. But ethical problems surrounding this testing are as ominous as the diseases themselves

by John Rennie, *staff writer*

John Rennie, "Grading the Gene Tests", Scientific American, June 1994 pp. 88-97. Reprinted by permission of Scientific American.

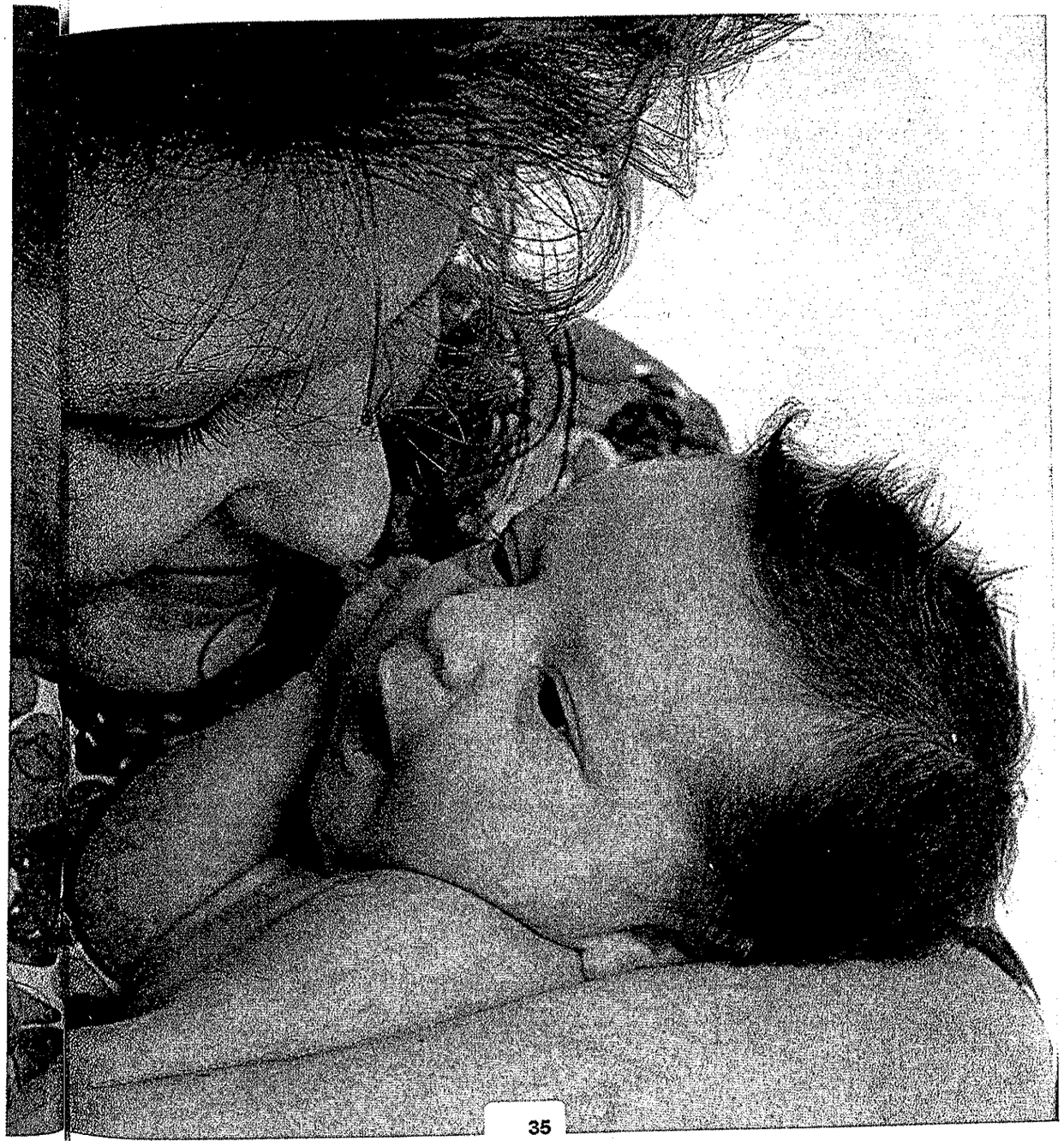


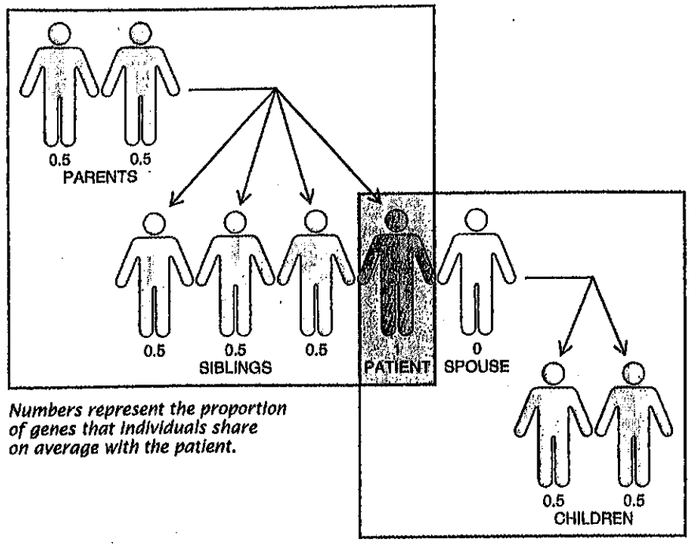
Almost nine months before she was born, Brittany Nicole Abshire passed the most important test she will ever take. Her parents, Renee and David, are both healthy carriers of the trait for Tay-Sachs disease, a cruelly disabling and ultimately lethal inheritable disorder. After they lost one daughter to Tay-Sachs in 1989, they swore they would never have another child unless they could be sure that it would be free of the disease. Genetic tests could diagnose the condition before birth, but the Abshires' religious beliefs ruled out abortion as a way of screening for healthy fetuses.

There seemed to be no hope until the Abshires learned about a new technology called preimplantation genetic testing. The experimental procedure had already been used to screen more than a dozen children for a different genetic disorder, cystic fibrosis. Gary D. Hodgen and specialists at the Jones Institute for Reproductive Medicine at the Eastern Virginia Medical School collected ova and sperm from the Abshires and successfully fertilized seven ova in vitro. After three days, when those seven had developed to about the eight-cell stage, Hodgen's team plucked a cell from each pre-embryo and tried to analyze its DNA.

For four of the pre-embryos, the analysis worked: one of them showed the deadly combination of genes, but three were not even carriers. Those three pre-embryos were implanted in Renee, and one survived to become Brittany, who was born this past January. Courtesy of genetic testing, Brittany is the first child ever certified to be free of Tay-

***EIGHT-CELL EMBRYOS** like the one shown at the left can now be screened for the presence of some genetic illnesses. Baby Brittany Nicole Abshire* (right) *was tested in this way because both of her parents are carriers of the fatal Tay-Sachs disease gene.*





Numbers represent the proportion of genes that individuals share on average with the patient.

GENES ARE SHARED by members of a family. If one person carries a gene for a disease, then each of his or her parents, siblings and children has a 50 percent chance of carrying the same gene. That fact affects the privacy of genetic data.

Sachs disease before entering her mother's womb.

As the era of genetic testing dawns, miracles such as Brittany could become commonplace. Genetic testing is the fastest-growing area in medical diagnostics: according to the Office of Technology Assessment (OTA), the number of genetic tests will increase 10-fold over the next decade. "Potential new genetic tests roll off the conveyor belt of the Human Genome Project almost once a week," remarks Norman Fost of the University of Wisconsin-Madison Medical School. Hundreds of thousands of fetuses are already being tested every year by techniques such as amniocentesis and chorionic villus sampling.

Tests are not just for the unborn: many can also be used to diagnose illnesses more accurately in children and adults. In the past year alone, researchers have found genes associated with Alzheimer's disease, Huntington's disease and colon cancer; they expect to find a breast cancer gene almost any day now. Tests based on those and other discoveries could warn people that they are at special risk for those diseases. And used in conjunction with prospective therapies that replace defective genes with working ones, genetic tests could lead to real cures.

But many human geneticists and other observers are concerned that the rapid growth of genetic testing is already posing ethical, legal, social and scientific quandaries for which there will be no easy answers. They fear that new tests are proliferating without adequate supervision. Because the genetics of disease is proving to be more complex than anticipated, the predictive power and utility of some tests are in question. Yet states are enthusiastically instituting programs for screening newborns that may be unnecessary. Meanwhile investigators are beginning to see evidence that "genetic discrimination" is costing some people jobs and insurance.

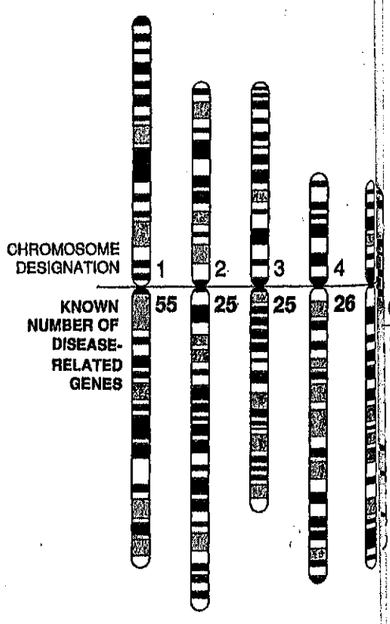
"We need to proceed cautiously, because there is a potential for doing harm with this technology," warns geneticist Michael M. Kaback of the University of California at San Diego, a pioneer in population screening. When we know more about a human's genetic makeup than ever before, will we know what to do with all that information?

A Mythological Model

Genetic testing is not a single technology. Rather it refers to a broad range of methods for gauging the presence, absence or activity of genes in cells. At the relatively low-tech end, researchers can count the chromosomes in a patient's cells or measure the amount of telltale proteins in his or her blood. At the most sophisticated level, researchers assay a cell's DNA with molecular probes that can find a specific genetic sequence among the three billion base pairs that make up human DNA. Some tests cost as little as $50, whereas others are more than $1,000. With these tests, medical geneticists can try to predict the course of a patient's health.

Unfortunately, the more that researchers have learned about human genetics, the more they have come to appreciate that even seemingly straightforward diseases are complicated. Notions of genetic illness have often been built around the single-gene model, in which a defect in a gene causes a particular health deficit. Some diseases do work this way: the deformed blood cells of sickle cell anemia are caused by a gene that makes an abnormal form of hemoglobin; the fatal miseries of Tay-Sachs result from the lack of an enzyme that breaks down fatty substances in neurons. But this model is turning out to be an oversimplification.

No more than about 3 percent of all human diseases are caused by defects in a single gene, and none of those are major killers, as are heart disease and cancer. The more complex conditions involve a host of genes that merely nudge a person's predisposition to develop an illness. According to most estimates, everyone carries at least five to 10 genes that could make him or her sick under the wrong circumstances or could adversely affect children. "We're all mutants," Kaback summarizes. "Everybody is genetically defective."



The truth is that the rules for what constitutes a genetic disease are not clear-cut. If researchers someday find a gene that confers a 60 percent predisposition for gross obesity, is that a genetic defect? What about a gene that gives a 25 percent predisposition for cardiovascular disease at age 55? Or—moving into an even more ambiguous area—a gene that predisposes to antisocial behavior?

Furthermore, even some diseases that once appeared to fit the single-gene model on the basis of their hereditary patterns are more variable than had been assumed. Cystic fibrosis, one of the most common hereditary disorders among people of European descent, is a useful example. Its symptoms include the accumulation of suffocatingly thick mucus in the airways and often severe digestive problems. Today drug treatments allow half of all cystic fibrosis sufferers to live to about age 30, but just a couple of decades ago patients rarely survived into their twenties, and some still die in infancy.

Researchers had often prayed for a genetic test that could find carriers of the disease in the general population. Then, in 1989, investigators at the University of Michigan and the University of Toronto found the gene responsible for cystic fibrosis on chromosome 7; it encodes a protein in cell membranes that affects the intracellular balance of chloride ions. DNA-based tests for mutations commonly associated with the disease soon appeared.

But those tests have revealed a new class of cystic fibrosis patients—people with relatively minor symptoms, such as asthma or bronchitis, who never thought of themselves as genetically ill. Some male patients are perfectly healthy except that they are infertile—for reasons not yet understood, they lack a vas deferens, the tube in the reproductive system that conducts sperm cells from the testicles. Basically, cystic fibrosis is not a single disease after all.

Moreover, molecular biology has revealed that cystic fibrosis is not caused by a single type of mutation. Although one mutation is associated with 70 percent of all cases, and two others with another 15 to 20 percent, more than 360 mutations have been linked to cystic fibrosis so far. No one has yet been able to correlate firmly the severity of the disease with different mutations. And DNA tests designed to catch one mutation will miss others.

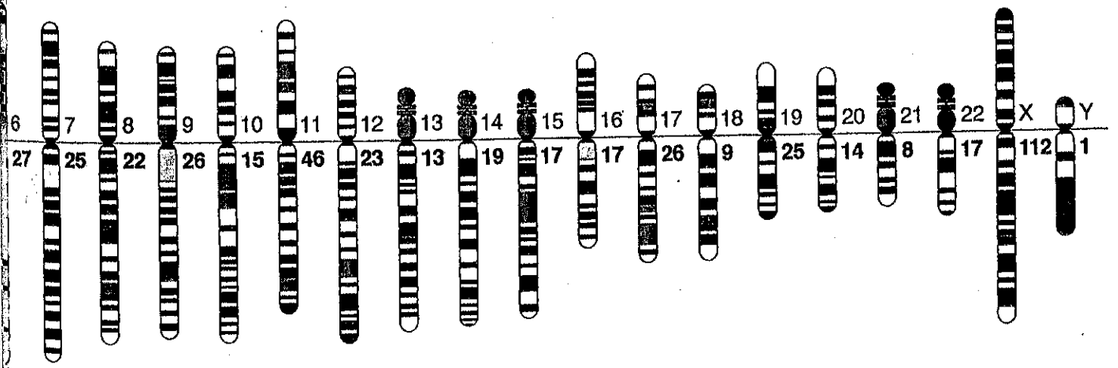
All these discoveries make it much harder to interpret the results of genetic tests for cystic fibrosis. A positive test result does not indicate how severely afflicted a patient will be, and a negative test result could be misleadingly reassuring. Thus, the DNA tests usually need to be confirmed by biochemical assays and monitoring for symptoms.

The problem confounding the single-gene disease model and the straightforward interpretation of the tests is what many observers call the myth of genetic determinism. "Genetic determinism is one of these simpleminded errors that we were prone to commit when we thought genes linked to diseases in a kind of inevitable, ineluctable fashion," explains Thomas H. Murray, director of the Center for Biomedical Ethics at the Case Western Reserve University School of Medicine and former head of a task force for the Human Genome Project. "It invites you to think that 'genes equal fate.'" Environmental circumstances, in the form of modified diets, therapeutic drugs, behavioral changes and other influences, can avert many disastrous outcomes foretold in the DNA. Conversely, because cystic fibrosis, heart disease, cancer, autoimmune disorders, multiple sclerosis and other conditions arise from an unfortunate confluence of genetic and environmental factors, genetic tests for those illnesses can never by themselves predict an individual's future with perfect clarity.

Damned by DNA

Against this backdrop of genetic interpretation (and misinterpretation), the drama of population screening is being played. In recent decades, several screening programs aimed at detecting genetic diseases in large groups of people have been attempted, some with good results, some with bad.

