

## Is health only skin-deep?

Do advances in genomics mandate racial profiling in medicine?

The USA is witnessing a growing debate about the apparent disparities between the health status of white Americans and racial minorities, most notably African Americans and Hispanics. In 1993, the US government admitted that there are significant differences and responded by establishing the Minority Health Initiative to investigate and redress these discrepancies. The National Cancer Institute started the Center for Reducing Cancer Health Disparities in 2000, and last spring, the National Academies of Sciences' Institute of Medicine (IOM) in Washington, DC, released a study sponsored by the government's Department of Health and Human Services entitled 'Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care'. More than a mere academic exercise, this research raises an important question: does race impact on the emergence and progression of disease, or is race merely skin-deep? And if race does indeed have biological correlations, should racial profiling influence a physician's diagnosis and choice of treatment?

This growing awareness has been heightened by various confounding trends, first and foremost advances in human genetics. While numerous scientists—most notably Francis Collins and Craig Venter—have declared that genetics and the sequence of the human genome prove that there is no such thing as race, another camp of experts in population genetics and pharmacogenomics point out that naturally occurring polymorphisms impact on the frequency of particular diseases in certain populations, such as diabetes in Pima Indians or breast cancer and Tay-Sachs disease in Ashkenazi Jews. Individuals of some ethnic groups also assimilate drugs differently—some drug companies are testing new and existing drugs accordingly and have started to market them to those with similar genetic backgrounds.

And an increasing number of studies show that some ethnic minorities in the USA do have higher morbidity and mortality rates. According to a study conducted by the Commonwealth Fund,

77% of African Americans over 50 years old have been diagnosed with hypertension, coronary heart disease or cancer, compared with 68% of Hispanics and 64% of white Americans. In general, one in five Hispanics, one in six African Americans and one in four Asian Americans have a chronic condition compared to only one in seven white Americans. 'The difference is even more striking when taking into account that the minority population is, on average, younger than the white population, and would therefore be expected to be healthier,' the authors of the study commented.

But whatever the reason, race cannot and should not be used for diagnosis and treatment, according to Elijah Saunders, Professor of Medicine at the University of Maryland School of Medicine in Baltimore, himself African American.

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### If race is more than skin-deep and has biological correlations, should racial profiling influence a physician's diagnosis and choice of treatment?

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'The difference in the rates of mortality and morbidity from hypertension among blacks and Hispanics in this country cannot be explained by genetics,' he said. 'Being Hispanic or poor is also a marker for hypertension.' Although one in three blacks have hypertension, compared to one in four Caucasians, Saunders maintains that this is more likely to be caused by a complex interaction of socioeconomic status, environmental factors and salt sensitivity in many African Americans. 'While genetics may set the stage for developing hypertension, I favour the environmental-socioeconomic explanation as a cause for high prevalence of the disease,' he said.

Furthermore, as many blacks are more salt-sensitive and more likely to have low plasma renin levels, they are less sensitive to ACE (angiotensin-converting enzyme) inhibitors and ARBs (angiotensin II receptor blockers), which makes the disease

more difficult to control in this population. Saunders recently presented a study showing that African Americans respond better to a new drug, eplerenone, that selectively blocks aldosterone, a hormone that causes the body to retain sodium, whereas ACE inhibitors and ARBs do not fully restrict the hormone's action. At the meeting of the International Society for Hypertension in Blacks in Miami this year, the Association of Black Cardiologists presented a similar heart failure study specifically targeted to African Americans in which the nitric oxide-enhancing drug BiDil was found to have a significant effect only in blacks, who some believe to have low nitric oxide activity. But even given these results, Saunders cautioned against categorical assumptions that race is a determining factor. 'We're not talking about race as a genetic situation, we're talking about it as a marker,' he said.

