Annotation: Preventive Screening for Health Risks among Adolescents

As I turned off the radio to start writing this annotation, a child expert was saying, "Adolescents have many serious questions about their health and about related aspects of their lives that they would like to discuss with their doctors, but usually are not given the chance." In this issue's "Don't Ask, They Won't Tell: The Quality of Adolescent Health Screening in Five Practice Settings," Blum and colleagues examine the frequency with which physicians in different practice settings ask questions about risk behaviors that would encourage adolescents to voice these concerns.[1]

The authors examined a total of 788 charts of adolescents aged 13 to 17 years randomly selected from five practice settings: private pediatric and family practices, a community family practice clinic, a high school clinic, and a community teen clinic. Blum et al. measured the frequency with which questions were recorded concerning 21 health risks derived from the Guidelines for Adolescent Preventive Screening (GAPS). These included biomedical, physical, and psychological risks, substance abuse, and sexual behavior.

The total proportion of the 21 risks screened and recorded varied from 19% in the private practice settings to 67% in the teen clinics. Contrary to their expectations, the extent of screening did not differ by age or sex.

As a pediatrician on the periphery of the specialized fields of adolescent medicine and epidemiology, I believe this is an important study. It serves as an example of the value of an epidemiologic enquiry of a medical-sociologic problem about which there are commonly held but unmeasured assumptions. In this case, the findings not only support the assumption that health screening of adolescents is inadequate, but also, for the first time, provide data on the extent of the problem, thereby underscoring the urgency of meeting it.

The focus in this study was solely on the frequency of screening in different clinical settings. Future investigations by the authors or by others using their protocols could provide valuable data on several other variables. The authors discussed but did not assess the attitudes, education, and training of physicians in different practice settings and suggested reasons why physicians in private practice are more reluctant to ask questions and discuss social and behavioral issues that underlie the major causes of adolescent morbidity and mortality. The reasons include inadequate relevant medical education and resident training, time limitations, and mistaken biases that high-risk behaviors are less likely to occur among the predominantly middle- and upper-income adolescents in their practices than among inner-city youth often seen in community and school teen clinics.

Several of my younger colleagues with whom I discussed the paper, including some in private practice, insisted that they had been well prepared and that they not only felt comfortable in discussing all aspects of preventive care of adolescents recommended by GAPS, but also considered it an important and a rewarding part of their practices. This response was voiced most emphatically by physicians in the teen clinics, suggesting that medical education and resident training designed for students preparing for such careers should be given greater emphasis in programs for all students. If this were done, more physicians would *ask* and more adolescents would *tell* and seek help about many of their most serious unvoiced concerns. □

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Reference

1. Blum RW, Beuhring T, Wunderlich M, Resnick MD. Don't ask, they won't tell: the quality of adolescent health screening in five practice settings. *Am J Public Health.* 1996;86: 1767–1772.

Editor's Note. See related article by Blum et al. (p 1767) in this issue.

Comment: Genetics and Public Health

The demonstration about 40 years ago that an inborn error of metabolism, phenylketonuria (PKU), could be diagnosed at birth so that children treated with an appropriate diet would avoid becoming mentally retarded exploded two myths about genetics: first, that genetic effects are immutable and, second, that "nature" and "nurture" were competing explanations, rather than interacting factors, in health and disease.

The introduction of prenatal diagnosis of specific chromosomal and inherited disorders about 25 years ago provided tools for determining whether a particular baby was affected or not affected with the disorder about which the prospective parents had reason to worry. No longer were genetic counselors and caregivers restricted to probabilistic statements about the recurrence or occurrence of the particular disorder. These developments stimulated an avalanche of important and clinically useful advances in human genetics.

Nevertheless, both of these examples presented complications. In the diagnosis of phenylketonuria, we were slow to recognize that increased levels of phenylalanine in the blood of the newborn could be due to multiple mutations, not just phenylketonuria, reflecting the general rule of heterogeneity of etiology and heterogeneity of mutations. Only about half of the infants who were positive on the screening test actually had phenylketonuria, and some, fortunately rare, infants had a mutation that made them need more than normal phenylalanine in the diet to develop normally. In prenatal diagnosis, we had to take great pains to emphasize to parents, referring physicians, and the media that no test could guarantee a "normal child"; the tests were directed at specific diagnosable conditions, which are still a minority of those for which reliable diagnoses are desired. Meanwhile, the capacity to test the chromosomes made possible the determination of the sex of the fetus, with the specter that some parents might use this test to choose the sex of their baby. That proved to be quite infrequent and was discouraged. Controversy did arise, of course, from the fact that parents facing a diagnosis of a severe, untreatable condi-

Editor's Note: See related article by Khoury et al. (p 1717) in this issue's Public Health Policy Forum.

tion might choose to terminate the pregnancy. In fact, fully informed, they generally would not have the test unless they were already very likely to terminate the pregnancy; overall, therefore, many more pregnancies have been saved by prenatal diagnoses showing that the fetus was unaffected with the condition the parents feared.