One nightmarish example of well-intentioned testing gone wrong is the screening campaign for sickle cell anemia during the early 1970s. In response to a groundswell of demands that something be done about the disease, which is a scourge of the African-American community, the federal government funded a screening program to detect carriers of the sickle cell gene. The program was easy to implement because carriers could be identified from just one drop of blood through an inexpensive test. At first, the screening enjoyed popular support. Some ministers conducted tests on their congregations; some members of the Black



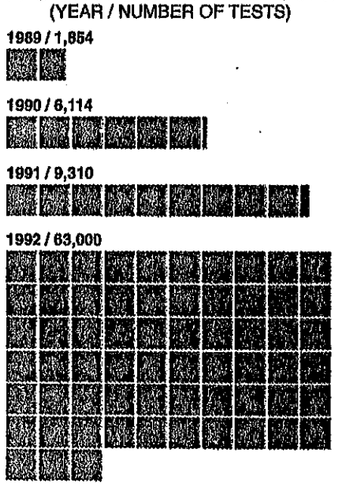
CHROMOSOME MAPS of the genetic traits for a variety of illnesses are still being compiled. Disease-related genes have already been located on each of the chromosomes, and new ones are constantly being discovered. The relation between genes and diseases is rarely simple, however. Almost all diseases are likely to have some genetic component.

MASS SCREENING for sickle cell anemia was at first popular among African-Americans during the early 1970s. Boxer Joe Frazier (*center*) is shown promoting one screening drive. Because the public was poorly educated about the meaning of the tests, the results were sometimes misused to discriminate against healthy carriers of the trait.

Panthers were offering the tests door-to-door in black communities.

But soon things turned ugly. Because people were rarely educated about the meaning of the tests, many perfectly healthy carriers of the trait were led to believe they were sick. This ignorance extended to some state governments as well. The Massachusetts legislature, for instance, passed a law requiring that all children at risk for "the diseases" sickle cell anemia and sickle cell trait be screened before enrollment in school. "By legislative fiat, sickle cell trait became a disease," Kaback moans.

GROWTH IN THE USE OF CYSTIC FIBROSIS CARRIER TESTS
(YEAR / NUMBER OF TESTS)



SOURCE: Office of Technology Assessment, 1992

TESTING FOR CARRIERS of cystic fibrosis has mushroomed in recent years.

Some insurance companies began to deny coverage to black carriers on the grounds that they had a preexisting medical condition or that their children were bad risks. The U.S. Air Force Academy rejected black applicants who were carriers. Some commercial airlines refused to hire carriers as flight attendants because of the erroneous belief that such individuals were particularly likely to faint at high altitudes. Prominent scientists suggested on network television that the best solution to the anemia problem would be for blacks carrying the gene to forgo breeding—a suggestion that naturally fed fears that the screening was really genocidal in intent. In short, the testing did more harm than good by becoming a tool of long-standing prejudices.

The Tay-Sachs program, which Kaback organized, is a shining example of what can go right with such an effort. Tay-Sachs disease is especially prevalent among Jews of eastern European descent. (The Abshires are not Jewish, but they come from a small community in Louisiana where the disease is also common.) Since the early 1970s more than a million Jews throughout the world have volunteered for testing to learn whether they are carriers of the recessive Tay-Sachs trait. When couples who both carry the mutation decide to have children, they typically elect to have prenatal testing. If a fetus has the disease, they usually abort it rather than give birth to a child who would succumb within five years to a horribly slow, painful death. More important, however, the tests also set at ease the minds of fearful couples who might otherwise never risk having children.

Why did the Tay-Sachs program succeed where the one for sickle cell failed? Kaback and others credit the care that went into its implementation. Before the pilot programs in Baltimore and Washington, D.C., began, 14 months were spent establishing contacts within the Jewish community and educating potential patients about the tests and their implications. People received extensive genetic counseling both before and after the tests. Unlike the screening for sickle cell anemia, the Tay-Sachs program was always voluntary, which meant that people had the opportunity to prepare for the consequences of the testing.

Another important difference, Kaback argues, lies in the diseases themselves. Because Tay-Sachs is always so uniformly hideous in its progression, extremely few people believe an affected child should be brought into the world. Because testing can prevent that tragedy, it carries a clear benefit. The benefits of sickle cell testing are less distinct. The severity of the disease is variable and intermittent, and with prompt medical attention, immunizations and antibiotic treatments (which alleviate the frequent bacterial infections that accompany the anemia), patients can live for many decades. Relatively few people believe aborting an anemic fetus on the basis of a genetic test is humane, so the test has less obvious utility.

Learning the Lessons

The Tay-Sachs model for screening has been successfully adapted for some other diseases. For instance, prudent testing has greatly cut the incidence of thalassemia, a genetic blood disorder common among many people of Mediterranean descent: in Sardinia, the rate of thalassemia has declined from one in 250 births to one in 1,200 births during the past 20 years.

Applying the lessons learned from the Tay-Sachs and sickle cell experiences is not always easy, however, especially for diseases in which the population at risk is extremely large. Once again cystic fibrosis serves as a useful example. In families with histories of the disease, screening is usually accurate and beneficial. But 80 percent of the children with cystic fibrosis are born to families without such histories, so nearly all couples in the U.S. would need to be screened to prevent most cases. "How do you get four million pregnant women a year into an educational setting?" Fost asks. Given that the number of professional genetic counselors in the U.S. is barely more than 1,000, cystic fibrosis screening alone would swamp the country's counseling resources. Most patients would have to get counseling information from their primary physicians—many of whom have little or no training in genetics, according to surveys of the medical profession.

Yet many researchers believe, as Fost puts it, cystic fibrosis screening is "metastasizing, despite the lack of any evidence that it works." For the past eight years, investigators in Wisconsin have been conducting a double-blind study to determine whether biochemically screening newborns for cystic fibrosis is beneficial. So far they have found no evidence that identifying the children at birth is better than waiting for any symptoms to emerge. Nevertheless, in 1989 the states of Colorado and Wyoming both made cystic fibrosis screening mandatory for all newborns.

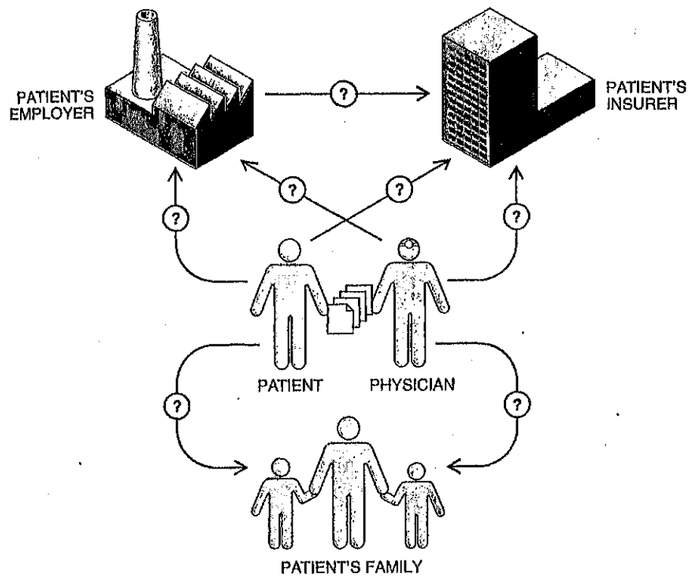
Because all genetic tests have some margin of error, excessive newborn testing has the capacity to do harm, if only by worrying parents unnecessarily. One study looked at families in which a child was initially diagnosed as having cystic fibrosis but was later shown to be healthy; one fifth of the parents nonetheless continued to fear that their children had the disease. Geneticists and ethicists often express concern about how stigmatizing children with a disease label may warp personal development.

In a report issued last November, the Institute of Medicine (IOM) of the National Academy of Sciences offered numerous recommendations about how genetic testing should be conducted to minimize its potentially adverse effects. All testing, it suggests, should be voluntary, and the results should be kept confidential to prevent misuse. All testing should be linked to genetic counseling, so that the patient understands the results and their implications. For the most part, tests should be restricted to those conditions for which some beneficial intervention is possible, either as therapy or as reproductive planning. Tests should not usually be performed purely for information's sake; rather the patient should be able to use the result to make an informed decision about an issue of immediate relevance, such as having a child or electing a medical treatment. The IOM also strongly believes an individual should decide freely whether or not to be tested, without social pressure or financial inducement.

Unregulated Testing

As good as those guidelines may be, abiding by them will be difficult. One problem with trying to set any limits is that genetic testing is so easy to do; another is that the field is largely unregulated. "Currently there is very little to stop someone from implementing genetic tests on a population basis without the sort of institutional review and informed consent required for other new technologies," Fost says.

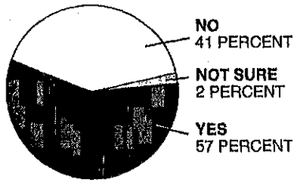
Neil A. Holtzman, a health policy expert at the Johns Hopkins University Hospital and an editor of the IOM report, notes that most companies in the business of genetic testing offer it as a laboratory service and not as a kit for physicians to use. They are therefore not obliged to submit their methods for appraisal and approval by the Food and Drug Administration. The companies do fall under the jurisdiction of the Clinical Laboratory Improvement Amend-



WHO SHOULD KNOW the results of genetic tests is an unsettled ethical and legal issue. Because the results of genetic tests may carry health and financial implications for others, a patient or physician may be obliged to divulge that information. In a 1992 poll, a majority of Americans said the privacy of test results should not be absolute.

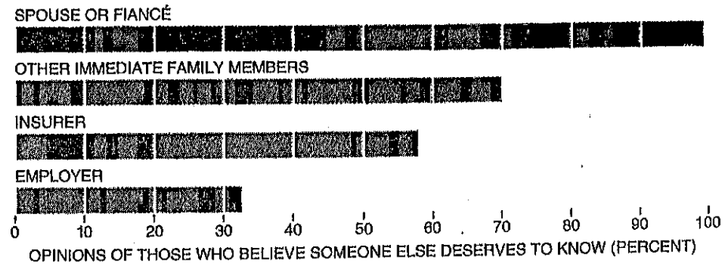
THE RIGHT TO KNOW

If someone is a carrier of a defective gene or has a genetic disease, does someone else deserve to know?



SOURCE: March of Dimes/Lou Harris, 1992

WHO SHOULD KNOW?



BREE WALKER LAMPLEY, a television and radio celebrity in Los Angeles, has ectrodactyly, a genetic condition that causes a deformity of the hands and feet. She was publicly criticized for having a baby in 1991 because her child had a 50 percent chance of inheriting that trait. (Her son did indeed inherit that gene.) Her case illustrates the social pressures that can be imposed on individuals who carry genetic defects.

ments of 1988. This law ensures that laboratories conducting interstate commerce in Pap smears and other biomedical tests meet certain standards of reliability. Unfortunately, Holtzman says, the Health Care Financing Administration, the agency empowered with enforcing those rules, "has really dragged its feet on setting up guidelines for these new genetic tests."

According to the IOM report, only 10 states have established any licensing requirements for genetic testing laboratories, and only New York State has comprehensive regulations that pertain to DNA tests. This lack of oversight worries Holtzman and the rest of the IOM committee about the possible margin of error in the test results. "I think we've already seen a couple of examples of companies seemingly getting tests out there without any regulatory brakes being put on," Holtzman charges. "If we don't get the proper regulatory authority in place, it's going to become a problem of too little, too late."

Critics also point out that many genetics researchers have financial ties to companies in the business of testing. "What I see my colleagues doing is isolating a gene, finding a single mutation and then jumping into population screening. That's not the way it should happen, in my opinion," Kaback says. "We've got entrepreneurial interests influencing judgments that people are making about when tests are ready to be deployed in the population."

Kaback and the rest of the IOM committee also worry about pressures being put on physicians to use genetic tests. "There are private companies sending letters to doctors all over the country, telling them they should be offering cystic fibrosis carrier testing to all their pregnant couples," he says. In these litigious times, many doctors may feel it is safer to order a test than to face charges of negligence.

Because of such concerns, several professional groups have issued statements that emphasize the experimental status of most genetic tests. The American Society of Human Genetics has twice announced that offering screening for cystic fibrosis carriers to the general public should not be considered the standard in medical practice. This past March, the National Advisory Council for Human Genome Research at the National Institutes of Health warned that screening for cancer should not be performed widely until more research on its reliability and consequences could be determined.

Genetic Privacy

Even if the accuracy and utility of genetic testing are assured, maintaining the privacy of that information will remain a problem. Your genes are not exclusively your own: you share half of them with each of your parents, siblings and children. If you discover that you carry a worrisome gene, you may have an ethical, if not legal, obligation to tell them. "There are ripples from genetic testing that don't have analogues in most other kinds of medical testing," remarks Arthur Caplan, a bioethicist at the University of Minnesota.

A 1992 March of Dimes poll reported that 57 percent of the public thinks someone other than a patient deserves to know that he or she carries a defective gene. Of those who believed so, 98 percent thought a spouse or betrothed should know. More surprisingly, however, 58 percent thought insurance companies should also be informed, and 33 percent thought an employer should be told. In a different study, physicians themselves disclosed a willingness to violate patient-doctor confidentiality in some cases: 54 percent said that, even over a patient's objections, they would tell relatives at risk about the results of a test for Huntington's disease (a lethal neurodegenerative disorder that usually manifests in middle age). Twenty-four percent said they would tell the patient's employer, and 12 percent would tell an insurance company.

Industry has also revealed an appetite for individuals' genetic information, although the limited predictive ability and high cost of the current tests seem to have restricted their appeal. A survey by the OTA released in 1991 tried to determine whether employers were conducting genetic tests as conditions of employment; such tests could theoretically reveal workers who would be particularly bad (or expensive) health risks. It found that in 1989 only 12 of 330 Fortune 500 companies were monitoring or screening for any reason. But more than half of the polled companies found the idea of monitoring acceptable, and 40 percent admitted that a person's health insurance costs might affect his or her chance of employment.

Bioethicist Thomas Murray has also found interest in genetic data among insurance companies. "If you ask the question narrowly, 'Are insurers requiring DNA tests of customers?', the answer is no," he says. "The tests are too expensive, not cost-effective, there aren't enough of them yet—there are a lot of reasons. But are insurers interested in genetic information, and will they be in the future? The answer to that is a resounding yes. The best genetic information right now comes not from genetic testing but from one's personal health history—what did your parents die of?"

The insurance industry itself confirms that view. A joint report issued in 1991 by the American Council of Life Insurance and the Health Insurance Association of America stated that although insurers would not be requiring tests in the foreseeable future, they should be

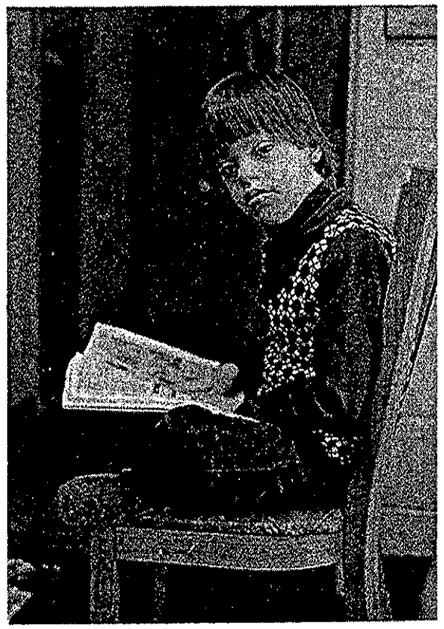
entitled to know the results of any genetic tests or other evidence of possible disease in a policyholder's record. Insurers maintain that they need this information not to discriminate genetically but to set fair rates for all policyholders. It would be wrong, they argue, to make healthy people pay higher premiums because they had been lumped in with those at higher risk. They also do not want to exempt genetic testing results from scrutiny because they say this precedent might someday preclude them from using other medical and statistical indicators of risk.

