lated disciplines who awakened the nation to the dangers of and cures for those problems.

Now, as many of the social and health problems from our past are once again with us—seemingly in a more virulent form—it is time that we resurrect the coalitions of public health, urban planning, and social work professionals who were so effective in that earlier age. Social and public health problems such as those linked to homelessness are not discrete pathologies. If we wish to arrest the rise in infant mortality, tuberculosis, AIDS, drug abuse, and the other individual manifestations of a tattered social contract, we must convince a cynical nation that good schools, decent housing, good transportation, day care, rational health planning and good nutrition for *all* our citizens are imperative social policies for many reasons. They are important because the children of America are all our children, because they are the only effective way to make urban streets civil places to live and work, and finally because they help us to be effective competitors in a new world economy in which we must be team members and not club owners.

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Can Genetic Constitution Affect the 'Objective' Diagnosis of Nicotine Dependence?

Accurate diagnosis of nicotine dependence and detection of relapse in treated tobacco dependent persons can be augmented by quantitative biochemical assessment.[1] The reliability of biochemical assessment may, however, be limited by the genetic constitution of the individual. Three studies published in this issue of the Journal describe possible sources of measurement error and indicate the need for more basic research in the biochemical verification of cigarette smoking and other forms of tobacco use.[2–4] As suggested by these reports, individual genetic heritage may quantitatively affect the expired air carbon monoxide (CO) and plasma cotinine levels measured in cigarette smokers.

In brief, McNeill, *et al.*,[2] demonstrated that the elevated expired-air hydrogen levels which occur in the expired air of lactose intolerant persons can result in considerably elevated measurements of expired air CO. Lactose intolerance is common in persons of Asian and African heritage.[5] Wagenknecht, *et al*,[3] found that serum cotinine levels were higher in a group of young Black smokers than in young White smokers even though the latter had higher estimated daily nicotine exposure and serum thiocyanate. The authors ruled out a reporting bias and differences in nicotine intake as explanations for the population difference, and suggested that either the rate of metabolism of nicotine or the rate of excretion of cotinine differed between these populations. These findings supplement a previous report of racial differences in serum cotinine levels of young children exposed to environmental tobacco smoke.[6] Finally, Perez-Stable, *et al*,[4] found that among a Mexican-American cohort, more than one in five persons who reported smoking less than 10 cigarettes per day had higher than expected ratios of serum cotinine levels to daily cigarette consumption. Perez-Stable, *et al*, concluded that the Mexican American smokers were underreporting their cigarette consumption; the possibility of genetic differences in nicotine metabolism and/or cotinine excretion was considered as an alternative explanation of their findings. These authors also speculate that lighter smokers, regardless of genetic background, may metabolize nicotine and/or clear cotinine more slowly than their heavier smoking counterparts.

Although the findings of these three studies are preliminary, the possibility of heritable population differences and the likelihood that expired air CO levels are affected by lactose intolerance persons confirms the need for more developmental work in the area of biochemical assessment of tobacco use status. Idle[7] also discussed individual variability in nicotine metabolism and other factors that could complicate biochemical measures of tobacco use. Idle, however, probably overstated the demonstrated variance in saliva assays, as well as the apparent degree of individual variability[8] and contamination by non-tobacco vegetable sources of nicotine/cotinine.

Some perspective may be gained from the biochemical assessment of other forms of drug use, since these issues are not unique to the assessment of tobacco use and nicotine dependence. It has long been known that individuals vary considerably in their metabolism and elimination of drugs and that some differences are related to the genetic constitution.[9] Such variation in the pharmacokinetic profile of drugs across individuals can complicate clinical pharmacotherapeutics by altering the duration and magnitude of the effects of the medication. It seems to be less generally appreciated, however, that individual variation in drug kinetics can also complicate the use of bioassays in quantifying prior drug exposure. The accuracy of individual estimates of the amount of drug taken as well as the estimate of time since its administration is limited by a variety of factors, including the rate at which that individual metabolizes and eliminates the drug, and by other individual differences in the production of drug-by-products.[10]

These issues are of practical significance in the treatment of drug dependent persons where practitioners must be able to objectively determine whether or not a person has ingested a target substance of abuse. The value of the threshold criterion ("cutoff" point) for the conclusion that drug use has occurred can affect the frequency and type of errors that are

made in the assessment of tobacco and other forms of substance use.[10,11] For example, increasing the values of the cutoff point results in fewer false positive conclusions (classifying subjects as users when they really are abstinent) but also reduces the likelihood of detecting any occurrence of drug use.

Studies that evaluate the efficacy of tobacco cessation strategies, should include biochemical means of assessment to objectively verify abstinence. Cotinine assessment is probably the most accurate and specific means of quantitating tobacco intake. Even if the possible quantitative differences in cotinine metabolism suggested by the present studies are verified, cotinine assessment should, nonetheless, continue to serve as a useful means of assessing level of tobacco exposure. While Wagenknecht, *et al,* reported an adjusted 83 ng/ml difference in serum cotinine levels between Blacks and Whites, the differences in the cotinine levels between Blacks and Whites, the difference in the misclassification rate of self-reported nonsmokers was two percentage points (i.e., 6.5% of Blacks and 4.5% of Whites who reported themselves to be nonsmokers but were classified as smokers by the biochemical assessment procedure). This latter difference may be due less to differences in the rate of misclassified nonsmokers in the two groups and more to differences in the rate of metabolism of nicotine and/or the rate of clearance of cotinine. Verification of any racial/ethnic differences in nicotine metabolism, for example, should result in the calculation of optimal cutoff points for each appropriate racial/ethnic group.

Cotinine assessment can also be complicated when individuals swallow nicotine, as often occurs among users of smokeless tobacco or nicotine polacrilex gum; the first-pass liver metabolism may produce levels of plasma cotinine that are higher in proportion to nicotine intake than those levels that result as a function of parenterally absorbed nicotine.[1]

Assessing expired air CO is a convenient means of estimating tobacco smoke exposure. However, until manufacturers of devices for this assessment provide a means of eliminating hydrogen gas contaminations of the results, such instruments should be used with caution. The use of CO assessment is already limited because of the variety of other sources of contamination of results (e.g., environmental carbon monoxide, consumption of alcohol) and the fact that expired air CO measurements do not reveal if the person has substituted a smokeless form of tobacco for the smoked form. Where possible, one can reduce the error rate associated with this technique by using filters to reduce the effects of recent alcohol consumption and asking study participants whether they have lactose intolerance or have been exposed to other sources of contamination.

A major health promoting strategy is to both encourage tobacco users to quit and provide help for those who seek it.[12] Objective determination of tobacco intake may facilitate achievement of such goals. Several methods of biochemical assessment of tobacco are available, each with various advantages and disadvantages.[1] Therefore, even the possible constraints given of biochemical assessment of tobacco use suggested by the papers published in this issue of the Journal[2-4] and by Idle,[7] it remains important to encourage health care providers to include biochemical diagnoses in their evaluations of the tobacco use. Feedback on biological markers of nicotine dependence may even be therapeutic.[13] Manufacturers of devices for measuring expired air carbon monoxide should be encouraged to reduce the impact of hydrogen gas contamination of results. It remains important to attempt to replicate the currently discussed findings and to provide as definitive information as possible regarding the possible extent of sources of biological differences among individuals that may lead to diagnostic and measurement error.

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