Public health and medical care are characterized by choices, hopefully choices well informed by good science, guided by compassionate values, and supported by effective communication among caregivers, patients and their families, and public health officials. Knowledge of genetics, use of genetic tools, and interpretation of genetic variation in the highly outbred species we know as humans should permeate all fields of public health research, public health practice, and public health education. We do not do too well, at present. Thus, the paper in this issue of the Journal from the Genetics Working Group at the Centers for Disease Control and Prevention is a welcome attempt to highlight the role of genetics in prevention.[1] The authors relate genetic tests to the broad framework of primary, secondary, and tertiary prevention and to the core functions of assessment, policy development, and assurance. There is no doubt that population-based epidemiologic studies are needed to characterize the predictive value of gene-based diagnostic tests and guide their appropriate uses in medicine and public health. We should be cautious in accepting high relative risk estimates, including some of those in the article by Khoury et al., because of the bias of publication and the uncertainty of generalizability. Furthermore, the roles of genetics in public health are much broader than genetic testing.

Epidemiologic and biostatistical study designs should account explicitly for variation in the population. A startling, continuing example of failure is the set of generic guidelines for diagnosis and treatment of elevated serum cholesterol or LDL-cholesterol values across the whole population, ignoring knowledge of multiple diagnosable underlying mechanisms of hypercholesterolemia, associated with different preferred treatments.[2] Also, the guidelines were applied to the entire adult population despite lack of data and then contrary data on the value of routine cholesterol testing and treatment in the elderly.[3] Much less attention has been given to another important cardiovascular risk factor, elevated plasma levels of the thrombogenic and atherogenic amino acid homocysteine. This risk factor can be reduced by increasing circulating levels of folic acid, with both genetically variable folate metabolism and dietary or supplemental vitamin intake being important influences.[4] Knowledge of genetically variable biotransformation enzymes involved in the metabolism of the drug should be incorporated into study designs for clinical trials for new pharmacologic agents. In fact, we should not let the use of the standard error of the mean, rather than the standard deviation, make the interindividual variation in pharmacological or other quantitative studies seem small.

Epidemiology itself is undergoing a transformation to put greater emphasis on underlying biological mechanisms, not just statistical associations, and to test findings from observational epidemiology in prevention clinical trials, like the recently completed, shocking trials of beta-carotene as a chemopreventive agent against lung cancer and heart disease.[5–7] The discovery, cloning, and sequencing of the breast cancer genes (BRCA1 and BRCA2), cited by Khoury et al., provide a basis for diagnostic testing of predisposition to breast and ovarian cancers in women in high-risk families, Ashkenazic Jewish women, and potentially many more women, as the many different mutations in these genes are sorted out with regard to breast cancer risk and appropriate counseling is defined, hopefully together with women's health groups like the Breast Cancer Resource Committee. Moreover, if the functions of those genes can be elucidated, we may have wholly new ideas and approaches to treatment and prevention of breast cancer, which is almost surely a highly heterogeneous diagnosis. That would close what is called the "therapeutic gap."

In environmental health and risk assessment, we use genetic tests for mutations (genotoxicity) as indicators of risk of cancers from those mutagenic agents and investigate interactions of exposures to environmental agents with genetic variation (from predisposition to resistance) in the "host," a subfield we now call ecogenetics. Here we must distinguish germline (heritable) mutations, expressed in all the cells of the body, from somatic mutations, occurring in a single cell and affecting the clonal descendants of that cell.

Current models show at least five genes involved in the pathogenesis of colon cancer, for example. Such knowledge may force us to revamp our standard assumptions about linear extrapolation of dose–response relationships for mutagenic (genotoxic) chemicals, which currently assume that zero cancer risk occurs only at zero dose.[8] For example, interactive mechanisms and repair of DNA lesions might make the response fall more rapidly than the dose at low exposures. Interindividual variation and mechanistically understood differences between rodents and humans were highlighted in the June 1996 report of the Presidential/Congressional Commission on Risk Assessment and Risk Management ("The Risk Commission").[9]

The use of biomarkers of exposure, of early or pre-clinical effects, and of variation in susceptibility is expected to facilitate bridging of our knowledge between toxicology and epidemiology. Practical tests of biomarkers would help health officers identify subgroups or even individuals who may be at high risk of subsequent disease and may be most appropriate for surveillance among those with known or potential exposure. Congress long ago sought to protect highly susceptible subgroups under the Clean Air Act and all workers under the Occupational Safety and Health Act, but our research and risk assessments have lagged on that mandate.

Genetic tests have already proved of crucial value in prompt diagnosis and epidemiologic tracking of infections, including toxigenic *Escherichia coli* and drug-resistant *Mycobacterium tuberculosis.* As noted by the Risk Commission in the wake of the cryptosporidiosis epidemic in Milwaukee, Wis, the contaminated hamburger epidemic in Seattle, Wash, and resurging and emerging infections everywhere, it is worth reminding ourselves and the rest of the world that not just chemicals but microbes and radiation are serious environmental hazards. Risks should be assessed and acted upon in a broad public health context.[9]

Personal behaviors and responses to interventions aimed at promoting healthful behaviors or decreasing unhealthy behaviors play on a biologic substrate of variation, too, as do neurologic and psychiatric diseases, from epilepsy to depression. Genetic variation is only one of many sources of "host" differences; others include nutrition, pharmacologic agents (including alcohol and illegal drugs), smoking and other often confounding behaviors, previous and concurrent occupational, recreational, and environmental exposures, personal protective measures, and interpersonal stress. Particular care is needed in dealing with

behavioral characterizations, including especially analyses of genetic factors, because societal definitions of what is normal or widely accepted behavior have so many cultural, racial, and historical biases.