These arguments do not persuade Murray. "Insurers are applying a model of 'actuarial fairness' and justice they developed in the realm of commercial insurance," he replies. Those principles, in his opinion, are not relevant to health insurance, which serves social and humanitarian functions that deserve consideration. Because no one can control his or her genetic makeup, it seems wrong to penalize individuals for it.

Many observers also doubt the ability of insurance companies and other agencies to interpret genetic information wisely. Paul R. Billings, a geneticist now at the Palo Alto Veterans Administration Medical Center, has been collecting examples of people who were apparently discriminated against because of genetic information that became known to insurers, employers, health maintenance organizations (HMOs) and adoption agencies. He and his colleagues first published some of their results in the *American Journal of Human Genetics* in 1992. Several of the cases they described concerned people who were healthy carriers of genetic diseases or had extremely mild symptoms yet were still denied jobs or insurance coverage. One woman who applied to become an adoptive parent was rejected because her family history of Huntington's disease made her "too great a risk."

In another case, parents who had one child with cystic fibrosis conceived again, and prenatal testing confirmed that this second child, too, would have the disease. When the family's HMO learned that the couple intended to proceed with the pregnancy, it moved to withdraw or limit the entire family's health coverage. Only after threats of a lawsuit did the HMO change its mind.

Billings says a second report, listing about 100 cases of genetic discrimination, is almost done. With funding from the Human Genome Project, he and his co-workers have also been conducting a further survey of 30,000 people with genetic conditions. "Our preliminary view of that study is that it confirms genetic discrimination is occurring," he notes. A 1992 OTA report also found that about 15 percent of genetic counselors said some of their clients had experienced discrimination in insurance.



DOWN SYNDROME patients, who carry three copies of chromosome 21, exhibit a range of mental and physical impairments. But given the proper education and medical attention, many of them are accomplishing much more than was once believed possible. Predicting the limits of people with genetic handicaps is uncertain.

Outside the Law

Anyone looking to the law for protection from genetic discrimination would find a thin shield at best. At the federal level, most experts agree, the strongest statute for barring discrimination in the workplace is the 1990 Americans with Disabilities Act. But the relevance of that act to genetic information is still uncertain. The Equal Employment Opportunity Commission, which enforces the act, has already offered the opinion that healthy carriers of genetic diseases would probably not qualify as having a disability.

Some states have laws that protect the carriers of genes for sickle cell anemia and a few other specific traits found disproportionately among African-Americans and other groups whose members have been historical targets of discrimination. Somewhat broader legislation has been passed in Wisconsin and a few other states and is being debated in a number of others. In 1991 the California legislature passed a law that prevented any form of genetic discrimination, but it was subsequently vetoed by Governor Pete Wilson.

Because most concern about discrimination revolves around insurance coverage, insurance reform may be the key to a solution. "Our task force recommended that all individual risk information be excluded from decisions about who gets insured, what they get insured for and how much they get charged," Murray says. "We see no other practical, sustainable plan for health care coverage than community rating." Community rating, which was the basis for the first health insurance programs during the 1930s, is a system in which a customer's premiums are determined by the health profile of his or her community. Genetic information about individuals would be irrelevant.

The IOM committee and others also favor community rating for that reason. Insurers disagree, arguing that individual risk rating serves the public welfare more equitably at less expense. Nevertheless, for many reasons, the popularity of individual risk rating has been declining. In recent years, New York, Maine and a few other states have shifted to programs based at least partially on community rating.

Both insurers and their critics agree that reforms in health care financing are likely to render moot some—but not all—of the disputes about genetic discrimination in insurance. The details of the new health care system will be important. For example, some insurance plans that would meet the Clinton administration's standard of universal coverage might still be able to disallow coverage for certain genetic conditions. People with those traits might then have to buy additional insurance or pay some costs out of pocket. Under the current system, insurance companies and HMOs often resist paying for many genetic tests or for the costs of genetic counseling. It remains to be seen how reforms in health care financing will affect those policies.

Universal, comprehensive coverage could also become the in-

strument of a demon that has long haunted genetic technology: eugenics. The word immediately summons memories of the Nazi genocidal horrors and other atrocities, such as the forced sterilization of 30,000 people as "mental defectives" in the U.S. before World War II. Yet eugenics can arise through a seemingly more benign movement to ration social resources. Last December, China announced a policy of discouraging people at risk for hereditary diseases from having children, on the grounds that the genetically ill impose too much of a burden on society.

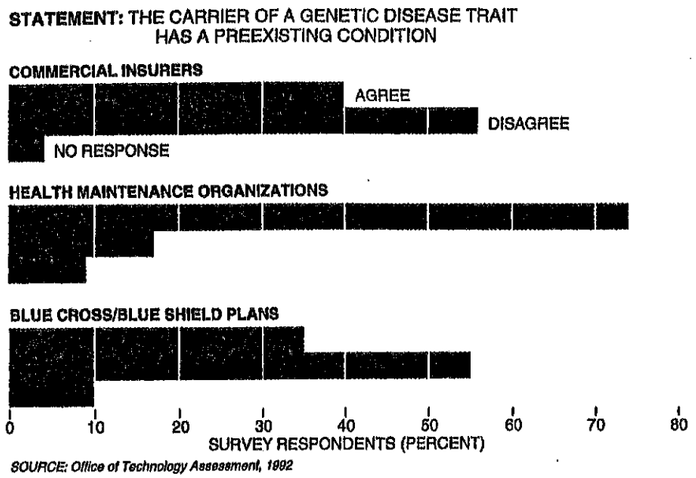
A Eugenic Democracy

The U.S. is not immune from such thinking. "If we get universal health care, people are going to want to know why they should be paying for the 'genetically irresponsible,'" Caplan believes. "In this country, eugenics is not going to come from a Hitlerian dictator saying, 'You must do this.' It's probably going to come from a society saying, 'You can have a kid like that if you want, but I'm not paying.'"

A counterargument might be that in a democracy, the public should be entitled to set limits on what costs individuals can impose on everyone. Yet such arguments, like those surrounding insurance, invariably depend on a definition of fairness. Moreover, whatever motivations lie behind the pressures being put on people making reproductive choices, their net effect is the same: society influences who will or will not be born. As Billings says, "Whether we want to dress it up in economic incentives, if you have to sell your house and go broke to have a child of a certain type, that's eugenics."

Because of its history, "eugenics" is perhaps too loaded a word to describe some applications of genetic testing. Holtzman and many others prefer to reserve it to describe circumstances in which a government or other agency intervenes in reproductive decisions. That is why, Holtzman says, the IOM committee so emphasized the importance of preserving personal autonomy: couples should weigh for themselves whether the risks of having a sick child outweigh other considerations.

"I think the goal of eliminating diseases and disabilities is a good one," Caplan affirms. "I don't think there's anything wrong with encouraging women at risk to be screened for spina bifida or to ask Jewish couples of eastern European descent to be screened for Tay-Sachs. It's wrong to confuse the goal of eliminating disease with the moral problem of coercion."



INSURERS' ATTITUDES toward people who carry the genes for disease traits may shape policies concerning the eligibility of those persons and their offspring for health care coverage. Critics worry that genetic discrimination could occur.

The troublesome fact remains, however, that the line between genetic diseases and undesirable traits is blurred. Caplan cites the example of albinism, which is not a disease but is associated with a higher risk for skin cancer, faulty vision and social stigma. "I think the standard that medicine wants to go with is, is there clear dysfunction or disorder? If not, I would argue that medicine ought not to be testing for it and counseling for it. If we're in the gray zone, I suspect we should try to stay out of those areas, because there's so much else of clear value that we could be doing," he suggests.

Yet Caplan admits that—as much as he would like to—he cannot frame a convincing standard that would allow parents to select some of their children's traits but not their sex, height or other cosmetic features, presuming technological feasibility. Distaste for abortion will stop many parents from exercising that veto for now. But such choices could be circumvented by emerging technologies for screening embryos before they are implanted—or even before conception. "So I think the stance that we will deal only with clear-cut disorders will last about five minutes," Caplan answers ruefully. "Once you can actually do that testing, the interest will swamp my objections. The ability to choose the traits of your child will roar through with a whoosh."

The consequences of those choices may be very hard to predict. Murray recalls that at a meeting of the American Society for Human Genetics a few years ago, he heard about a deaf couple who had asked one geneticist whether the hearing ability of a fetus could be determined prenatally: they wanted to go through with the pregnancy only if they knew that the child *would* be deaf.

As Brittany Abshire and millions of other healthy children and adults prove, genetic testing can immeasurably improve the quality of life for individuals, even entire families. To ignore the good it can do would be an act of immoral blindness and cowardice. But using these technologies wisely will demand foresighted social and legal policies. The record is discouraging: in the past, when genetic discoveries have made tests possible, policymakers have often either encouraged them prematurely or acted too late.

"The paradigms of eugenics are programs of unsurpassed evil. They're not going to get any less evil just because our genetics got better," Murray muses. "We need to be very conscious of what we're dabbling in."

FURTHER READING

CYSTIC FIBROSIS AND DNA TESTS: IMPLICATIONS OF CARRIER SCREENING. Congress of the United States, Office of Technology Assessment. Report OTA-BA-532, August 1992.

MOLECULAR BIOLOGY: IMPACT ON HUMAN DISEASE. Theme issue of *FASEB Journal*, Vol. 6, No. 10; July 1993.

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TRENDS IN HUMAN GENETICS

Vital Data

by Tim Beardsley, *staff writer*

Tim Beardsley, "Vital Data", Scientific American, March 1996, pp.100-105.
Reprinted by permission of Scientific American.

Later this year, if a biotechnology company called Myriad Genetics has its way, thousands of healthy women in the U.S. will hear doubly bad news. First, a close relative—perhaps a sister—will announce that she has breast cancer. Second, the patient's physician thinks this particular cancer has probably been caused by a mutation that the healthy relative has an even chance of also carrying. The patient has been advised to suggest to all her female relatives that they be tested for the mutation. Women who share it may be urged to consider a prophylactic double mastectomy, as they, too, are likely to develop breast cancer. How likely? Hard to say—the mutations have not yet been thoroughly studied—but the likelihood could be as much as 85 percent.

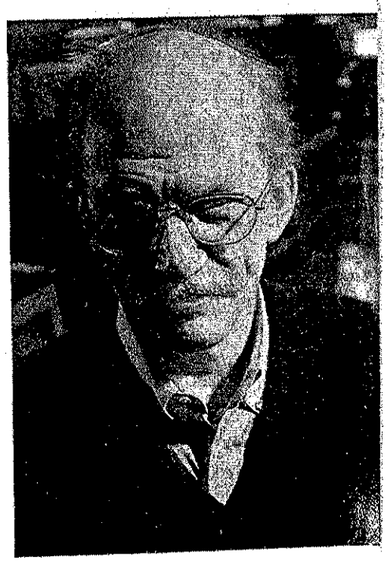
Most people have yet to confront the dilemmas posed by tests for genes associated with serious diseases. But *BRCA1*, the breast cancer gene that Myriad proposes to start testing on a large scale this year, is merely one of what may become dozens that physicians will soon routinely order checked for mutations. The tests are all, to varying degrees, spin-offs of the Human Genome Project, an audacious 15-year, $3-billion federal effort to analyze the human genetic heritage in its ultimate molecular detail.

Although the project was formally launched only five and a half years ago, progress is outstripping expectations. Francis S. Collins, director of the National Center for Human Genome Research (NCHGR) at the National Institutes of Health, thinks the job might be done "maybe even two years early"—by 2003. Technologies developed in response to the effort have already quadrupled the rate of discovery of human disease genes, according to NCHGR's estimate. A medically significant wisp of DNA is now characterized almost every week, and the pace will soon increase again, as the final assault on the genome gets under way. Eventually, a new gene will be sequenced—that is, have the order of its chemical subunits determined—every hour.

The project was launched because it seemed to promise the best hope for ultimately defeating not only diseases long known to be inherited but also others that have a more subtle link with genes, including cancer. Yet the road to that genetic nirvana will be a long one. Early results from one of the most eagerly awaited developments, gene therapy, have been disappointing. And at least one genome biologist, Daniel W. Drell of the Department of Energy, foresees a "vicious legal evolution" of gene-based patent claims, as corporations frantically seek to lock up sequences of DNA with commercial value. The commercialization of humankind's common endowment has prompted protests from activists who see it as an affront to natural dignity. Meanwhile one prominent geneticist has warned that gene-based therapies will be too expensive for widespread use.

Abuses of the new genome science, on the other hand, have arrived already. Compelling evidence demonstrates that children, whom genetic counselors agree should not be tested for certain traits, in fact are being tested in substantial numbers, to their likely detriment. Conversely, because people at risk for a genetic condition are often turned down for either health insurance, life insurance or employment, patients are now declining genetic testing for themselves or their children, even when it would be medically valuable. Others seek testing under false names.

Leaders of the genome project have acknowledged from the start



GENOME SEQUENCING CENTER (*top*) at the Washington University School of Medicine, headed by Robert H. Waterston (*bottom*), should begin large-scale sequencing of human chromosomes (*inset, right*) this year.

Observed correlations in IQ or educational attainment between parents and children in three studies of adoption

Study	Correlations		
	Foster Child with Foster Mother	Biological Child with Biological Mother	Foster Child with Biological Mother
Burks	.19	.46	—
Leahy	.20	.51	—
Skodak and Skeels	.02	—	.32

much lower than the correlation of the children with their biological parents. A careful examination of these studies by Kamin, however, raises some serious questions about their design. The study by Burks included many severely retarded children, which, of course, greatly reduced the IQ correlation with the adoptive parents, who in general come from higher socioeconomic categories and have higher IQ scores than the average for the population as a whole. In both the Burks study and the Leahy study, the matching of biological and foster families was poor. Adoptive parents were older, had incomes that were higher by 50%, and had fewer children, as might be expected. They were, in general, much less variable than the biological families in nearly every respect. In the Skodak and Skeels study, there were selective adoptions, with children of highly educated mothers being placed in higher-status homes. So, from such studies we really do not know what the heritability of IQ is.

The most striking and consistent feature of adoption studies is not usually much commented upon by those interested in demonstrating genetic effects: Whatever the correlations may be between the IQs of children and those of their biological parents, *the phenomenon of adoption raises children's IQ significantly*. In the study by Skodak and Skeels, the biological mothers' IQs averaged only 86, one standard deviation below the average for the population. By contrast, the mean IQ of their children who were raised by adoptive families was 117, one standard deviation above the mean for the population. In a study of orphanage children in the United Kingdom, the same phenomenon was seen. Children taken into the orphanage in early infancy had an average IQ of 105 if they remained in the orphanage until they were about 5 years old, 100 if they were returned to their biological mothers, but 115 if they were adopted. These observations are just what is to be expected from the social characteristics of adopting parents: They are generally middle-class and upper-middle-class couples, with few or no children of their own, who have the financial power, the motivation, and the class background to produce "intelligent" children. There is, of course, no contradiction between this adoption effect and the possibility that IQ scores may be highly heritable. "Genetic" does not mean "unchanging." No matter how high the heritability of IQ might prove to be, upper-middle-class families tend to produce upper-middle-class children.

THE FIVE SEXES

Why Male and Female Are Not Enough

by ANNE FAUSTO-STERLING

Anne Fausto-Sterling, "The Five Sexes," The Sciences, March/April 1993.
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IN 1843 LEVI SUYDAM, a twenty-three-year-old resident of Salisbury, Connecticut, asked the town board of selectmen to validate his right to vote as a Whig in a hotly contested local election. The request raised a flurry of objections from the opposition party, for reasons that must be rare in the annals of American democracy: it was said that Suydam was more female than male and thus (some eighty years before suffrage was extended to women) could not be allowed to cast a ballot. To settle the dispute a physician, one William James Barry, was brought in to examine Suydam. And, presumably upon encountering a phallus, the good doctor declared the prospective voter male. With Suydam safely in their column the Whigs won the election by a majority of one.