Joseph Graves Jr, Professor of Evolutionary Biology at the University of Arizona in Phoenix, goes even further, saying that physicians should not use skin colour to diagnose and treat individuals, but only family history. 'What most people would describe as African American, 80% of that individual's genes originate somewhere in Africa. But others with the same appearance might have inherited varying amounts of genes from American Indians, Europeans and Africans,' Graves said. 'African Americans do have unique health needs,' he acknowledges, but he also felt that the complex interaction between socioeconomic and environmental conditions contributed more than genetics. For instance, 90% of Africans in Nigeria have the 235T mutation in the ACE gene locus—a marker for hypertension—but only 10% actually have hypertension. Compare that with 85% of African Americans with the mutation, and over 30% who have the disease, Graves pointed out. Scientists like Saunders may thus be reaching the right answer for the wrong reason, he suggested. Saunders concluded that taking race into account in diagnosing and treating disease could



be useful but also dangerous when attributing health aspects to race and genetics ‘when we just don’t know.’

Others, however, firmly maintain that taking race into account could improve diagnosis and treatment of disease. Physician and ethicist Sally Satel, in her article ‘I am a Racially Profiling Doctor’ in *The New York Times Magazine*, builds a case that taking into account the skin colour of her patients improves her diagnosis and treatment. When prescribing Prozac, for example, she starts an African American patient on a lower dose than a white patient, ‘in part because clinical experience and pharmacological research show that many blacks metabolise antidepressants more slowly than Caucasians and Asians. As a result, levels of the medication can build up and make side-effects more likely.’ Skin colour itself is not the issue, Satel explains, but ‘the evolutionary history indicated by skin colour.’

‘Skin colour can convey some useful information beyond skin colour, e.g. a higher risk of sickle cell disease or a higher likelihood of response to certain hypertensives,’ acknowledges Catarina Kiefe, from the Department of Medicine at the University of Alabama in Birmingham. But she believes that Satel’s approach is ultimately a dangerous impediment to the practice of medicine. ‘In our society, skin colour also conveys a lot of misinformation, e.g. blacks are at a higher risk of living in neighbourhoods that have poorer schools,’ she commented. ‘Satel demonstrates a rather

puzzling lack of understanding of these complexities. Her simplistic statements totally belittle the immense burden of suffering that has resulted from erroneous associations between biological traits more prevalent in subgroups and sociological attributes made to the entire subgroup.’

Another area under investigation is the different outcomes of black and white Americans following cancer diagnosis. Although blacks have poorer survival rates after diagnosis, this cannot be attributed to a difference in disease biology between the races, concluded Peter Bach, a pulmonologist and epidemiologist at New York’s Memorial Sloan-Kettering Cancer Center. His assessment is based on a study he recently published in the

cancer biology between racial groups are unlikely to be responsible for a substantial portion of the survival discrepancy.’ He concluded that, instead, ‘differences in treatment, stage of the cancer at presentation and mortality from other diseases in addition to the cancer should represent the primary targets of research and interventions designed to reduce disparities in cancer outcomes.’

Obviously, there are other factors at work, which Bach investigated in an earlier study published in the *New England Journal of Medicine*. He examined racial differences in the treatment of early-stage non-small-cell lung cancer and found that the rate of surgery for black patients was nearly 13% lower than for white patients with the same health coverage and stage of disease. There were, however, no differences in the survival rates between the two groups if they had surgery. His studies indicate that US medical care providers discriminate against racial minorities. This is also the conclusion of both the Center for Reducing Cancer Health Disparities and the IOM. In a nation with a history of discrimination against racial minorities, many believe that searching for a biological basis for different rates of illness and death is an extension of earlier ‘social hygiene’ policies developed at the end of the 19th Century. Moreover, racial minorities are less willing to participate in clinical trials due to a history of health discrimination capped by the Tuskegee syphilis trial, in which poor black sharecroppers were left untreated—although a cure for syphilis existed—in order to observe the disease’s progress.

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*Journal of the American Medical Association* in which he reviewed all articles in English from 1966 to January 2002 describing the outcomes of 32 004 black and 189 877 white cancer patients. It addresses what Bach calls ‘the biological hypothesis’—that cancer progression is determined by race—and comes to the conclusion that it is not. ‘Only modest cancer-specific survival differences are evident for blacks and whites treated comparatively for similar-stage cancer,’ Bach noted. ‘Therefore, differences in

The debate continues about whether genetic variations among human individuals occur frequently enough to support the concept of race. Race in humans corresponds to subspecies in animals, but the subtle genetic differences among humans from differing geographic origins are not synonymous with race, Graves noted. About 85% of all genetic variation occurs at the individual level, and there is far greater variation among Africans than between Africans and Caucasians, for instance. ‘There is no scientific debate,’

Graves said. Instead, 'there is a confusion between geographic variation [in humans] with subspecies among other species.'

