GENETIC ISSUES IN PUBLIC HEALTH AND MEDICINE

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With an Introduction by

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Advancing genetic technology has given rise to certain controversial issues, the import of which extends far beyond the walls of the classroom or laboratory. Calling on a number of involved professionals, this book offers the scientist trenchant analyses of the ethical, religious, legal, political and philosophical implications of the questions which present themselves when genetic, medical and community interests intersect.

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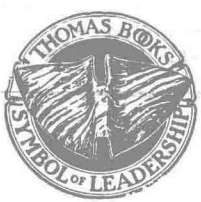

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TO OUR PROGENY

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PREFACE

THE MANY ADVANCES in human genetics and their contingent problems and implications make it increasingly necessary to understand the converging relationships with other fields. The interaction between genetics and medicine, medicine and the community, and genetics and the community, are obvious. However, the point where the three sets of concerns intersect comprises issues of social, political, legal, economic, and moral-ethical impact. Some issues are simply tangential, but others that are more controversial reach to the philosophical core of scientific inquiry itself. That intersection of issues prompted this collection, which was sparked by a series of seminars. So that present and future decision makers can deal effectively with these growing reciprocal concerns and their consequences—real and potential—they need an overview of the significant genetic issues in public health.

Our approach has been to focus mainly on the applications of genetic knowledge and on its various concomitant problems. In addition to general remarks in the Foreword and comments preceding each section, transitional introductions precede chapters where necessary.

For a book of this nature, we decided that the contributors, chosen for their varied expertise, should treat topics in their own manner without having to conform to any specific point of view or to a rigid style of presentation. On matters where there are differences of opinion within the scientific community, such as the explanation of HLA-disease associations, the risks of administering Rh Immune Globulin during pregnancy, ethical considerations in counseling and intervention, and/or the hazards of recombinant DNA, the interpretations of the contributors were honored. Moreover, we felt that any resultant overlap in subject areas between chapters would afford a multifaceted view. At the

same time, although intending to include many aspects, we have not attempted to achieve a panoramic scope. For example, the role of genetic factors in common disorders of complex etiology, such as heart disease, cancer, and stroke, are not dealt with per se. However, the basic principles of genetic-environmental interaction and the heterogeneity of late-onset chronic disorders presented in the more straightforward examples of eco-genetics illustrated in diabetes mellitus provide the fundamental models for their elucidation.

In another vein, the authors point out legal problems but in general do not discuss them at length. As there are already books that deal extensively with those problems, a comprehensive treatment of that topic would be unnecessary. Furthermore, because the thread of legal problems weaves throughout the book, an in-depth discussion at every turn would be redundant as well as inconsistent with our purpose.

In presenting the thoughts of some of those close to the issues, we have attempted to give the readers—public health students and administrators, medical students and physicians, and all types of health researchers and practitioners—an appreciation of some of the significant genetic issues with public health implications.

B.H.C.
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EDITORS' FOREWORD

That genetics is a health issue is apparent from the burgeoning list of disorders with a simple genetic basis as well as from the growing recognition of the interaction of hereditary with environmental factors in diseases of complex etiology. The proportion of admissions to hospital pediatric wards for genetically mediated conditions attests to the magnitude of the problem not only in special subsegments but also in the general population. Moreover, with the advent of intervention techniques, the issues have taken on ethical, moral, social, and even legal significance. No longer are they limited solely to the affected individuals or their families, but rather they have become pertinent to issues for the total community.

Recognizing the pivotal role of genetics with regard to health and disease, Joshua Lederberg succinctly pointed out that

> at least 25 percent of our health burden is of genetic origin. This figure is a very conservative estimate in view of the genetic component of such griefs as schizophrenia, diabetes, atherosclerosis, mental retardation, early senility, and many congenital malformations. In fact, the genetic factor in disease is bound to increase to an even larger proportion, for as we deal with infectious disease and other environmental insults, the genetic legacy of the species will compete only with traumatic accidents as the major factor in health. . . . Given the problem of the number of new, suspicious compounds now pervading the environment, we face a formidable task in putting our genetic house in order (1).

To accomplish that task requires an ongoing appreciation of the dimensions of the role involved. The advances of the past quarter century have been phenomenal in scope and impact both in basic molecular genetics and in application to specific clinical situations.

Fundamental to the fulfillment of the charge is the recognition that DNA is the hereditary vehicle, the gene, and that a gene manifests itself through a series of definable biological

processes. Now not only is the phenotypic expression of certain genes within the realm of chemical interpretation but also DNA repair and recombination (Huang).

In addition to the alterations in the genetic material at both the molecular and gross chromosomal level mediated by radiation and other clastogenic and mutagenic agents (Merz), much of genetic expression depends on the environment. The realization that differential response to extrinsic agents is often genetically determined has generated the new "eco-genetics." This area of genetics is of particular significance in public health because of the increasing use of new drugs and exposure to a wide variety of environmental pollutants and other extrinsic agents ingested, inhaled, injected, and touched (Omenn/Motulsky).