Barry's diagnosis, however, turned out to be somewhat premature. Within a few days he discovered that, phallus notwithstanding, Suydam menstruated regularly and had a vaginal opening. Both his/her physique and his/her mental predispositions were more complex than was first suspected. S/he had narrow shoulders and broad hips and felt occasional sexual yearnings for women. Suydam's "feminine propensities, such as a fondness for gay colors, for pieces of calico, comparing and placing them together, and an aversion for bodily labor, and an inability to perform the same, were remarked by many," Barry later wrote. It is not clear whether Suydam lost or retained the vote, or whether the election results were reversed.

Western culture is deeply committed to the idea that there are only two sexes. Even language refuses other possibilities; thus to write about Levi Suydam I have had to invent conventions—*s/he* and *his/her*—to denote someone who is clearly neither male nor female or who is perhaps both sexes at once. Legally, too, every adult is either man or woman, and the difference, of course, is not trivial. For Suydam it meant the franchise; today it means being available for, or exempt from, draft registration, as well

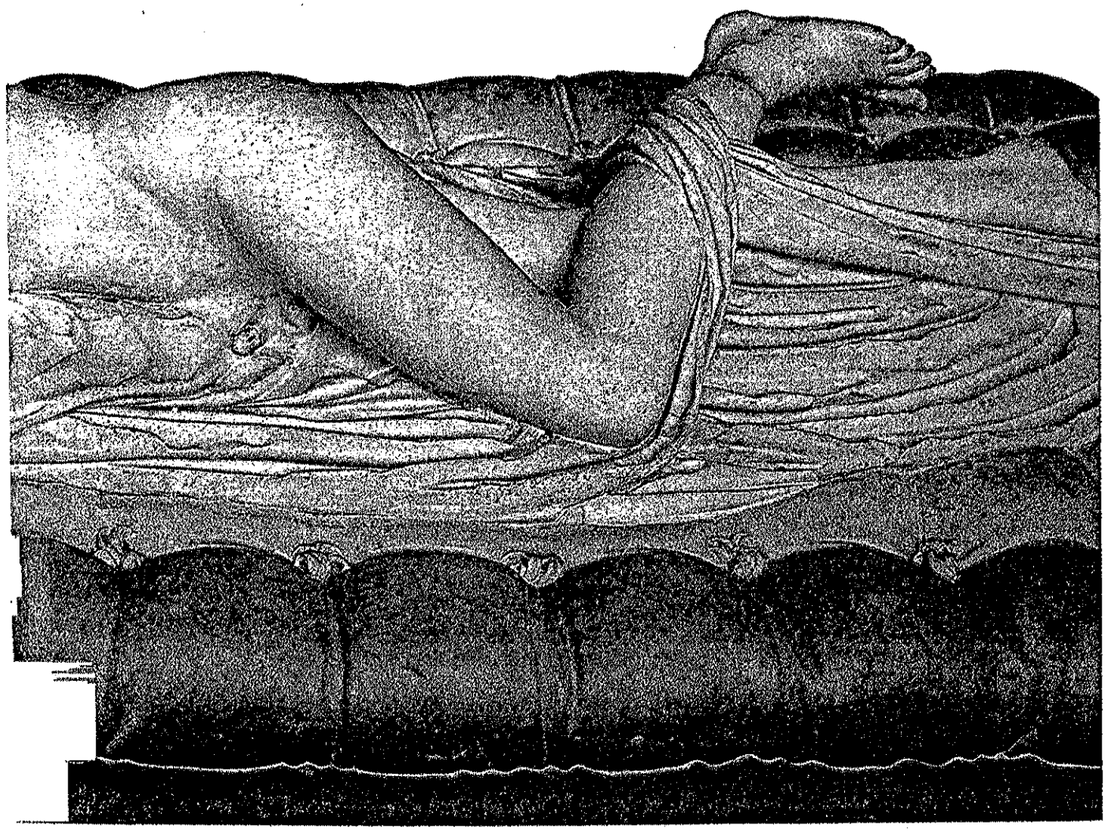
as being subject, in various ways, to a number of laws governing marriage, the family and human intimacy. In many parts of the United States, for instance, two people legally registered as men cannot have sexual relations without violating anti-sodomy statutes.

But if the state and the legal system have an interest in maintaining a two-party sexual system, they are in defiance of nature. For biologically speaking, there are many gradations running from female to male; and depending on how one calls the shots, one can argue that along that spectrum lie at least five sexes—and perhaps even more.

For some time medical investigators have recognized the concept of the intersexual body. But the standard medical literature uses the term *intersex* as a catch-all for three major subgroups with some mixture of male and female characteristics: the so-called true hermaphrodites, whom I call herms, who possess one testis and one ovary (the sperm- and egg-producing vessels, or gonads); the male pseudohermaphrodites (the "merms"), who have testes and some aspects of the female genitalia but no ovaries; and the female pseudohermaphrodites (the "ferms"), who have ovaries and some aspects of the male genitalia but lack testes. Each of those categories is in itself complex; the percentage of male and female characteristics, for instance, can vary enormously among members of the same subgroup. Moreover, the inner lives of the people in each subgroup—their special needs and their problems, attractions and repulsions—have gone unexplored by science. But on the basis of what is known about them I suggest that the three intersexes, herm, merm and ferm, deserve to be considered additional sexes each in its own right. Indeed, I would argue further that sex is a vast, infinitely malleable continuum that defies the constraints of even five categories.

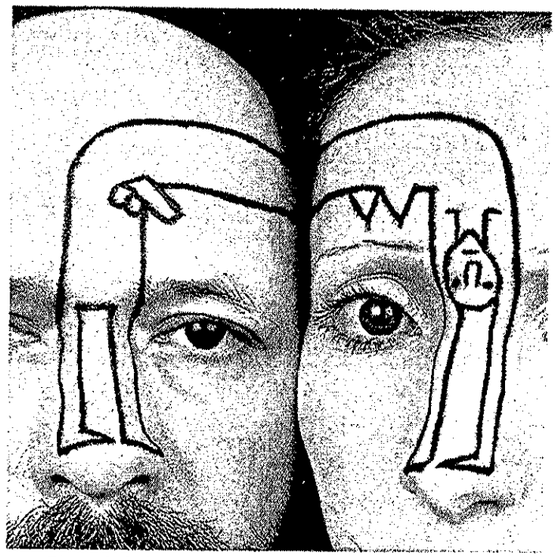
NOT SURPRISINGLY, it is extremely difficult to estimate the frequency of intersexuality, much less the frequency of each of the three additional sexes: it is not the sort of information one volunteers on a job application. The psychologist John Money of Johns Hopkins University, a specialist in the study of congenital sexual-organ defects, suggests intersexuals may constitute as many as 4 percent of births. As I point out to my students at Brown University, in a student body of about 6,000 that fraction, if correct, implies there may be as many as 240 intersexuals on campus—surely enough to form a minority caucus of some kind.

In reality though, few such students would make it as far as Brown in sexually diverse form. Recent advances in physiology and surgical technology now enable physicians to catch most intersexuals at the moment of birth. Almost at once such infants are entered into a program of hormonal and surgical management so that they can slip quietly into society as "normal" heterosexual males or females. I emphasize that the motive is in no way conspiratorial. The aims of the policy are genuinely humanitarian, reflecting the wish that people be able to "fit in" both physically and psychologically. In the medical community, however, the assumptions behind that wish—that there be only two sexes, that heterosexuality alone is normal, that there is one true model of psychological health—have gone virtually unexamined.



Sleeping Hermaphrodite, Roman, Second Century B.C.

THE WORD *hermaphrodite* comes from the Greek names Hermes, variously known as the messenger of the gods, the patron of music, the controller of dreams or the protector of livestock, and Aphrodite, the goddess of sexual love and beauty. According to Greek mythology, those two gods parented Hermaphroditus, who at age fifteen became half male and half female when his body fused with the body of a nymph he fell in love with. In some true hermaphrodites the testis and the ovary grow separately but bilaterally; in others they grow together within the same organ, forming an ovo-testis. Not infrequently, at least one of the gonads functions quite well, producing either sperm cells or eggs, as well as functional levels of the sex hormones—androgens or estrogens. Although in theory it might be possible for a true hermaphrodite to become both father and mother to a child, in practice the appropriate ducts and tubes are not configured so that egg and sperm can meet.



Rimma Gerlovina and Valeriy Gerlovin, Romulus and Remus, *1989*

In contrast with the true hermaphrodites, the pseudohermaphrodites possess two gonads of the same kind along with the usual male (XY) or female (XX) chromosomal makeup. But their external genitalia and secondary sex characteristics do not match their chromosomes. Thus merms have testes and XY chromosomes, yet they also have a vagina and a clitoris, and at puberty they often develop breasts. They do not menstruate, however. Ferms have ovaries, two X chromosomes and sometimes a uterus, but they also have at least partly masculine external genitalia. Without medical intervention they can develop beards, deep voices and adult-size penises.

No classification scheme could more than suggest the variety of sexual anatomy encountered in clinical practice. In 1969, for example, two French investigators, Paul Guinet of the Endocrine Clinic in Lyons and Jacques Decourt of the Endocrine Clinic in Paris, described ninety-eight cases of true hermaphroditism—again, signifying people with both ovarian and testicular tissue—solely according to the appearance of the external genitalia and the accompanying ducts. In some cases the people exhibited strongly feminine development. They had separate openings for the vagina and the urethra, a cleft vulva defined by both the large and the small labia, or vaginal lips, and at puberty they developed breasts and usually began to menstruate. It was the oversize and sexually alert clitoris, which threatened sometimes at puberty to grow into a penis, that usually impelled them to seek medical attention. Members of another group also had breasts and a feminine body type, and they menstruated. But their labia were at least partly fused, forming an incomplete scrotum. The phallus (here an embryological term for a structure that during usual development goes on to form either a clitoris or a penis) was between 1.5 and 2.8 inches long; nevertheless, they urinated through a urethra that opened into or near the vagina.

By far the most frequent form of true hermaphrodite encountered by Guinet and Decourt—55 percent—appeared to have a more masculine physique. In such people the urethra runs either through or near the phallus, which looks more like a penis than a clitoris. Any menstrual blood exits periodically during urination. But in spite of the relatively male appearance of the genitalia, breasts appear at puberty. It is possible that a sample larger than ninety-eight so-called true hermaphrodites would yield even more contrasts and subtleties. Suffice it to say that the varieties are so diverse that it is possible to know which parts are present and what is attached to what only after exploratory surgery.

The embryological origins of human hermaphrodites clearly fit what is known about male and female sexual development. The embryonic gonad generally chooses early in development to follow either a male or a female sexual pathway; for the ovo-testis, however, that choice is fudged. Similarly, the embryonic phallus most often ends up as a clitoris or a penis, but the existence of intermediate states comes as no surprise to the embryologist. There are also uro-genital swellings in the embryo that usually either stay open and become the vaginal labia or fuse and become a scrotum. In some hermaphrodites, though, the choice of opening or closing is ambivalent. Finally, all mammalian embryos have structures that can become the female uterus and the fallopian tubes, as well as structures that

can become part of the male sperm-transport system. Typically either the male or the female set of those primordial genital organs degenerates, and the remaining structures achieve their sex-appropriate future. In hermaphrodites both sets of organs develop to varying degrees.

INTERSEXUALITY ITSELF is old news. Hermaphrodites, for instance, are often featured in stories about human origins. Early biblical scholars believed Adam began life as a hermaphrodite and later divided into two people—a male and a female—after falling from grace. According to Plato there once were three sexes—male, female and hermaphrodite—but the third sex was lost with time.

Both the Talmud and the Tosefta, the Jewish books of law, list extensive regulations for people of mixed sex. The Tosefta expressly forbids hermaphrodites to inherit their fathers' estates (like daughters), to seclude themselves with women (like sons) or to shave (like men). When hermaphrodites menstruate they must be isolated from men (like women); they are disqualified from serving as witnesses or as priests (like women), but the laws of pederasty apply to them.

In Europe a pattern emerged by the end of the Middle Ages that, in a sense, has lasted to the present day: hermaphrodites were compelled to choose an established gender role and stick with it. The penalty for transgression was often death. Thus in the 1600s a Scottish hermaphrodite living as a woman was buried alive after impregnating his/her master's daughter.

For questions of inheritance, legitimacy, paternity, succession to title and eligibility for certain professions to be determined, modern Anglo-Saxon legal systems require that newborns be registered as either male or female. In the U.S. today sex determination is governed by state laws. Illinois permits adults to change the sex recorded on their birth certificates should a physician attest to having performed the appropriate surgery. The New York Academy of Medicine, on the other hand, has taken an opposite view. In spite of surgical alterations of the external genitalia, the academy argued in 1966, the chromosomal sex remains the same. By that measure, a person's wish to conceal his or her original sex cannot outweigh the public interest in protection against fraud.

During this century the medical community has completed what the legal world began—the complete erasure of any form of embodied sex that does not conform to a male–female, heterosexual pattern. Ironically, a more sophisticated knowledge of the complexity of sexual systems has led to the repression of such intricacy.

In 1937 the urologist Hugh H. Young of Johns Hopkins University published a volume titled *Genital Abnormalities, Hermaphroditism and Related Adrenal Diseases.* The book is remarkable for its erudition, scientific insight and open-mindedness. In it Young drew together a wealth of carefully documented case histories to demonstrate and study the medical treatment of such "accidents of birth." Young did not pass judgment on the people he studied, nor did he attempt to coerce into treatment those intersexuals who rejected that option. And he showed unusual even-handedness in referring to those people who had had sexual experiences as both men and women as "practicing hermaphrodites."

One of Young's more interesting cases was a hermaphrodite named Emma who had grown up as a female. Emma had both a penis-size clitoris and a vagina, which made it possible for him/her to have "normal" heterosexual sex with both men and women. As a teenager Emma had had sex with a number of girls to whom s/he was deeply attracted; but at the age of nineteen s/he had married a man. Unfortunately, he had given Emma little sexual pleasure (though *he* had had no complaints), and so throughout that marriage and subsequent ones Emma had kept girlfriends on the side. With some frequency s/he had pleasurable sex with them. Young describes his subject as appearing "to be quite content and even happy." In conversation Emma occasionally told him of his/her wish to be a man, a circumstance Young said would be relatively easy to bring about. But Emma's reply strikes a heroic blow for self-interest:

> Would you have to remove that vagina? I don't know about that because that's my meal ticket. If you did that, I would have to quit my husband and go to work, so I think I'll keep it and stay as I am. My husband supports me well, and even though I don't have any sexual pleasure with him, I do have lots with my girlfriends.

YET EVEN AS YOUNG was illuminating intersexuality with the light of scientific reason, he was beginning its suppression. For his book is also an extended treatise on the most modern surgical and hormonal methods of changing intersexuals into either males or females. Young may have differed from his successors in being less judgmental and controlling of the patients and their families, but he nonetheless supplied the foundation on which current intervention practices were built.

By 1969, when the English physicians Christopher J. Dewhurst and Ronald R. Gordon wrote *The Intersexual Disorders,* medical and surgical approaches to intersexuality had neared a state of rigid uniformity. It is hardly surprising that such a hardening of opinion took place in the era of the feminine mystique—of the post–Second World War flight to the suburbs and the strict division of family roles according to sex. That the medical consensus was not quite universal (or perhaps that it seemed poised to break apart again) can be gleaned from the near-hysterical tone of Dewhurst and Gordon's book, which contrasts markedly with the calm reason of Young's founding work. Consider their opening description of an intersexual newborn:

> One can only attempt to imagine the anguish of the parents. That a newborn should have a deformity . . . [affecting] so fundamental an issue as the very sex of the child . . . is a tragic event which immediately conjures up visions of a hopeless psychological misfit doomed to live always as a sexual freak in loneliness and frustration.