And while some genetic traits, such as the gene for sickle cell anaemia or Tay-Sachs disease, occur with high frequency among African Americans and Ashkenazi Jews, respectively, these diseases can also be found in populations in the Mediterranean, such as Greece, Syria, and Israel. Tay-Sachs disease is also found in populations of French Canadians and the Amish—groups who tend to marry within themselves. Yet, some have concluded that Tay-Sachs and breast cancer due to the *BRCA1* gene are Ashkenazi Jewish diseases, simply because this group has been studied.

Others still defend the notion of race. George Gill, Professor of Anthropology at the University of Wyoming and a forensic anthropologist for the Wyoming State Crime Laboratory, thinks that the idea that race is only skin-deep is simply not true. 'Forensic anthropologists are overwhelmingly in support of the idea of the basic biological reality of human races,' he commented. Utilising a combination of

new and traditional methods of bone analysis, forensic biologists can give an accurate assessment of race, Gill said. He thus believes that 'race denial' is not based on science, but on socio-political motivation. Both Gill and Kiefe also noted that, although scientists may not sub-

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scribe to the concept of race, they still identify individuals as part of one or another race. 'My answer is that we can often function within systems that we do not believe in,' Gill said. Unless the putative differences are acknowledged, human discrimination will continue, he added.

Indeed, 'The concept of race as a definable biological entity persists in the medical literature,' Kiefe wrote recently in the *Journal of the American Medical Association*. Medicine is part of society, and

people in health care are thus driven by the same culture, prejudices and emotions as others, she explained. Bach agrees: 'In cancer and other diseases, biology has always been out there as an explanation for poor outcomes among racial minorities.'

The authors of the IOM report wrote that 'the committee was persuaded by the evidence it gathered that disparities can partly be attributed to a complex, often fragmented, and economically driven health care environment,' and urges researchers to replace the notion of 'race' with 'ethnic group'. But whatever causes the differences in health status—be it polymorphisms or different treatments due to discrimination—the report concludes 'the real challenge lies not in debating whether disparities exist, because the evidence is overwhelming, but in developing and implementing strategies to reduce and eliminate them.'

*Vicki Brower*

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## The biochemistry of beauty

### The science and pseudo-science of beautiful skin

**T**he moment the US Food and Drug Administration (FDA) authorised the use of botulinum toxin A this April for the treatment of glabellar lines, those unsightly furrows that form between the eyebrows, it was party time for beauty clinics from Los Angeles to Milan. But not half as much as for Allergan, the company in Irvine, CA, that exclusively produces and markets the purified bacterial toxin. Botox, the tradename for botulinum toxin A, could henceforth be marketed as 'Botox Cosmetic™' in a growing billion dollar market.

In fact, people have been having their faces periodically immobilised by Botox for at least 5 years, but the FDA authorisation is an important milestone in the progress of the toxin out of the world of clinical indications and into the funfair of

vanity. Due to its paralysing properties, botulinum toxin A was originally used by clinicians to treat strabismus (cross-eyedness) via injection into the periocular muscles, and has since proven very bene-

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ficial in the treatment of blepharospasm (uncontrollable microcontractions of the eyelid muscles), cervical dystonia and certain types of spasticity in children. However, Botox has not appeared in recent newspaper and magazine headlines

because of its clinical applications, but rather its use in so-called 'Botox clinics', where an explosively growing number of well-off customers are having unsightly facial wrinkles and furrows removed together with all traces of emotion and expression. Not only has the toxin become popular in the media, it has long since made its way into the American language as well: a synonym for face lifting, 'botoxing' things has become all the rage.

According to the American Society for Aesthetic Plastic Surgery, 8.5 million surgical and non-surgical cosmetic procedures were performed in 2001. Botulinum toxin A and B alone accounted for 1.6 million of these, and, with an increase of more than 20-fold in its use over the last 5 years, has made it to the top of the league for rapidly growing beauty treatments.