Since Sir Archibald Garrod's concept of "inborn errors of metabolism" ushered in human biochemical genetics, the list of genetic disorders traceable to a specific molecular cause has grown steadily—in the past decade, logarithmically. Concurrently, from the late 1950s on, advances in cytogenetics have paralleled these developments, and with further technological developments, precise diagnosis of certain conditions has become feasible by biochemical or cytogenetic assays on cultured tissues. The use of tissue culture systems is certainly a major breakthrough in human genetics (Puck). Cultured cells apparently reflect the enzymatic and chromosomal complements of an individual although not the organismic differentiation. From the identification of sex (by the presence of the Barr body of the female, as required of Olympic athletes) to the identification of Down's syndrome (by the appearance of an extra chromosome or portion thereof), progress in somatic cell genetics has been both basic and practical. These advances also have not been without their dilemmas, e.g., as in the sociocultural, legal, and other complications surrounding the identification of XYY-males.

Diagnosis of organic disorders in humans has been utilized for prevention as well as for directing therapy. Prenatal diagnosis for genetic disease by amniocentesis has helped to spare anxiety and anguish in both the parents and the unborn. The precise techniques involved are now generally practicable

(Migeon), and the consequences have received favorable evaluation through the National Amniocentesis Registry (Lowe).

Diagnostic screening for birth defects involves not only scientific (genetic, biochemical, and medical) expertise but also individual and societal decisions. Often complex, the problems require resolution through careful planning and judgment as well as technological skill and precision (Thomas). The medical personnel offering the screening must consider whether the test itself is infallible, whether a positive result is acceptable emotionally and socially, what kind of defect is unacceptable, and finally, when an abortion is recommendable, if acceptable (Kazazian). When total population screening is undertaken, especially if by law, as for phenylketonuria, noninvasive diagnostic procedures and effective means of therapeutic intervention are a particular concern, although even when attained, they do not eliminate all the pitfalls (Holtzman).

Despite the absence of simple specific therapies, neonatal screening is valuable for providing otherwise unavailable data for health services planning as well as for incidence statistics and genetic interpretation (Robinson). Ongoing surveillance on a community scale has additional advantages besides those afforded by diagnostic screening of individuals or single-episode screening of population samples (Oakley *et al.*). In all, a long-standing issue in screening programs for both clinic and community-dwelling populations has been informed consent, although this need not be considered a formidable obstacle (Borgaonkar).

The studies of genetic disorders that aggregate in special population segments, definable ethnic subgroups, or mating isolates are carried out for many different reasons: to gain a better insight into the nature of a disease in order to learn how to prevent or ameliorate it as well as to apply existing therapeutic and/or preventive techniques. Tay-Sachs disease (Kaback) and sickle-cell anemia (Murray), respectively, have well-documented simple genetic bases, although they provide a contrast in management and application of procedures that entail both resolved and unresolved issues. With a disease like diabetes, however, even in a definable gene pool, the situation is more complicated, both in genetic basis and the interaction of environmental fac-

tors (Bannerman). The availability of highly inbred groups, such as the Old Order Amish, has been informative in studies of multifactorial conditions (e.g., cervical cancer) as well as for more conventional applications in chromosomal aberrancy and mendelian-type genetic variation (McKusick). These investigations have not only provided medical genetic knowledge but have yielded fringe benefits of available diagnosis and ameliorative measures to the populations studied.

While the primary concern of the geneticist is directed toward better understanding of etiological factors and their mechanism of operation, the primary concern of the individual or the population at risk is centered on prognosis and possible intervention. As a consequence, genetic counseling has become an important branch in preventive medicine (Childs). Intervention procedures vary with the condition: for certain affected individuals there is substitution therapy; for some others, dietary restriction; for couples, the decisions could be whether to refrain from reproducing at all, whether to risk conception relying on prenatal tests for a subsequent decision regarding abortion, or whether to take a calculated risk of having a child whose health will depend on further corrective medicine (Childs; Murphy *et al.*).

The rapid advances of science and medicine have now provided us with many ways to improve health and survivorship on both an individual and population basis. Moreover, the advances in immunology have made it possible to virtually eliminate Rh erythroblastosis fetalis by prevention of maternal Rh immunization (Bowman) and are helping to make organ transplantations not only promising but a reality (Bias).

Although the issues about artificial insemination and embryo culture *in vitro* (the so-called "test tube babies") have been more newsmaking than practical, the recent development of recombinant DNA has realized one aspect of genetic engineering (Sinsheimer). Consequently, certain critical issues arise: on the one hand, there is the difficulty of protecting against the misuse of this technology in perturbing human genetic endowment; on the other hand, there is the urgent need for safeguarding against the escape of biological hazards from the laboratory.