Dewhurst and Gordon warned that such a miserable fate would, indeed, be a baby's lot should the case be improperly managed; "but fortunately," they wrote, "with correct management the outlook is infinitely better than the poor parents—emotionally stunned by the event—or indeed anyone without special knowledge could ever imagine."

Scientific dogma has held fast to the assumption that without medical care hermaphrodites are doomed to a life of misery. Yet there are few empirical studies to back up that assumption, and some of the same research gathered to build a case for medical treatment contradicts it. Francies Benton, another of Young's practicing hermaphrodites, "had not worried over his condition, did not wish to be changed, and was enjoying life." The same could be said of Emma, the opportunistic hausfrau. Even Dewhurst and Gordon, adamant about the psychological importance of treating intersexuals at the infant stage, acknowledged great success in "changing the sex" of older patients. They reported on twenty cases of children reclassified into a different sex after the supposedly critical age of eighteen months. They asserted that all the reclassifications were "successful," and they wondered then whether reregistration could be "recommended more readily than [had] been suggested so far."

The treatment of intersexuality in this century provides a clear example of what the French historian Michel Foucault has called biopower. The knowledge developed in biochemistry, embryology, endocrinology, psychology and surgery has enabled physicians to control the very sex of the human body. The multiple contradictions in that kind of power call for some scrutiny. On the one hand, the medical "management" of intersexuality certainly developed as part of an attempt to free people from perceived psychological pain (though whether the pain was the patient's, the parents' or the physician's is unclear). And if one accepts the assumption that in a sex-divided culture people can realize their greatest potential for happiness and productivity only if they are sure they belong to one of only two acknowledged sexes, modern medicine has been extremely successful.

On the other hand, the same medical accomplishments can be read not as progress but as a mode of discipline. Hermaphrodites have unruly bodies. They do not fall naturally into a binary classification; only a surgical shoehorn can put them there. But why should we care if a "woman," defined as one who has breasts, a vagina, a uterus and ovaries and who menstruates, also has a clitoris large enough to penetrate the vagina of another woman? Why should we care if there are people whose biological equipment enables them to have sex "naturally" with both men and women? The answers seem to lie in a cultural need to maintain clear distinctions between the sexes. Society mandates the control of intersexual bodies because they blur and bridge the great divide. Inasmuch as hermaphrodites literally embody both sexes, they challenge traditional beliefs about sexual difference: they possess the irritating ability to live sometimes as one sex and sometimes the other, and they raise the specter of homosexuality.

BUT WHAT IF things were altogether different? Imagine a world in which the same knowledge that has enabled medicine to intervene in the management of intersexual patients has been placed at the service of multiple sexualities. Imagine that the sexes have multiplied beyond currently imaginable limits. It would have to be a world of shared powers. Patient and physician, parent and child, male and female, heterosexual and homosexual—all those oppositions and others would have to be dissolved as sources of division. A new ethic of medical treatment would arise, one that would permit ambiguity in a culture that had overcome sexual division. The central mission of medical treatment would be to preserve life. Thus hermaphrodites would be concerned primarily not about whether they can conform to society but about whether they might develop potentially life-threatening conditions—hernias, gonadal tumors, salt imbalance caused by adrenal malfunction—that sometimes accompany hermaphroditic development. In my ideal world medical intervention for intersexuals would take place only rarely before the age of reason; subsequent treatment would be a cooperative venture between physician, patient and other advisers trained in issues of gender multiplicity.

I do not pretend that the transition to my utopia would be smooth. Sex, even the supposedly "normal," heterosexual kind, continues to cause untold anxieties in Western society. And certainly a culture that has yet to come to grips—religiously and, in some states, legally—with the ancient and relatively uncomplicated reality of homosexual love will not readily embrace intersexuality. No doubt the most troublesome arena by far would be the rearing of children. Parents, at least since the Victorian era, have fretted, sometimes to the point of outright denial, over the fact that their children are sexual beings.

All that and more amply explains why intersexual children are generally squeezed into one of the two prevailing sexual categories. But what would be the psychological consequences of taking the alternative road—raising children as unabashed intersexuals? On the surface that tack seems fraught with peril. What, for example, would happen to the intersexual child amid the unrelenting cruelty of the school yard? When the time came to shower in gym class, what horrors and humiliations would await the intersexual as his/her anatomy was displayed in all its nontraditional glory? In whose gym class would s/he register to begin with? What bathroom would s/he use? And how on earth would Mom and Dad help shepherd him/her through the mine field of puberty?

IN THE PAST THIRTY YEARS those questions have been ignored, as the scientific community has, with remarkable unanimity, avoided contemplating the alternative route of unimpeded intersexuality. But modern investigators tend to overlook a substantial body of case histories, most of them compiled between 1930 and 1960, before surgical intervention became rampant. Almost without exception, those reports describe children who grew up knowing they were intersexual (though they did not advertise it) and adjusted to their unusual status. Some of the studies are richly detailed—described at the level of gym-class showering (which most intersexuals avoided without incident); in any event, there is not a psychotic or a suicide in the lot.

Still, the nuances of socialization among intersexuals cry out for more sophisticated analysis. Clearly, before my vision of sexual multiplicity can be realized, the first openly intersexual children and their parents will have to be brave pioneers who will bear the brunt of society's growing pains. But in the long view—though it could take generations to achieve—the prize might be a society in which sexuality is something to be celebrated for its subtleties and not something to be feared or ridiculed. •

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Human Ecology, Vol. 10, No. 4, 1982

The Ecology of Human Birth Seasonality

R. G. Condon[1] and Richard Scaglion[2]

This article examines birth seasonality in two environmentally and ethnographically distinct societies: the Copper Inuit of the Central Canadian Arctic and the Samukundi Abelam of Papua New Guinea. Although the regions inhabited by these societies differ dramatically in degrees of seasonal variation, both populations display significant seasonality in conceptions and births. For the Copper Inuit, such seasonal variation was found to be the consequence of social and economic responses to extreme environmental change. Birth seasonality for the Samukundi Abelam is also pronounced and was determined to be the result of social ideologies which are only indirectly linked to environmental factors. The article also proposes a research paradigm designed to facilitate the cross-cultural investigation of birth seasonality in human populations.

KEY WORDS: birth seasonality; Inuit; Abelam; biorhythms; sociorhythms.

R.G. Condon and R. Scaglion, "The Ecology of Human Birth Seasonality," Human Ecology, Volume 10, April 1982, pp. 495-511. Reprinted by permission of Human Ecology.

INTRODUCTION

Yearly patterns in human natality were initially documented in 1826 by Quetelet. Since that time, birth seasonality has been recognized as an ecologically responsive phenomenon linked to a complex network of environmental and cultural variables. Recent studies have focused upon the effects of a limited number of variables such as high temperature and humidity (Chang *et al.*, 1963; Cowgill, 1966a,b; McDonald, 1966; Pasamanick *et al.*, 1959, 1960; Stoeckel and Choudhury, 1972; Zelnik, 1969); heat stress, protein deficiency and/or poor nutrition during the warm months (Malina and Himes, 1977; McDonald, 1966; Pasamanick *et al.*, 1960; Zelnik, 1969); spontaneous abortion rates (Pasamanick *et al.*, 1959);

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and fetal death rates (Pasamanick *et al.*, 1959). Cultural factors such as religious festivals (Cowgill, 1966a,b; Johnson *et al.*, 1975; Takahashi, 1964), business cycles (Kirk, 1960), and the existence of occupations requiring the temporary absence of the husband (Stoeckel and Choudhury, 1972) have also been cited as important determinants of birth seasonality.

More recent investigations have analyzed birth seasonality in an ecological framework using controlled comparison techniques (Mosher, 1979; Pasternak, 1978). Still others (Condon, 1981; Malina and Himes, 1977; Scaglion, 1978; Scaglion and Condon, 1979) have concentrated upon small-scale and relatively homogeneous societies in order to examine a wide range of social and environmental correlates of birth seasonality. Despite the abundance of such material, no attempt has yet been made to construct a research paradigm for the comparative investigation of natality rhythms in an ecological context.

The goal of this article is to compare the birth patterns of two societies located in markedly different environmental zones, the Samukundi Abelam of Papua New Guinea and the Copper Inuit of the Central Canadian Arctic. After delineating the social-environmental interactions giving rise to the pronounced birth seasonality in both regions, we will construct a preliminary research paradigm designed to facilitate the cross-cultural investigation of such rhythms. Given the obvious differences in environmental parameters between the two regions and the markedly different cultural patterns characterizing each society, we draw upon a wide range of variables from the fields of anthropology, chronobiology, and human demography to explain the existence and perpetuation of human natality rhythms.

MATERIALS AND METHODS

Data on birth seasonality were gathered on separate field trips to both regions. Fieldwork among the Samukundi Abelam was conducted by R.S. between November 1974 and January 1976 in Neligum village, located in the East Sepik Province of Papua New Guinea. During this period, nutritional and demographic data were collected through intensive interviews with local residents. Fieldwork among the Copper Inuit was carried out by R.G.C. between September 1978 and January 1980 in the settlement of Holman Island in the Northwest Territories of Canada. Nutritional and demographic data were collected through interviews and through the examination of individual medical files at the local nursing station. In both field sites, extensive ethnographic materials were collected through interviews and participant observation.

The forest-dwelling midges, it seems, had gone through a population explosion when the settlers started clearing the forest and planting cacao for chocolate. After the farmers harvested their cacao beans, they discarded the hulls in piles that were an ideal breeding ground for midges, which spread the virus to humans all along the Amazon roads.

During the time when this mystery was being solved, many other examples came to light of pathogens emerging when a natural habitat is cleared. Those findings made such an impression on the field that by 1992 a panel of infectious disease experts produced a report for the Institute of Medicine stating that "environmental changes probably account for most emerging diseases."

Yet the evidence for that conclusion was—and is—largely circumstantial. "A lot of this is hypothetical," says Jenkins. "We look back after disease has broken out and try to project mechanisms for how this occurred." To prove the hypothesis, prospective studies are needed in place of the retrospective ones Jenkins is describing. In prospective studies, the population's health would be followed closely not only after a project that alters natural habitat, but also before and during the disruption. That is what Jenkins and her team are up to in Papua New Guinea: "What we're trying to do is go in before the logging begins and then watch for changes in the health of people living in the area for 3 years, maybe 6 years."

Jenkins learned from contacts in the government that Sovereign Hill Pty. Ltd., a subsidiary of the giant Malaysian logging company Rimbunan Hijau, had been given permission to exercise logging rights bought from villagers in the Hawain River valley north of Wewak. Before the loggers landed, Jenkins met with villagers in the region to get permission to study them. The plan for her network of graduate students, Peace Corps workers, and researchers from the Christensen Research Institute and the University of Papua New Guinea was to study people from four villages—two in the logging region and two in areas that remain pristine—to see how logging affects the villagers' health.

WILLIAM SCHERLIS

Control data. People from the village of Arin—in an unlogged area—serve as a control in Jenkins' study.

By the time the loggers arrived, Jenkins' team was mostly in place. The researchers had to move quickly to get baseline health data on 1000 people in the four villages before their environment was disturbed. They began by collecting blood to search for antibodies to a series of viruses, including those that cause AIDS, herpes infections, and those carried by mosquitoes, such as Ross River and Dengue fevers. Emerging viruses are just part of the picture, however—they also will test for other nonviral microbes, such as the bacteria and parasites that cause typhoid and malaria. And they will be on the alert for the spread of sexually transmitted diseases, because where there are all-male logging camps, there usually are prostitutes.

WILLIAM SCHERLIS

Viral nursery? Forest cleared by logging in Papua New Guinea could be a source of "new" infectious diseases.

At the same time, entomologists and a virologist on the team are scrutinizing mosquitoes and other insects that might transmit diseases. Institute of Medical Research virologist Ray Sanders has started to isolate viruses carried by mosquitoes, which should give researchers an idea of what to look for in humans and a way to identify emerging arboviruses (viruses carried by insects and other arthropods). Biologists have netted dozens of birds, rodents, bats, and other forest-dwelling creatures to sample their blood. Predicts Sanders: "I suspect we'll find some completely new viruses—or variants of known species."

While Jenkins' study was getting under way, Shope was making plans to return to Brazil to help start another study that may provide data on how the diseases of the Amazon are spread to humans. The Rockefeller Foundation has provided $600,000 in funding for the first year of the 3-year study, which is a collaboration with the School of Forestry and Environmental Studies at Yale and Brazilian researchers.

The researchers will focus attention on inhabitants of islands in the Amazon, 60 kilometers inland from Belém. The settlers who live there have been clearing the forests so they can plant fruit trees, including the acai fruit that is a staple of their diet. As in the Papua New Guinea study, researchers will aim at determining how deforestation affects human health. They will start with baseline studies of the health of about 300 people in the municipality, Abaetetuba, with particular emphasis on malaria, Leishmaniasis, Leptospirosis (a disease that plagued British troops in the jungle of Malaya), and arboviruses, of which more than 150 types are known in Brazil, some 30 disease-causing. At the same time, biologists will collect insects and wild animals to see what pathogens they harbor.

The study has one extra dimension that takes it beyond observation of what is happening when nature is devastated by development. The Yale and Brazilian researchers are setting up an experiment to find out how farmers can grow their crops with the least damage. "The goal is to find out how to grow crops in the forest without destroying the forest—and to keep the best public health possible," says Shope.

The team will divide the study area into four experimental plots. On one, settlers will cut down the forest and plant cash crops, as they always have done. On the second, they will do the same—but also mix into their usual crops fruit trees native to the forest. On the third, only a small part of the forest will be cut down to make room for the planting of more native fruit trees. The fourth will serve as a control; the forest will be left intact. As settlers tend their plots, the researchers will check the health of the farmers three to four times a year, as well as draw blood from insects and wild animals.

Shope hopes the data the team collects will not only pin down the relation between deforestation, agriculture, and the spread of disease, but will provide information the Brazilian government could use to formulate policy recommendations on how to settle that region of Amazonia with the least possible destruction.

The studies by Shope and Jenkins are just now getting off the ground, and it will be at least 3 years before conclusions can be drawn. But when those results do arrive, Morse at Rockefeller is hopeful they will provide "scientifically valid data" that will help nail down theories about emerging infections and viruses. "I'd like to see more studies like these," says Morse. "Only by fully understanding how viruses interact with their hosts can we hope to rationally devise effective preventive and therapeutic strategies." And in the age of AIDS, that isn't a trivial outcome of research.

–Ann Gibbons

A Pox upon Our Genes

Smallpox vanished twelve years ago, but its genetic legacy may still linger within us

by Jared Diamond

Human evolution holds a special fascination for us. Granted, it's much easier to study natural selection in creatures like bacteria and fruit flies, which we manipulate experimentally without compunction. Granted, the general principles thereby uncovered may also apply to humans. But let's face it: bacteria and general principles aren't what we're most curious about. What we really want to know are the particulars of how we came to be who we are.

Unfortunately, attempts to study natural selection in humans face daunting obstacles. You can't take any woman you choose and mate her to any man you choose in order to observe the resultant progeny. You can't irradiate, heat shock, or dissect humans. You can't inoculate them with lethal diseases, although that experiment would be especially interesting because diseases were a major selective force on us until the advent of modern medicine.