The development of the Human Genome Project by the National Institutes of Health and the Department of Energy in the United States and similar initiatives in France, the Nordic countries,[10] and elsewhere have brought great attention to the technology, potential applications, and ethical issues involved in sequencing the human genome and applying that knowledge. To begin with, of course, there was the question of whose genome would be sequenced and whether there might be proprietary implications. Fears of the misguided eugenics movement of the early decades of this century were reignited.

Thus, it was wise of James Watson to respond to a reporter's inquiry with the impromptu announcement that he, as initial Director of the Human Genome Project in 1988, would earmark a portion of the funding for consideration of the Ethical, Legal, and Social Implications (ELSI) of the Project.[11] Thus was born a complex and generally admirable effort to define the issues, anticipate the implications, engage social scientists, ethicists, historians, and philosophers, and convene highly interdisciplinary groups of researchers, policy folks, and other groups, including representatives of insurers, employers, and workers. It is certainly true that science, in general, and genetics, in particular, are not and should not be conducted as if isolated from the larger society. That society properly impinges on what is done and certainly what is funded, and the society is affected by what is investigated and learned.

As illustrated above by the breast cancer genes, there is particular angst about the capacity to diagnose a genetically determined disease (such as Huntington disease) or a genetic predisposition (such as specific BRCA1 mutations) if there is no effective or desirable preventive or therapeutic response for the clinical condition. In the case of untreatable Tay-Sachs disease, it was possible to move earlier in the chain of events and offer community-based counseling and specific carrier testing for this autosomal recessive condition, so that matings or pregnancies at risk for Tay-Sachs disease could be averted on the initiative of the individuals most likely to be gene carriers. In general, those of us in public health would prefer preventive approaches over later efforts at effective therapy for conditions already diagnosed clinically. In the case of cystic fibrosis, the many mutations greatly complicate carrier detection. No specific population subgroup could be targeted for community-based counseling and screening, and the disease is not nearly as severe or untreatable as Tay-Sachs. Thus, carrier detection programs largely were deferred as both the American Society for Human Genetics and the National Institutes of Health Ethical, Legal, and Social Implications program launched social impact assessments and recommended caution.

Important issues about informed consent remain. First, who may decide/consent for children?[12] Then, can Institutional Human Subjects Review Boards approve genetic tests on stored samples collected as part of epidemiologic studies or clinical trials? An extensive proposal and review has focused primarily on samples retained from clinical services.[13] Very complex family-specific issues arise from trying to contact or asking probands to contact their relatives for genetic studies.

Privacy and discrimination issues have dogged genetics for many years. Insurers are particularly suspect as they compete for low-risk customers with approaches that have been sophisticated actuarially, but inappropriate genetically.[14,15] Both health and life insurance are at risk, and both insurability and rates can be affected. Colorado, I believe, was the first legislature to enact state-level protection against the use of genetic information to deny health insurance. Pre-employment and post-employment discrimination is another concern.[16,17] After extensive discussion and negotiation, an Ethical, Legal, and Social Implications working group elicited a decision from the Equal Employment Opportunities Commission of the federal government that, for the purposes of implementing the Americans with Disabilities Act, all forms of pre-employment genetic testing would fall under the Act's protection.[11] Previously, the Equal Employment Opportunities Commission had held that genetic risk assessments and carrier tests did not identify existing disabilities. Less productively, another Ethical, Legal, and Social Implications working group on insurance issues chose to seek total reform of the US health care system to eliminate the need for individual risk underwriting altogether, which, of course, has not occurred! The action, in general, on insurance issues lies with the individual states.

In public health education, I believe we have a long way to go to ensure that our enrolled students and continuing-education students gain an adequate introduction to genetics. The subject comprises a formidable array of molecular and cell biology, clinical medicine, ecogenetics, genetic epidemiology, statistical genetics, evaluation of screening and testing methods, ethics, and public policy.[18] Such interdisciplinary educational initiatives are underway at the University of Michigan and University of Washington Schools of Public Health and perhaps elsewhere. Probably, genetics should be one of the core fields for public health training.

We can be certain that genetics will grow further in importance in public health as the public becomes more knowledgeable and more demanding of genetic services, and as knowledge of our genes and their functions permits more effective strategies for treatment and especially for prevention, the special responsibility of public health. □

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Call for Abstracts for the 1997 APHA Meeting

The 125th American Public Health Association Annual Meeting will be held November 9–13, 1997, in Indianapolis, Ind. The meeting's theme will be "Communicating Public Health." The Call for Abstracts was published in the November 1996 issue of the Journal and has *February 10, 1997*, as the deadline for submission.

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