Annotation:

Human Ecology, an Expanding Role for the Human Geneticist

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As noted recently by the editor of this *Journal* [1], human genetics has grown considerably in the last 20 years, and "few areas of human biology have remained untouched by this evolving field." However, I would like to ask two interrelated questions: (1) Has the development of the "discipline" of human genetics kept pace with the amount of interest and research in the field? and (2) Are human geneticists seriously neglecting an area of involvement in which all scientists have a responsibility and in which human geneticists should have some expertise, that is, the interaction of man and his environment? I will present some thoughts on the second question, and then return to the first.

Many people, including many scientists, believe that we are facing an environmental crisis of such proportions that our very existence is threatened. The first task of those who are trying to change our current course is to make a case to the general population of the fact of an environmental crisis; this will make it possible to accomplish the second task, which is to establish methods for controlling population growth, the basic cause of environmental deterioration. The arguments advanced so far in support of the fact of an environmental crisis have followed three general lines: (1) aesthetic, (2) depletion of resources (food, water, etc.), and (3) the health hazard of pollution and uncontrolled environmental change. Of these, the third may be the most effective, and here the door is open to the human geneticist.

In the last few years we have become aware of the tremendous genetic variability in natural populations such as man. With 30% or more of our loci polymorphic, it is not surprising that there is unique biochemical individuality. Our emerging subdiscipline of pharmacogenetics has taught us that all of this variability provides a fertile opportunity for biologically active drugs to find a genetically susceptible target. And the frequency of such targets in a population may be high; for example, G6PD deficiency has a gene frequency of .13 in the American Negro.

Now we may be seeing the first tip of the iceberg of "ecogenetics." Recent studies have clearly demonstrated an association between a gene producing a deficiency of serum α_1 antitrypsin and emphysema. Evaluation of two series of patients with emphysema revealed that about 5% and 25% of these patients are homozygous and heterozygous, respectively, for α_1-antitrypsin deficiency [2, 3]. A great increase in mor-

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tality and morbidity from emphysema has occurred in the United States during the last 20 years [4, 5]. Further, city dwellers have a 2.5-fold higher incidence than rural dwellers [5, 6]. Preliminary data indicate that cigarette smoking promotes development of emphysema in heterozygotes for α_1-antitrypsin deficiency, probably accounting for some of the increase in the frequency of emphysema [7]. Particulate matter in the smoke is thought to be the most likely pathogenic agent. Since the air of urban environments is polluted with particulate matter, it is a reasonable hypothesis, as yet untested, that the increase in emphysema in urban areas comes partly from the effects of air pollution upon the carriers of this gene. While many data remain to be gathered, indications are that air pollution may be contributing to morbidity and mortality in carriers of this gene and further study is urgently needed.

From our knowledge of genetic variability and pharmacogenetics, we can be sure that other pollutants are even now finding genetically susceptible targets (any disease showing an unexplained increase is suspect); as we contaminate our environment with higher levels and additional agents, the whole process will accelerate, all of us becoming, at some point, susceptible to one or more pollutants. A very important role of the human geneticist, in my opinion, is to use his training to uncover additional genetic-environment interactions, such as the relationship between emphysema and α_1 antitrypsin, and once uncovered, to explore fully the various ramifications. These efforts will take full advantage of the demographic and statistical capabilities of human population geneticists and of the biochemical and clinical capabilities of many other human geneticists. The development of emphysema in carriers of the α_1-antitrypsin deficiency and other "ecogenetic" topics should be fully examined in workshops and symposia of the annual meeting of the American Society of Human Genetics, and then further publicized as indicated.

At the beginning, I raised the question of the satisfactory progress of human genetics as a "discipline." By development of the discipline of human genetics, I mean the identification of what human geneticists are, what they do, and what they hope to accomplish.

The lack of clarity of our role and what we can contribute to medicine and society in general leads to a number of problems. For example, not very many medical schools have followed the pioneering few and set up sections or departments of human or medical genetics. While admitting the medical relevance of medical genetics by appointing genetically oriented physicians or Ph.D.'s to clinical and preclinical departments, they have failed in most cases to recognize the field as a discipline and unite the medical geneticists into a unit. Most of us would probably agree that, while the contribution of an isolated geneticist to a department can be great and his research can be markedly stimulated by his associates, the development of a cohesive discipline in terms of role and goals is not promoted very much by this arrangement. For example, I wonder how much progress pathology would have made as a discipline if most pathologists had been isolated in the various departments where special kinds of pathological material originated. I suspect that the quality of the practice of pathology would be much more variable, and the teaching of pathology to medical students much more fragmented, both of which are current characteristics of human genetics in most American medical schools.

The major problem to date is the lack of a central core of material unique to our discipline. Most basic science departments have such a core, but in all areas of basic science, human genetics overlaps with departments such as biochemistry, microbiology, pharmacology, etc. Most clinical departments have an organ system, an age group, or an area of technology more or less as an exclusive domain; human genetics does not. Small wonder that medical schools have realized that by adding a genetically oriented basic scientist or physician to some of their departments, they are "modern" without the difficulties inherent in development of a new unit or department.

I suggest that the incorporation of a proper amount of attention to and study of the environmental aspects of the gene-environment interaction will greatly strengthen our discipline, while properly serving one of the pressing needs of mankind. It does not really matter whether units which evolve for such studies go by the name of human genetics, medical genetics, human ecological genetics, or human ecology, as long as such units, involved in the problems of man's inheritance and the interaction of his inheritance with environment, are actually formed in our medical schools.

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