**The New England Journal of Medicine -- May 3, 2001 -- Vol. 344, No. 18**

Racial Profiling in Medical Research

Two articles in this issue of the Journal deal with the treatment of heart failure in white and black patients. One, concerning carvedilol, reports that the benefit of this beta-blocker is similar in nonblacks and blacks with chronic heart failure. ([1](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-1)) The other contends that enalapril, an angiotensin-converting-enzyme inhibitor, is more effective in whites than in blacks with left ventricular dysfunction. ([2](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-2)) The authors of both articles refer to "race," "racial groups," "racial differences," and "ethnic background" but offer no plausible biologic justification for making such distinctions. In a nod to the quandary faced by anyone who tries to explain the complex therapeutic effect of a drug along racial lines, the authors of the enalapril study acknowledge "the difficulty in ascertaining whether racial differences in outcomes are attributable to race or to other factors" and concede that "racial categorization [may be] only a surrogate marker for genetic or other factors." I maintain that attributing differences in a biologic end point to race is not only imprecise but also of no proven value in treating an individual patient.

Race is a social construct, not a scientific classification. In a 1999 position paper, the American Anthropological Association stated the following:

It has become clear that human populations are not unambiguous, clearly demarcated, biologically distinct groups.... Throughout history whenever different groups have come into contact, they have interbred. The continued sharing of genetic materials has maintained humankind as a single species.... Any attempt to establish lines of division among biological populations is both arbitrary and subjective. ([3](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-3))

Racial identification does have importance in the formulation of just and impartial public policies. However, recently released data from the 2000 U.S. Census show that even self-identification of race can be problematic. Following the decision by the Office of Management and Budget to allow multiple responses to a question on racial identification in the 2000 Census, almost 7 million people identified themselves as members of more than one race; about 800,000 respondents said they were both white and black. ([4](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-4)) This degree of multiracial identification underscores the heterogeneity of the U.S. population and the futility of using race as a biologic marker.

It is indisputable that social perceptions of what a person is or is not influence the availability, delivery, and outcome of medical care. It is incontrovertible that these perceptions apply with dismaying regularity to black people and other minorities in the United States. And it is undeniable that lifestyle, socioeconomic status, and personal beliefs are powerful influences on health. But these are matters of morality and culture, and we must clearly distinguish them from the biologic aspects of race-based medicine -- from the danger of attributing a therapeutic failure to the patient's "race" instead of looking for the real reason.

Sadly, the idea of race remains ingrained in clinical medicine. ([5](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-5)) On ward rounds, it is routine to refer to a patient as "black," "white," or "Hispanic," yet these vague epithets lack medical relevance. A racial designation in the context of medical management not only defies everything we have learned from biology, genetics, and history but also opens the door to inequities in medical care. Recently, the possibility of marketing drugs with the aim of promoting their use in particular races has emerged. ([6](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-6)) But since "race" is biologically meaningless, how will a physician know whether a given patient (who may identify with two races) has the combination of alleles that will ensure the efficacy of the drug? And what effect will racial profiling in the choice of therapy have on the bond of trust between patients and physicians?

Beyond the bedside, race-based medical research is widespread. The pseudoscience of race is well represented in clinical investigations. In March 2001, under the search term "Negroid race," Medline contained 13,592 citations, of which 1301 appeared in 1999 or 2000. Among these studies are race-based investigations of lipid metabolism, renal function, responses to vasodilators, sexual maturation, drug metabolism, neurodegenerative diseases, and even Dupuytren's contracture. Such research mistakenly assumes an inherent biologic difference between black-skinned and white-skinned people. It falls into error by attributing a complex physiological or clinical phenomenon to arbitrary aspects of external appearance. It is implausible that the few genes that account for such outward characteristics ([7](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-7)) could be meaningfully linked to multigenic diseases such as diabetes mellitus or to the intricacies of the therapeutic effect of a drug.

Some geographically or culturally isolated populations can properly be studied for genetic influences on physiological phenomena or diseases. The Pima Indians, who have unusual susceptibility to non-insulin-dependent diabetes mellitus, ([8](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-8)) and the people of Gambia, in whom polymorphisms in the NRAMP1 gene influence susceptibility to tuberculosis, ([9](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-9)) are examples. But even these cases are complex, since nongenetic factors also influence the outcome. Among these many factors is culture: for instance, the germ-line BRCA1 mutations that render Ashkenazi women susceptible to breast cancer ([10](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-10)) owe their prevalence in that population to the fact that for countless generations, Jews have married Jews.

After 400 years of social disruption, geographic dispersion, and genetic intermingling, there are no alleles that define the black people of North America as a unique population or race. Nevertheless, the prevalence of certain alleles does vary among populations. In some cases, these variant genes originated as mutations that proved advantageous under particular environmental conditions. In central and western Africa, for example, several independent mutations in the (beta)-globin gene gave rise to different sickle hemoglobins, each with a distinct geographic distribution and phenotype. These mutations spread through the population because they protect against malaria; they were dispersed in Greece, Saudi Arabia, Turkey, Iran, and elsewhere by migration and slavery.

Similar forces account for the different frequencies of certain blood-group alleles: they reflect geographic origins, not race. For all these reasons, hemoglobin S, susceptibility to breast cancer, blood type, skin color, and other manifestations of allelic variation do not define race in a biologically valid manner. This is not to deny that the frequencies of certain allelic variants or mutant genes among people who share a geographic origin or culture have medical value. Obviously, a screening program to detect sickle hemoglobin should focus on populations of African descent, and screening for Tay-Sachs disease in New York should be confined to Ashkenazi Jews.

The publication of the first draft of the sequence of the human genome ([7](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-7),[11](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-11)) should force an end to medical research that is arbitrarily based on race. The Human Genome Project now gives us the power to uncover the true origins of genetic variations; linking them to race has become passe. And instead of using polymorphisms to seek racial distinctions, we can spark real progress in clinical research by using genetic variations to track down clinically relevant alleles and pathogenic mutations. In another editorial in this issue of the Journal, Wood discusses allelic variations that may influence drug metabolism and the responses to treatment with certain drugs. ([12](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-12))

Education is also essential. Instruction in medical genetics should emphasize the fallacy of race as a scientific concept and the dangers inherent in practicing race-based medicine. Physicians everywhere must teach the immorality of racial discrimination in clinical practice. As for medical research, any investigation that entails so-called racial distinctions, whether a clinical trial or a laboratory study, should begin with a plausible, clearly defined, and testable hypothesis. Before studying a possible relation between skin color and sodium excretion, for instance, investigators should have a credible reason for believing that such a link could exist and a plan for finding the relevant genetic network. Research to root out social injustice in medical practice needs continued support, but tax-supported trolling of data bases to find racial distinctions in human biology must end.

Nature Genetics now obliges authors to "explain why they make use of particular ethnic groups or populations, and how classification was achieved." ([13](http://www.nejm.org/content/refs/2001/0344/0018/1392.asp" \l "ref-13)) The requirement to furnish a scientifically valid definition of the population under study should be adopted by all biomedical journals. It will be difficult to abandon long-held preconceptions, but perhaps the first benefit of the Human Genome Project will be to lead us to the understanding that in medicine, there is only one race -- the human race.

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