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The following summary is a crude outline of areas of genetic research that have some relevance to medicine.

HUMAN GENETICS

1. Hereditary factors in disease
   Statistical methodology. Pedigree analysis. Population analysis.
   Twin studies.
   Clinical genetics
      Single factor syndromes (e.g., hemophilia; retinoblastoma; xeroderma pigm.)
      Complex determination (e.g., epilepsy; diabetes)
   Biochemical or developmental analysis of genetic defects
      (e.g., alcaptonuria or phenylpyruvic oligophrenia; sickle cell anemia)
   Mutation rates

2. Individuality
   Blood groups
   Transplantation specificity
   Sensory modalities (e.g. phenylthiourea taste)
   Metabolic individuality (*1)
   antibody response (*2)
   anthropometry; skin and hair; features; 'race'

3. Cytogenetics

4. Genetic hygiene and population genetics
   Eugenics (*3)
   (Counselling) (*4)
   Environmental medicine (*5)
   Detection of heterozygous carriers

EXPERIMENTAL MAMMALIAN GENETICS (SELECTED TOPICS)

1. Mutation; radiation effects
2. Cytogenetics
3. Developmental analysis of gene effects
4. Biochemical do.
5. Experimental evolution
6. Transplantation— histocompatibility and acquired tolerance (*6)
7. Susceptibility to infectious disease (notably TB)
8. Cancer Research— host variations and genetics of tissue and tumor cells (*7)

MICROORGANISMS

Mutation. Radiation effects. Chemical mutaggenesis. Mechanisms of killing cells.
Evolutionary patterns in natural populations (esp. of pathogens)
Genetic factors in pathogenicity.
Genetic recombination analysis.
Nature and origin of viruses.

Notes:
Genetic research characteristically cuts across many other disciplines. This list already would imply zones of dependence on or collaboration with virtually any department in the medical school.

1. This is readily recognized in characteristic metabolic diseases, but may be equally important in personal differences, as Roger Williams has emphasized. Individuality may thus be reflected in characteristic patterns of excretion of various metabolites and has a large, certainly not an exclusive, genetic basis. It is also reflected in differences in therapeutic response, e.g., to isoniazide, and may be a too often neglected factor in idiosyncratic responses to other drugs. Explicit genetic analysis of the latter situations remains to be carried out.

2. For example, in the polio vaccination program, it has been noted that some children make a poor antibody response. It is not known whether this has a genetic basis, nor whether this is general unresponsiveness or a specific unreactiveness to the polio virus. Fink (at Colo.) and others have given experimental evidence for genetic variability in antibody response in mice. This field should be one of the more important areas of development for practical medical understanding. The general question of individualized reactions to pathogens is not far distant.

3. In my own opinion, the overzealous pushing of active eugenic controls (e.g., the sterilization of the so called "unfit") is largely responsible for the hindered development of medical genetics. Such negative controls are essentially futile for the reduction in incidence of rare recessive mutations in any event, and involve matters of public policy that far overreach the authority of the medical profession per se. Many modern students (cf. Neel and Shull) share the view that much more scientific knowledge of human genetics is needed before one can advocate any far reaching social controls of human reproduction. The present role of the human geneticist is to inform his colleagues and through them the public, rather than advocate drastic interference by society, especially when the calculated social effects are so small.

Medicine may someday be faced with formulating an attitude on another issue where genetic control may be more effective, namely the sex ratio. This has not been the subject of much work lately, but it is at least theoretically possible (in my own view almost probable) that techniques will ultimately be developed to enable the sex of offspring to be voluntarily controlled. Most of us would hope that day to be deferred indefinitely, but this illustrates the tremendous impact that human genetics is bound to have, ultimately, on medicine and on society. (Since this draft was first prepared, a credible report has been published on the separation of X and Y spermatozoa of rabbits by means of electrophoresis: Gordon, M. J., Control of Sex Ratio in Rabbits by Electrophoresis of Spermatozoa, Proc. Natl. Acad. Sci. U. S., 43:913-918, 1957).

4. Counselling. Many schools have set up "Heredity Clinics" as part of their program in medical genetics. These are valuable centers for the collection of data, and there can be no question of public interest in

these problems. I would not advocate such a service in which the genetic specialist dealt directly with the patient. The counsellor inevitably must influence the patients' reproductive decisions, matters so involved with his total personality that such consultation should ordinarily be made with his own physician. The department should be in a position to consult with physicians, and inevitably will.

5. "Environmental medicine" is taken here to encompass the genetic hazards from industrial and professional operations, as well as from atomic bombs. Almost all the emphasis so far has been spent on radiations (from bombs, fluoroscopy or mineral extraction), and except that some hazard is involved, little enough is known. Without minimizing the tremendous importance of radiation hazards from, for example, fallout, it seems to me that there is a much broader problem of which radiation is only one part. Until recently, radiations were considered the only artificial agency by which mutations could be induced. It is now realized that a wide variety of chemical reagents can induce mutations. Radiations undoubtedly have freer access to the germ cells, but the mutagenicity of such compounds as hydrogen peroxide, formaldehyde, nitrogen mustard, azaserine, and caffeine raises the question whether genetic effects should be considered as one aspect of chronic toxicity of compounds which are part of the everyday environment of modern man.

6. Experimental studies have now firmly established the immunogenetic basis of transplantation compatibility in mammals. It is disheartening to see how often these factors are overlooked or underemphasized in surgical trials. The finding that prenatal exposure of mice to heterologous tissue antigens provokes a tolerance to the postnatal transplantation of other heterologous tissues is a new and important lead to the overcoming of this difficulty. A technique for overcoming histocompatibility barriers would open up a vast new territory of surgical replacement of defective tissues and organs. It might also answer one of the mysterious questions of immunology: why does the organism fail to produce antibodies to its own antigens.

7. Most of the emphasis in genetic cancer research has been in the properties of specific lines of mice, which are indeed indispensable research tools. More recently, technical advances are leading to closer examination of the genetics of the tissue cell itself, as in the ascites tumor studies of Hauschka and Klein, and the tissue culture of single clones of human cells by Puck.