This piece is about an ingenious attempt to study natural selection in humans without resorting to morally unacceptable manipulations. Twenty-five years ago, nature visited a tragic experiment on rural areas of India in the form of a virulent outbreak of smallpox. Nature used abominably excellent experimental design, matching children who died against brothers or sisters who survived. Analysis of the results by two scientists yielded insights into the scars that smallpox, one of the great modern killers of humans, has left on our genes.

The study that resulted was unique in the annals of medicine. It will never be repeated because smallpox itself has been eliminated. Thus, it will be remembered as our last, and best, chance to understand what may have been an important determinant of our blood groups.

Despite the virtual halt in human skeletal evolution since the end of the Ice Age, the genes for our soft tissues (including blood cells) continue to undergo changes in response to natural selection. However, the important selective agents are no longer large, visible enemies, like lions, but tiny, invisible ones: microbes. With the beginnings of agriculture about 10,000 years ago, infectious diseases probably began to claim an increasing toll of human life, eventually becoming the leading cause of our mortality. As human numbers soared, we became susceptible to diseases that tend to die out in small populations but that can maintain themselves in large ones, which offer continuing supplies of not-yet-infected victims. Agriculture also made us sedentary, and we began to live in the midst of our own effluents and hence to infect one another more easily with pathogens in our feces, urine, and exhaled air. As we domesticated animals and came to live amidst them, we caught still other diseases.

It's true of some infectious diseases, as of some other causes of death, that certain people are genetically more susceptible than others. Since more resistant individuals are more likely to survive and to leave more offspring, selection operating over the last 10,000 years must have caused a genetic revolution in our soft tissues. In a previous column ("Blood, Genes, and Malaria," February 1989), I discussed genetic resistance to malaria, the leading infectious disease of the Old World tropics. But a disease much more familiar to Americans and Europeans is smallpox. Until the recent eradication of smallpox, American citizens traveling abroad required two pieces of paper in order to reenter the United States: a valid passport and proof of recent smallpox vaccination.

Smallpox is caused by one of a group of microbes called pox viruses. While the virus (and hence the disease) is confined to humans, it is closely related to viruses that cause similar diseases in various domestic animals, including cows (cowpox), sheep, goats, horses, and pigs. The smallpox virus probably developed by mutations from one of these animal viruses after we began living in close association with animals.

Imagine smallpox suddenly being introduced into a small and isolated population without any previous exposure to smallpox or related viruses. If all the people have plenty of contact with one another, then smallpox will quickly spread, infecting everybody. Many people will die, but those who survive will develop antibodies to smallpox and will thereby become resistant. As a result, smallpox will have killed or immunized the whole population and will die out, because the virus doesn't infect animals.

Although the disease thus can't persist for long in a small, isolated population, it can last indefinitely as it spreads through a large population in contact with other large populations. Going from one area to another, it can return to an area after a new crop of previously unexposed babies has become available for infection. This need for large numbers of hosts, plus the close similarity of the smallpox virus to domestic animal viruses, is the reason for believing that smallpox probably appeared only after the rise of agriculture.

Just where and when did smallpox first

infect us? It must have evolved somewhere in the Old World, since the New World was free of smallpox until it arrived with Spanish conquistadors about 1507. Our oldest certain evidence consists of three Egyptian mummies, dating from the period 1570–1085 B.C., with well-preserved skins that show the characteristic rash caused by smallpox. One of the mummies was Pharaoh Ramses V, whose titles of Mighty Bull, Repulser of Millions, Golden God of the Sun, and Lord of the Two Lands were powerless to protect him against this virus. Smallpox is also known to have existed in India and China before the time of Christ. But it remains unclear how much earlier than 1570 B.C., and exactly where within the Old World, the fatal mutation that transformed some animal virus into smallpox first occurred.

Many devastating smallpox epidemics are known to have killed one-quarter to one-half of the affected populations. Thus, smallpox has often changed the course of human history. It may have caused the famous plague that decimated Athens in 430 B.C. and helped seal her doom in her war against Sparta. Epidemics beginning about A.D. 165 may have contributed to the decline of the Roman Empire. Titled victims besides Ramses V include Marcus Aurelius of Rome, Peter II of Russia, and Louis XV of France.

But the most far-reaching effects of smallpox were in the New World, where Spanish explorers carrying the disease encountered Indian populations large enough to sustain smallpox but with no previous exposure and no antibodies. Hence the disease played a decisive role in the astonishing conquests of the Aztec and Inca empires, each with millions of inhabitants, by groups of just a few hundred Spaniards. In Mexico, after Cortés had lost two-thirds of his tiny force and retreated to the coast from the Aztec capital of Tenochtitlán (modern Mexico City), a smallpox epidemic killed half of the Aztecs, including Montezuma's successor, Cuitláhuac. In Peru an epidemic that spread southward from Central America, before Pizarro and other Spaniards reached the area, killed the Inca emperor Huayna Capac, killed his designated heir, Ninan Cuyoche, and plunged the empire into civil war between the rival would-be emperors Huáscar and Atahualpa. Cortés and Pizarro triumphed not only because smallpox had killed so many Indian soldiers, including their commanders, but also because a disease that killed Indians, and spared the already resistant Spaniards, demoralized those Indians who survived the epidemic.

As is true of other diseases, individuals must vary in their genetic resistance to smallpox, and the more resistant individuals are more likely to survive epidemics. In populations exposed to the virus for many generations, the frequencies of genes associated with resistance must have risen. Today, only twelve years since smallpox claimed its last victim, those resistant genes should still be common. What might those genes be? For reasons that I shall mention, the genes responsible for our so-called ABO blood types are likely candidates. I must now digress for a simplified crash course in hematology.

Blood is typed according to various protein-and-sugar compounds occupying the surfaces of our red blood cells (hence the name "blood group substances"). While most such substances are found only on our red cells, the ABO substances, which are the best known, are also present on other cells of our body. Each of us has either substance A alone, B alone, both A and B, or neither, and is correspondingly classified as having blood type A, B, AB, or O, respectively. (Strictly speaking, we have two copies of each gene, one inherited from our father and one from our mother, and each copy may be either the A, B, or O form, or allele. Thus, a type-A person has either two As or else one A and one O allele, while a type-O person must have two O alleles.)

In addition, each of us in infancy develops antibodies to the substances he or she lacks. People of type O develop antibodies to both the A and B substances; those of type A develop antibodies only to the B substance, and vice versa; and those of type AB develop neither antibody.

We pay attention to our blood types mainly when they cause us trouble. For example, if a patient of type B receives a transfusion of type-A blood, the transfused cells with the A substance are destroyed by the patient's anti-A antibody, with possibly lethal consequences to the patient. This problem appeared only with the rise of modern medicine and blood transfusions, but a similar problem can arise naturally when a woman is pregnant with a fetus bearing a blood group substance against which she has antibodies. For instance, if a type-O mother carries a fetus that inherited group A from the father, the mother's anti-A antibodies may cause the fetus to abort or may leave it damaged at birth. That doesn't mean, though, that all you type-O women should reject a type-A or type-B suitor, or that you should fret through your pregnancy if you marry that suitor. Only a small fraction of pregnancies in ABO-incompatible marriages actually result in medical complications.

Why, since almost all known effects of blood group substances are thus harmful, do we have differing blood types at all? The reason remains unclear. Perhaps they function as chemical passwords to help us distinguish our own cells from invading microbes or cancer cells that we ought to destroy.

In almost all human populations the O allele is more frequent than the A and B alleles combined. The occasional loss of type-A or type-B fetuses because of incompatibility with their mothers would therefore tend to eliminate the A and B alleles if there were no other important selective factors acting on ABO genes. In fact, as predicted by this reasoning, the O allele tends to be especially common in isolated human populations on islands or mountains out of the mainstream of migration and, therefore, out of the path of infection. But A and B are common in mainstream populations of the Old World, with A being especially frequent in Europe, B in Asia. What compensating advantage peculiar to group A in Europe accounts for its higher frequency there, and similarly for group B in Asia?

One possibility is that certain of the ABO blood groups might confer resistance against fatal diseases common (or formerly common) on certain continents but not on others. Beginning in 1953, convincing associations between ABO blood type and susceptibility to cancer began to be discovered. For example, the risk of stomach cancer is 20 percent higher for Europeans of type A for than those of type O. But cancers are not major causes of death in children and young adults and therefore should not be the major determinants of blood type.

A much more plausible explanation for ABO gene frequencies is that they were influenced by the infectious diseases that were major killers of humans. A potential mechanism for such an influence is that the surfaces of some microbes prove to bear substances similar to the ABO blood groups. This suggests a clever evolutionary trick by the microbes to deceive their hosts. For instance, if a microbe's surface is coated with the microbe's own peculiar substances, the host is likely to recognize the microbe as foreign, develop antibodies against it, and destroy it. But a microbe coated with the A substance would slip past the defenses of a type-A person, since we do not normally develop antibodies against our own proteins.

In the 1960s two kinds of evidence were advanced for a susceptibility of type-A people to smallpox. The first was a still-unresolved claim that a virus closely related to the smallpox virus does have substances like group A on its surface. The second consisted of two statistical studies that compared how frequencies of blood group A and of smallpox varied among different areas of India and Africa. Areas with high frequencies of smallpox proved to have low frequencies of group A, suggesting that smallpox had killed off people with group A.

As recently as the 1960s, in rural areas of India, lack of resources for vaccination, limited access to modern medical care, and lack of understanding of hygiene and disease transmission combined to make smallpox epidemics virtually annual occurrences. Children sick with smallpox shared the same room, and often the same bed, with their brothers and sisters, thereby insuring widespread exposure to the disease. As many as half of the smallpox patients died.

In 1965 and 1966 two scientists, Dr. F. Vogel and Dr. M. R. Chakravartti, realizing that a comparative study of survivors and victims might yield clues about genetic resistance to the disease, attempted to locate all cases of smallpox during severe epidemics in some villages and small towns. They found a total of 415 unvaccinated smallpox patients. For all but eight of these patients, they were also able to find a healthy brother or sister to consider as a "control subject"—that is, someone as similar as possible genetically to the patient and living in the same house, but differing in not having contracted smallpox despite close exposure. Drops of blood drawn from the fingertips sufficed to identify the ABO blood types of the patients and their siblings. Although 52 percent of the patients—217 out of 415—died in this severe epidemic, risk of death varied greatly with ABO blood type.

Among the 415 patients, 261 carried blood group A (that is, their blood type was A or AB), while 154 lacked A (their blood type was B or O). Among the 407 healthy subjects, only 80 carried group A, while 327 lacked it—which strongly suggests that the As were susceptible and the non-As resistant. The ratio of A to non-A among the patients (261:154), divided by the ratio of A to non-A among the controls (80:327), was 7—meaning that a person with group A had a seven times greater risk of contracting smallpox than someone without group A.

The 415 patients were then classified according to the severity or the mildness of their symptoms. Among the 283 severe cases, most (201) had blood group A, and only 82 lacked it. Among the mild cases, only 60 had group A, while 72 lacked it. Hence, once they had contracted smallpox, patients with group A were three times more likely to develop a severe case.

When the 415 patients were classified as to whether they died or survived, most (155) of the 217 who died had group A, and only 62 lacked it. The proportions were more nearly equal among those who survived: 106 had group A, and 92 lacked it. Hence, once a person had contracted smallpox, patients with group A had a doubled risk of dying.

Since people with group A are much more likely to contract smallpox, to develop a severe case of it, and to die of it, why hasn't the gene for group A been virtually eliminated in India, Europe, and other areas where smallpox has been a major killer for a long time, leaving all the survivors with group O or B?

Perhaps the answer is that other, equally widespread infectious diseases spared people with group A and penalized those with other blood groups. There is suggestive evidence that the Black Death (bubonic plague), which killed about one-third of medieval Europe's population, preferentially attacked the bearers of group O, as does cholera, whose death toll in India rivaled that of smallpox. These two diseases may have favored A at the expense of O in India and Europe. Conversely, those with blood type O may be relatively resistant to syphilis, which may have originated in the New World and thus contributed to the very high frequencies (approaching 100 percent) of group O among Central and South American Indians. Thus, ABO blood group frequencies may represent a compromise among the selective effects of numerous diseases. If so, why do geneticists consider the evidence little more than speculative?

In the case of smallpox, although the study by Vogel and Chakravartti yielded a clear picture, three other studies in India and one in Brazil failed to detect differences in ABO frequencies between smallpox patients and controls. Vogel and Chakravartti noted many reasons why they considered their 1965–66 study much more convincing. Most of their patients were unvaccinated children without medical care, exposed to an especially virulent epidemic, while many patients in the other studies were apparently vaccinated adults receiving medical care in large urban hospitals and possibly exposed to a less virulent epidemic. As a result, mortality in the other studies was only 0–16 percent, compared to 52 percent in the 1965–66 study. Vogel and Chakravartti studied all patients that they could locate in a small area and compared the patients with siblings living in the same house. The other studies used the biased sample of patients presenting themselves at an urban hospital and compared their blood groups with those of "control subjects" from other areas. However, blood group frequencies vary greatly with caste, religion, ethnic affiliation, and locality within India. Thus, Vogel and Chakravartti appear to me correct in claiming that their study involved a much less biased set of "experimental" subjects, a set of control subjects much better matched to the experimental subjects, and a much greater selective effect of the smallpox epidemic, which in this case was severe.

If the study had involved mice, these claims, counterclaims, and discrepancies would have been resolved by further studies. Larger blood samples would have been drawn to permit measurement of other possible genetic resistance factors besides ABO blood groups. But—thank God—the opportunity to continue studies of smallpox in humans has vanished. As a result of a major effort that began in 1966 to eliminate smallpox throughout the world, no natural cases have been recorded since Ali Maow Maalin developed the telltale rash in Merka Town, Somalia, on October 26, 1977. Hence, the study by Vogel and Chakravartti will remain unique. Similarly, our prospects for learning more about the genetic influences of bubonic plague and syphilis are slim, since plague has virtually vanished except in remote areas, while syphilis can now be treated as soon as it is detected.

Does this mean that these killers of the past are now of purely academic interest? Not at all. First, the slow-healing scars that they left on our genes, possibly in the form of altered ABO frequencies, will linger in us for many generations. But—perhaps more important—what they did to us in the past serves as a model for what AIDS is doing to us today.

It's well known that individuals exposed to AIDS vary in their risk of becoming infected, and that infected individuals vary in the rate at which their disease progresses. These facts suggest the possibility of genetic differences in susceptibility to AIDS, as is true of many other diseases. In some areas of the world the eventual AIDS-related mortality rate may come to rival that of the great past epidemics of smallpox and plague. If so, AIDS too may be in the process of causing big shifts in human gene frequencies, although we can't yet specify which genes are involved. Natural selection is not a theoretical postulate, but a grimly continuing reality.

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The Arrow of Disease

When Columbus and his successors invaded the Americas, the most potent weapon they carried was their germs. But why didn't deadly disease flow in the other direction, from the New World to the Old?

BY JARED DIAMOND

Illustrations by Richard Downs

Jared Diamond, "The Arrow of Disease," Discover, October 1992. Reprinted by permission of Discover.

The three people talking in the hospital room were already stressed out from having to cope with a mysterious illness, and it didn't help at all that they were having trouble communicating. One of them was the patient, a small, timid man, sick with pneumonia caused by an unidentified microbe and with only a limited command of the English language. The second, acting as translator, was his wife, worried about her husband's condition and frightened by the hospital environment. The third person in the trio was an inexperienced young doctor, trying to figure out what might have brought on the strange illness. Under the stress, the doctor was forgetting everything he had been taught about patient confidentiality. He committed the awful blunder of requesting the woman to ask her husband whether he'd had any sexual experiences that might have caused the infection. ■ As the young doctor watched, the husband turned red, pulled himself together so that he seemed even smaller, tried to disappear under his bed sheets, and stammered in a barely audible voice. His wife suddenly screamed in rage and drew herself up to tower over him. Before the doctor could stop her, she grabbed a heavy metal bottle, slammed it onto her husband's head, and stormed out of the room. It took a while for the doctor to elicit, through the man's broken English, what he had said to so enrage his wife. The answer slowly emerged: he had admitted to repeated intercourse with sheep on a recent visit to the family farm; perhaps that was how he had contracted the mysterious microbe.

This episode, related to me by a physician friend involved in the case, sounds so bizarrely one of a kind as to be of no possible broader significance. But in fact it illustrates a subject of great importance: human diseases of animal origins. Very few of us may love sheep in the carnal sense. But most of us platonically love our pet animals, like our dogs and cats; and as a society, we certainly appear to have an inordinate fondness for sheep and other livestock, to judge from the vast numbers of them that we keep.

Some of us—most often our children—pick up infectious diseases from our pets. Usually these illnesses remain no more than a nuisance, but a few have evolved into far more. The major killers of humanity throughout our recent history—smallpox, flu, tuberculosis, malaria, plague, measles, and cholera—are all infectious diseases that arose from diseases of animals. Until World War II more victims of war died of microbes than of gunshot or sword wounds. All those military histories glorifying Alexander the Great and Napoleon ignore the ego-deflating truth: the winners of past wars were not necessarily those armies with the best generals and weapons, but those bearing the worst germs with which to smite their enemies.

The grimmest example of the role of germs in history is much on our minds this month, as we recall the European conquest of the Americas that began with Columbus's voyage of 1492. Numerous as the Indian victims of the murderous Spanish conquistadores were, they were dwarfed in number by the victims of murderous Spanish microbes. These formidable conquerors killed an estimated 95 percent of the New World's pre-Columbian Indian population.

Why was the exchange of nasty germs between the Americas and Europe so unequal? Why didn't the reverse happen instead, with Indian diseases decimating the Spanish invaders, spreading back across the Atlantic, and causing a 95 percent decline in *Europe's* human population?

Similar questions arise regarding the decimation of many other native peoples by European germs, and regarding the decimation of would-be European conquistadores in the tropics of Africa and Asia.

NATURALLY, we're disposed to think about diseases from our own point of view: What can we do to save ourselves and to kill the microbes? Let's stamp out the scoundrels, and never mind what *their* motives are!

In life, though, one has to understand the enemy to beat him. So for a moment, let's consider disease from the microbes' point of view. Let's look beyond our anger at their making us sick in bizarre ways, like giving us genital sores or diarrhea, and ask why it is that they do such things. After all, microbes are as much a product of natural selection as we are, and so their actions must have come about because they confer some evolutionary benefit.

Basically, of course, evolution selects those individuals that are most effective at producing babies and at helping those babies find suitable places to live. Microbes are marvels at this latter requirement. They have evolved diverse ways of spreading from one person to another, and from animals to people. Many of our symptoms of disease actually represent ways in which some clever bug modifies our bodies or our behavior such that we become enlisted to spread bugs.

The most effortless way a bug can spread is by just waiting to be transmitted passively to the next victim. That's the strategy practiced by microbes that wait for one host to be eaten by the next—salmonella bacteria, for example, which we contract by eating already infected eggs or meat; or the worm responsible for trichinosis, which waits for us to kill a pig and eat it without properly cooking it.

As a slight modification of this strategy, some microbes don't wait for the old host to die but instead hitchhike in the saliva of an insect that bites the old host and then flies to a new one. The free ride may be provided by mosquitoes, fleas, lice, or tsetse flies, which spread malaria, plague, typhus, and sleeping sickness, respectively. The dirtiest of all passive-carriage tricks is perpetrated by microbes that pass from a woman to her fetus—microbes such as the ones responsible for syphilis, rubella (German measles), and AIDS. By their cunning these microbes can already be infecting an infant before the moment of its birth.

Other bugs take matters into their own hands, figuratively speaking. They

From our viewpoint,

diarrhea and coughing are "symptoms" of disease.

From a bug's viewpoint, they're clever evolutionary

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the bug's interests to make us "sick."

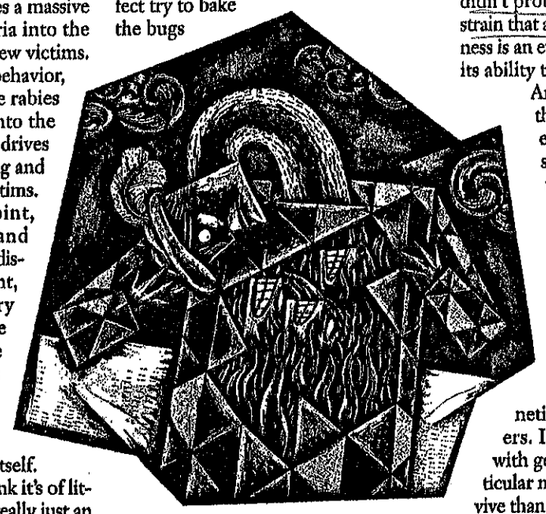
actively modify the anatomy or habits of their host to accelerate their transmission. From our perspective, the open genital sores caused by venereal diseases such as syphilis are a vile indignity. From the microbes' point of view, however, they're just a useful device to enlist a host's help in inoculating the body cavity of another host with microbes. The skin lesions caused by smallpox similarly spread microbes by direct or indirect body contact (occasionally very indirect, as when U.S. and Australian whites bent on wiping out "belligerent" native peoples sent them gifts of blankets previously used by smallpox patients).

More vigorous yet is the strategy practiced by the influenza, common cold, and pertussis (whooping cough) microbes, which induce the victim to cough or sneeze, thereby broadcasting the bugs toward prospective new hosts. Similarly the cholera bacterium induces a massive diarrhea that spreads bacteria into the water supplies of potential new victims. For modification of a host's behavior, though, nothing matches the rabies virus, which not only gets into the saliva of an infected dog but drives the dog into a frenzy of biting and thereby infects many new victims.

Thus, from our viewpoint, genital sores, diarrhea, and coughing are "symptoms" of disease. From a bug's viewpoint, they're clever evolutionary strategies to broadcast the bug. That's why it's in the bug's interests to make us "sick." But what does it gain by killing us? That seems self-defeating, since a microbe that kills its host kills itself.

Though you may well think it's of little consolation, our death is really just an unintended by-product of host symptoms that promote the efficient transmission of microbes. Yes, an untreated cholera patient may eventually die from producing diarrheal fluid at a rate of several gallons a day. While the patient lasts, though, the cholera bacterium profits from being massively disseminated into the water supplies of its next victims. As long as each victim thereby infects, on average, more than one new victim, the bacteria will spread, even though the first host happens to die.

SO MUCH FOR the dispassionate examination of the bug's interests. Now let's get back to considering our own selfish interests: to stay alive and healthy, best done by killing the damned bugs. One common response to infection is to develop a fever. Again, we consider fever a "symptom" of disease, as if it developed inevitably without serving any function. But regulation of body temperature is under our genetic control, and a fever doesn't just happen by accident. Because some microbes are more sensitive to heat than our own bodies are, by raising our body temperature we in effect try to bake the bugs



to death before we get baked ourselves.

Another common response is to mobilize our immune system. White blood cells and other cells actively seek out and kill foreign microbes. The specific antibodies we gradually build up against a particular microbe make us less likely to get reinfected once we are cured. As we all know, there are some illnesses, such as flu and the common cold, to which our resistance is only temporary; we can eventually contract the illness again. Against other illnesses, though—including measles, mumps, rubella, pertussis, and the now-defeated menace of smallpox—antibodies stimulated by one infection confer lifelong immunity. That's the principle behind vaccination—to stimulate our antibody production without our having to go through the actual experience of the disease.

Alas, some clever bugs don't just cave in to our immune defenses. Some have learned to trick us by changing their antigens, those molecular pieces of the microbe that our antibodies recognize. The constant evolution or recycling of new strains of flu, with differing antigens, explains why the flu you got two years ago didn't protect you against the different strain that arrived this year. Sleeping sickness is an even more slippery customer in its ability to change its antigens rapidly. Among the slipperiest of all is the virus that causes AIDS, which evolves new antigens even as it sits within an individual patient, until it eventually overwhelms the immune system.

Our slowest defensive response is through natural selection, which changes the relative frequency with which a gene appears from generation to generation. For almost any disease some people prove to be genetically more resistant than others. In an epidemic, those people with genes for resistance to that particular microbe are more likely to survive than are people lacking such genes. As a result, over the course of history human populations repeatedly exposed to a particular pathogen tend to be made up of individuals with genes that resist the appropriate microbe—just because unfortunate individuals without those genes were less likely to survive to pass their

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are now locked in an escalating evolutionary

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genes on to their children.

Fat consolation, you may be thinking. This evolutionary response is not one that does the genetically susceptible dying individual any good. It does mean, though, that a human population as a whole becomes better protected.

In short, many bugs have had to evolve tricks to let them spread among potential victims. We've evolved countertricks, to which the bugs have responded by evolving counter-countertricks. We and our pathogens are now locked in an escalating evolutionary contest, with the death of one contestant the price of defeat, and with natural selection playing the role of umpire.

THE FORM that this deadly contest takes varies with the pathogens: for some it is like a guerrilla war, while for others it is a blitzkrieg. With certain diseases, like malaria or hookworm, there's a more or less steady trickle of new cases in an affected area, and they will appear in any month of any year. Epidemic diseases, though, are different: they produce no cases for a long time, then a whole wave of cases, then no more cases again for a while.

Among such epidemic diseases, influenza is the most familiar to Americans, this year having been a particularly bad one for us (but a great year for the influenza virus). Cholera epidemics come at longer intervals, the 1991 Peruvian epidemic being the first one to reach the New World during the twentieth century. Frightening as today's influenza and cholera epidemics are, though, they pale beside the far more terrifying epidemics of the past, before the rise of modern medicine. The greatest single epidemic in human history was the influenza wave that killed 21 million people at the end of the First World War. The black death, or bubonic plague, killed one-quarter of Europe's population between 1346 and 1352, with death tolls up to 70 percent in some cities.

The infectious diseases that visit us as epidemics share several characteristics. First, they spread quickly and efficiently from an infected person to nearby healthy people, with the result that the whole population gets exposed within a short time. Second, they're "acute" illnesses: within a short time, you either die or recover completely. Third, the fortunate ones of us who do recover develop antibodies that leave us immune against a recurrence of the disease for a long time, possibly our entire lives. Finally, these diseases tend to be restricted to humans; the bugs causing them tend not to live in the soil or in other animals. All four of these characteristics apply to what Americans think of as the once more-familiar acute epidemic diseases of childhood, including measles, rubella, mumps, pertussis, and smallpox.

It is easy to understand why the combination of those four characteristics tends to make a disease run in epidemics. The rapid spread of microbes and the rapid course of symptoms mean that everybody in a local human population is soon infected, and thereafter either dead or else recovered and immune. No one is left alive who could still be infected. But since the microbe can't survive except in the bodies of living people, the disease dies out until a new crop of babies reaches the susceptible age—and until an infectious person arrives from the outside to start a new epidemic.

A classic illustration of the process is given by the history of measles on the isolated Faeroe Islands in the North Atlantic. A severe epidemic of the disease reached the Faeroes in 1781, then died out, leaving the islands measles-free until an infected carpenter arrived on a ship from Denmark in 1846. Within three months almost the whole Faeroes population—7,782 people—had gotten measles and then either died or recovered, leaving the measles virus to disappear once again until the next epidemic. Studies show that measles is likely to die out in any human population numbering less than half a million people. Only in larger populations can measles shift from one local area to another, thereby persisting until enough babies have been born in the originally infected area to permit the disease's return.

Rubella in Australia provides a similar example, on a much larger scale. As of 1917 Australia's population was still only 5 million, with most people living in scattered rural areas. The sea voyage to Britain took two months, and land transport within Australia itself was slow. In effect, Australia didn't even consist of a population of 5 million, but of hundreds of much smaller populations. As a result, rubella hit Australia only as occasional epidemics, when an infected person happened to arrive from overseas and stayed in a densely populated area. By 1938, though, the city of Sydney alone had a population of over one million, and people moved frequently and quickly by air between London, Sydney, and other Australian cities. Around then, rubella for the first time was able to establish itself permanently in Australia.

What's true for rubella in Australia is true for most familiar acute infectious diseases throughout the world. To sustain themselves, they need a human population that is sufficiently numerous and densely packed that a new crop of susceptible children is available for infection by the time the disease would otherwise be waning. Hence measles and other such diseases are also known as "crowd diseases."

CROWD DISEASES could not sustain themselves in small bands of hunter-gatherers and slash-and-burn farmers. As tragic recent experience with Amazonian Indians and Pacific Islanders confirms, almost an entire tribelet may be wiped out by an epidemic brought by an outside visitor, because no one in the tribelet has any antibodies against the microbe. In addition, measles and some other "childhood" diseases are more likely to kill infected adults than children, and all adults in the tribelet are susceptible. Having killed most of the tribelet, the epidemic then disappears. The small population

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size explains why tribelets can't sustain epidemics introduced from the outside; at the same time it explains why they could never evolve epidemic diseases of their own to give back to the visitors.

That's not to say that small human populations are free from all infectious diseases. Some of their infections are caused by microbes capable of maintaining themselves in animals or in soil, so the disease remains constantly available to infect people. For example, the yellow fever virus is carried by African wild monkeys and is constantly available to infect rural human populations of Africa. It was also available to be carried to New World monkeys and people by the transatlantic slave trade.

Other infections of small human populations are chronic diseases such as leprosy and yaws, that may take a very long time to kill a victim. The victim thus remains alive as a reservoir of microbes to infect other members of the tribelet. Finally, small human populations are susceptible to nonfatal infections against which we don't develop immunity, with the result that the same person can become reinfected after recovering. That's the case with hookworm and many other parasites.

ALL THESE TYPES of diseases, characteristic of small, isolated populations, must be the oldest diseases of humanity. They were the ones that we could evolve and sustain through the early millions of years of our evolutionary history, when the total human population was tiny and fragmented. They are also shared with, or are similar to the diseases of, our closest wild relatives, the African great apes. In contrast, the evolution of our crowd diseases could only have occurred with the buildup of large, dense human populations, first made possible by the rise of agriculture about 10,000 years ago, then by the rise of cities several thousand years ago. Indeed, the first attested dates for many familiar infectious diseases are surprisingly recent: around 1600 B.C. for smallpox (as deduced from pockmarks on an Egyptian mummy), 400 B.C. for mumps, 1840 for polio, and 1959 for AIDS.

Agriculture sustains much higher human population densities than does hunting and gathering—on average, 10 to 100 times higher. In addition, hunter-gatherers frequently shift camp, leaving behind their piles of feces with their accumulated microbes and worm larvae. But farmers are sedentary and live amid their own sewage, providing microbes with a quick path from one person's body into another person's drinking water. Farmers also become surrounded by disease-transmitting rodents attracted by stored food.

Some human populations make it even easier for their own bacteria and worms to infect new victims, by intentionally gathering their feces and urine and spreading it as fertilizer on the fields where people work. Irrigation agriculture and fish farming provide ideal living conditions for the snails carrying schistosomes, and for other flukes that burrow through our skin as we wade through the feces-laden water.

If the rise of farming was a boon for our microbes, the rise of cities was a veritable bonanza, as still more densely packed human populations festered under even worse sanitation conditions. (Not until the beginning of the twentieth century did urban populations finally become self-sustaining; until then, constant immigration of healthy peasants from the countryside was necessary to make good the constant deaths of city dwellers from crowd diseases.) Another bonanza was the development of world trade routes, which by late Roman times effectively joined the populations of Europe, Asia, and North Africa into one giant breeding ground for microbes. That's when smallpox finally reached Rome as the "plague of Antonius," which killed millions of Roman citizens between A.D. 165 and 180.

Similarly, bubonic plague first appeared in Europe as the plague of Justinian (A.D. 542–543). But plague didn't begin to hit Europe with full force, as the black death epidemics, until 1346, when new overland trading with China provided rapid transit for flea-infested furs from plague-ridden areas of Central Asia. Today our jet planes have made even the longest intercontinental flights briefer than the duration of any human infectious disease. That's how an Aerolíneas Argentinas airplane, stopping in Lima, Peru, earlier this year, managed to deliver dozens of cholera-infected people the same day to my city of Los Angeles, over 3,000 miles away. The explosive increase in world travel by Americans, and in immigration to the United States, is turning us into another melting pot—this time of microbes that we previously dismissed as just causing exotic diseases in far-off countries.

WHEN THE HUMAN population became sufficiently large and concentrated, we reached the stage in our history when we could at last sustain crowd diseases confined to our species. But that presents a paradox: such diseases could never have existed before. Instead they had to evolve as new diseases. Where did those new diseases come from?

Evidence emerges from studies of the disease-causing microbes themselves. In many cases molecular biologists have identified the microbe's closest relative. Those relatives also prove to be agents of infectious crowd diseases—but ones confined to various species of domestic animals and pets! Among animals too, epidemic diseases require dense populations, and they're mainly confined to social animals that provide the necessary large populations. Hence when we domesticated social animals such as cows and pigs, they were already afflicted by epidemic diseases just waiting to be transferred to us.

For example, the measles virus is most closely related to the virus causing rinderpest, a nasty epidemic disease of cattle and many wild cud-chewing mammals. Rinderpest doesn't affect humans. Measles, in turn, doesn't affect cattle. The close similarity of the measles and rinderpest viruses suggests that the rinderpest virus transferred from cattle to humans, then became the measles virus by changing its properties to adapt to us. That transfer isn't surprising, considering how closely many peasant farmers live and sleep next to cows and their accompanying feces, urine, breath, sores, and blood. Our intimacy with cattle has been going on for the 8,000 years since we domesticated them—ample time for the rinderpest virus to discover us nearby. Other familiar infectious diseases can similarly be traced back to diseases of our animal friends.

Given our proximity to the animals we love, we must constantly be getting bombarded by animal microbes. Those invaders get winnowed by natural selection, and only a few succeed in establishing themselves as human diseases. A quick survey of current diseases lets us trace four stages in the evolution of a specialized human disease from an animal precursor.

In the first stage, we pick up animal-borne microbes that are still at an early stage in their evolution into specialized human pathogens. They don't get transmitted directly from one person to another, and even their transfer from animals to us remains uncommon. There are dozens of diseases like this that we get directly from pets and domestic animals. They include cat scratch fever from cats, leptospirosis from dogs, psittacosis from chickens and parrots, and brucellosis from cattle. We're similarly susceptible to picking up diseases from wild animals, such as the tularemia that hunters occasionally get from skinning wild rabbits.

In the second stage, a former animal pathogen evolves to the point where it does get transmitted directly between people and causes epidemics. However, the epidemic dies out for several reasons—being cured by modern medicine, stopping when everybody has been infected and died, or stopping when everybody has been infected and become immune. For example, a previously unknown disease termed *o'nyong-nyong* fever appeared in East Africa in 1959 and infected several million Africans. It probably arose from a virus of monkeys and was transmitted to humans by mosquitoes. The fact that patients recovered quickly and became immune to further attack helped cause the new disease to die out quickly.

The annals of medicine are full of diseases that sound like no known disease today but that once caused terrifying epidemics before disappearing as mysteriously as they had come. Who alive today remembers the "English sweating sickness" that swept and terrified Europe between 1485 and 1578, or the "Picardy sweats" of eighteenth- and nineteenth-century France?

A third stage in the evolution of our major diseases is represented by former animal pathogens that establish themselves in humans and that do not die out; until they do, the question of whether they will become major killers of humanity remains up for grabs. The future is still very uncertain for Lassa fever, first observed in 1969 in Nigeria and caused by a virus probably derived from rodents. Better established is Lyme disease, caused by a spirochete that we get from the bite of a tick. Although the first known human cases in the United States appeared only as recently as 1962, Lyme disease is already reaching epidemic proportions in the Northeast, on the West Coast, and in the upper Midwest. The future of AIDS, deriving from monkey viruses even more secure, from the virus's perspective.

The final stage in this evolution is represented by the major, long-established epidemic diseases confined to humans. These diseases must have been the evolutionary survivors of many more pathogens that tried to make the jump to us from animals—and mostly failed.

Diseases represent evolution in progress, as microbes adapt by natural selection to new hosts. Compared with cow bodies, though, our bodies offer different immune defenses and different chemistry. In the new environment, microbe must evolve new ways to live and propagate itself.

The best-studied example of microbes evolving these new ways involves myxomatosis, which hit Australian rabbits in 19[illegible]. The myxoma virus, native to a wild species of Brazilian rabbit, was known to cause a lethal epidemic in European domestic rabbits, which are a different species. The virus was intentionally introduced to Australia in the hopes of ridding the continent of its plague of European rabbits, foolishly introduced in the nineteenth century. In the first year, myxoma produced a gratifying (to Australian farmers) 99.8 percent mortality in i

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fected rabbits. Fortunately for the rabbits and unfortunately for the farmers, the death rate then dropped in the second year to 90 percent and eventually to 25 percent, frustrating hopes of eradicating rabbits completely from Australia. The problem was that the myxoma virus evolved to serve its own interests, which differed from the farmers' interests and those of the rabbits. The virus changed to kill fewer rabbits and to permit lethally infected ones to live longer before dying. The result was bad for Australian farmers but good for the virus: a less lethal myxoma virus spreads baby viruses to more rabbits than did the original, highly virulent myxoma.

For a similar example in humans, consider the surprising evolution of syphilis. Today we associate syphilis with genital sores and a very slowly developing disease, leading to the death of untreated victims only after many years. However, when syphilis was first definitely recorded in Europe in 1495, its pustules often covered the body from the head to the knees, caused flesh to fall off people's faces, and led to death within a few months. By 1546 syphilis had evolved into the disease with the symptoms known to us today. Apparently, just as with myxomatosis, those syphilis spirochetes evolved to keep their victims alive longer in order to transmit their spirochete offspring into more victims.

HOW, THEN, does all this explain the outcome of 1492—that Europeans conquered and depopulated the New World, instead of Native Americans conquering and depopulating Europe?

Part of the answer, of course, goes back to the invaders' technological advantages. European guns and steel swords were more effective weapons than Native American stone axes and wooden clubs. Only Europeans had ships capable of crossing the ocean and horses that could provide a decisive advantage in battle. But that's not the whole answer. Far more Native Americans died in bed than on the battlefield—the victims of germs, not of guns and swords. Those germs undermined Indian resistance by killing most Indians and their leaders and by demoralizing the survivors.

The role of disease in the Spanish conquests of the Aztec and Inca empires is especially well documented. In 1519 Cortés landed on the coast of Mexico with 600 Spaniards to conquer the fiercely militaristic Aztec Empire, which at the time had a population of many millions. That Cortés reached the Aztec capital of Tenochtitlán, escaped with the loss of "only" two-thirds of his force, and managed to fight his way back to the coast demonstrates both Spanish military advantages and the initial naïveté of the Aztecs. But when Cortés's next onslaught came, in 1521, the Aztecs were no longer naive; they fought street by street with the utmost tenacity.

What gave the Spaniards a decisive advantage this time was smallpox, which reached Mexico in 1520 with the arrival of one infected slave from Spanish Cuba. The resulting epidemic proceeded to kill nearly half the Aztecs. The survivors were demoralized by the mysterious illness that killed Indians and spared Spaniards, as if advertising the Spaniards' invincibility. By 1618 Mexico's initial population of 20 million had plummeted to about 1.6 million.

Pizarro had similarly grim luck when he landed on the coast of Peru in 1531 with about 200 men to conquer the Inca Empire. Fortunately for Pizarro, and unfortunately for the Incas, smallpox had arrived overland around 1524, killing much of the Inca population, including both Emperor Huayna Capac and his son and designated successor, Ninan Cuyoche. Because of the vacant throne, two other sons of Huayna Capac, Atahuallpa and Huáscar, became embroiled in a civil war that Pizarro exploited to conquer the divided Incas.

When we in the United States think of the most populous New World societies existing in 1492, only the Aztecs and Incas come to mind. We forget that North America also supported populous Indian societies in the Mississippi Valley. Sadly, these societies too would disappear. But in this case conquistadores contributed nothing directly to the societies' destruction; the conquistadores' germs, spreading in advance, did everything. When De Soto marched through the Southeast in 1540, he came across Indian towns abandoned two years previously because nearly all the inhabitants had died in epidemics. However, he was still able to see some of the densely populated towns lining the lower Mississippi. By a century and a half later, though, when French settlers returned to the lower Mississippi, almost all those towns had vanished. Their relics are the great mound sites of the Mississippi Valley. Only recently have we come to realize that the mound-building societies were still largely intact when Columbus arrived, and that they collapsed between 1492 and the systematic European exploration of the Mississippi.

WHEN I WAS a child in school, we were taught that North America had originally been occupied by about one million Indians. That low number helped justify the white conquest of what could then be viewed as an almost empty continent. However, archeological excavations and descriptions left by the first European explorers on our coasts now suggest an initial number of around 20 million. In the century or two following Columbus's arrival in the New World, the Indian population is estimated to have declined by about 95 percent.

The main killers were European germs, to which the Indians had never been exposed and against which they therefore had neither immunologic nor genetic resistance. Smallpox, measles, influenza, and typhus competed for top rank among the killers. As if those were not enough, pertussis, plague, tuberculosis, diphtheria, mumps, malaria, and yellow fever came close behind. In countless cases Europeans were actually there to witness the decimation that occurred when the germs arrived. For example, in 1837 the Mandan Indian tribe, with one of the most elaborate cultures in the Great Plains, contracted smallpox thanks to a steamboat traveling up the Missouri River from St. Louis. The population of one Mandan village crashed from 2,000 to less than 40 within a few weeks.

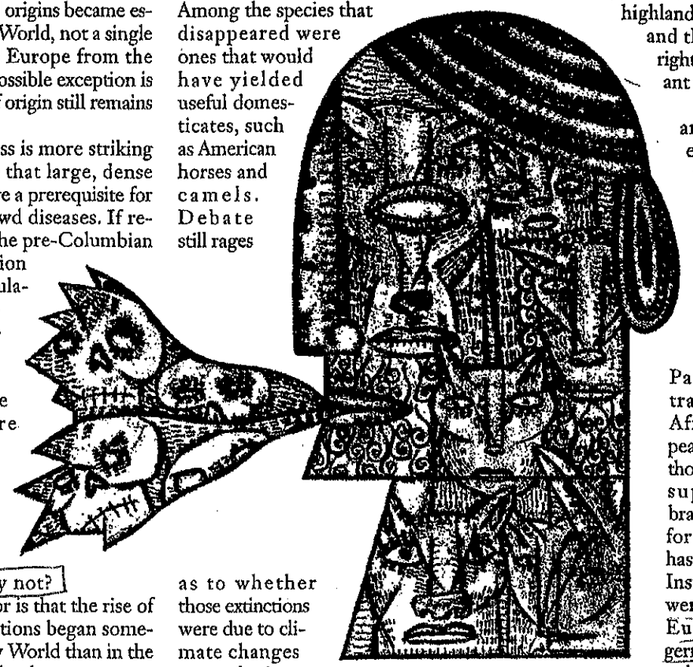
The one-sided exchange of lethal germs between the Old and New worlds is among the most striking and consequence-laden facts of recent history. Whereas over a dozen major infectious diseases of Old World origins became established in the New World, not a single major killer reached Europe from the Americas. The sole possible exception is syphilis, whose area of origin still remains controversial.

That one-sidedness is more striking with the knowledge that large, dense human populations are a prerequisite for the evolution of crowd diseases. If recent reappraisals of the pre-Columbian New World population are correct, that population was not far below the contemporaneous population of Eurasia. Some New World cities, like Tenochtitlán, were among the world's most populous cities at the time. Yet Tenochtitlan didn't have awful germs waiting in store for the Spaniards. Why not?

One possible factor is that the rise of dense human populations began somewhat later in the New World than in the Old. Another is that the three most populous American centers—the Andes, Mexico, and the Mississippi Valley—were never connected by regular fast trade into one gigantic breeding ground for microbes, in the way that Europe, North Africa, India, and China became connected in late Roman times.

The main reason becomes clear, however, if we ask a simple question: From what microbes could any crowd diseases of the Americas have evolved? We've seen that Eurasian crowd diseases evolved from diseases of domesticated herd animals. Significantly, there were many such animals in Eurasia. But there were only five animals that became domesticated in the Americas: the turkey in Mexico and parts of North America, the guinea pig and llama/alpaca (probably derived from the same original wild species) in the Andes, the Muscovy duck in tropical South America, and the dog throughout the Americas.

That extreme paucity of New World domestic animals reflects the paucity of wild starting material. About 80 percent of the big wild mammals of the Americas became extinct at the end of the last ice age, around 11,000 years ago, at approximately the same time that the first well-attested wave of Indian hunters spread over the Americas. Among the species that disappeared were ones that would have yielded useful domesticates, such as American horses and camels. Debate still rages as to whether those extinctions were due to climate changes or to the impact of Indian hunters on prey that had never seen humans. Whatever the reason, the extinctions removed most of the basis for Native American animal domestication—and for crowd diseases.



The few domesticates that remained were not likely sources of such diseases. Muscovy ducks and turkeys don't live in enormous flocks, and they're not naturally endearing species (like young lambs) with which we have much physical contact. Guinea pigs may have contributed a trypanosome infection like Chagas' disease or leishmaniasis to our catalog of woes, but that's uncertain. Initially the most surprising absence is of any human disease derived from llamas (or alpacas), which are tempting to consider as the Andean equivalent of Eurasian livestock. However, llamas had three strikes against them as a source of human pathogens: their wild relatives don't occur in big herds as do wild sheep, goats, and pigs; their total numbers were never remotely as large as the Eurasian populations of domestic livestock, since llamas never spread beyond the Andes; and llamas aren't as cuddly as piglets and lambs and aren't kept in such close association with people. (You may not think of piglets as cuddly, but human mothers in the New Guinea highlands often nurse them, and they frequently live right in the huts of peasant farmers.)

The importance of animal-derived diseases for human history extends far beyond the Americas. Eurasian germs played a key role in decimating native peoples in many other parts of the world as well, including the Pacific islands, Australia, and southern Africa. Racist Europeans used to attribute those conquests to their supposedly better brains. But no evidence for such better brains has been forthcoming. Instead, the conquests were made possible by Europeans' nastier germs, and by the technological advances and denser populations that Europeans ultimately acquired by means of their domesticated plants and animals.

So on this 500th anniversary of Columbus's discovery, let's try to regain our sense of perspective about his hotly debated achievements. There's no doubt that Columbus was a great visionary, seaman, and leader. There's also no doubt that he and his successors often behaved as bestial murderers. But those facts alone don't fully explain why it took so few European immigrants to initially conquer and ultimately supplant so much of the native population of the Americas. Without the germs Europeans brought with them—germs that were derived from their animals—such conquests might have been impossible. D