

GENETIC COUNSELING II

In the cases we have considered so far, the final outcome of counseling was the specification of a genetic risk. Various means to reduce such risks have been suggested or tried, ranging from directed mutation to selective abortion. With increasing genetic knowledge, more practical and satisfactory solutions will be found.

All known mutagenic agents are nonspecific, and it is not possible to produce at will a given genetic change. Therefore we cannot influence the composition of a given gamete, but in some cases it is possible to alter the odds that a given type of gamete will form a zygote or that the zygote will survive to parturition.

Some genetic conditions can be detected before birth. In dominant achondroplasia, the status of a patient's child can be determined by x-ray. In recessive amyotonia congenita, there may be almost complete absence of fetal movement, and the younger sibs of a patient may be classified as normal or abnormal in utero.

In countries like Denmark and Japan, induced abortion on grounds of a considerable risk of malformation or genetic disease is accepted and legal. In this country, with the exception of maternal rubella in some states, there is little precedent for such a course, except on grounds of maternal ill-health.

An interesting situation occurs when a male with a serious sex-linked disease is mildly enough affected to have children. This happens occasionally in Duchenne type muscular dystrophy, retinitis pigmentosa, peroneal atrophy, hemophilia, PTC disease, infantile agammaglobulinemia, anhidrotic ectodermal dysplasia and about 20 other sex-linked diseases. (Note: with the exception of hemophilia and PTC disease, not all cases of these diseases are sex-linked). Of the children from such a patient, all the boys are entirely normal, but

all the girls are carriers, and half their sons are expected to be affected. On the average, each daughter produced by a male with a serious sex-linked disease results in one affected boy, the expected number being $1/2$, $1/4$, $1/8$, etc., in the first, second, third, generations.

If an acceptable way could be found to assure that males with such diseases had only sons, they and their descendants would be normal. One way is through recognition of the sex of the fetus. Human cells from many tissues can be classified as to sex by the fifth month of gestation, from the fact that female cells show a characteristic "tag" at the margin of the nucleus, believed to be the paired heterochromatin of the X chromosomes. Many human fetuses have been classified from the epithelial cells in a small sample of amniotic fluid, and the predicted sex verified at birth. If induced abortion were acceptable and legal, the children of males with serious sex-linked diseases could all be healthy boys.

A more appealing means of achieving the same objective is suggested by the fact that in rabbits, X and Y sperm can be separated by electrophoresis. If this is generally feasible, bull calves and male chicks may become rarities, and the sex of children controlled without zygotic wastage.

Artificial insemination or "semi-adoption" has been used in this country in male sterility and in some cases in which the male carried a dominant or sex-linked gene for a serious disease. Recent court decisions throw doubt on the legitimacy of children from artificial insemination.

These methods to avoid transmission of a harmful gene without reducing fertility are unacceptable to many people. However, they indicate the beginning of a body of knowledge that will suggest other means to reduce genetic risks.

From this discussion of problems and possibilities in genetic counseling, the factors to be considered can be presented as a series of questions:

- (1) What is the statistical risk of the patient or his child being affected?
- (2) How serious is the defect, and what therapy is possible?
- (3) How much is another child wanted?
- (4) What measures are available to obtain a normal child or avoid a defective one?
- (5) Does the patient's attitude present a psychiatric problem not resolved by the measures available?
- (6) What will be the effects on future generations?

THE FAMILY HISTORY

Medical examinations usually include an inquiry into the health of close relatives. Properly taken, the family history can be of value in the diagnosis and treatment of hereditary disease. In addition, careful histories on consecutive patients provide information about medical risks in families that cannot be gotten from case reports in the literature, where there is usually a bias in favor of familial cases. In the absence of systematic studies, the risk figures available for genetic counseling may be highly inaccurate, and there is still very little reliable information about the risks of many diseases in relatives of patients. This lack is most serious for diseases of heterogeneous etiology, like high myopia, otosclerosis, or deaf-mutism.

The first step in taking a family history is to ask about the occurrence of the family of diseases or symptoms relevant to the patient's complaint. This is especially important if the disease is rare, or often hereditary. There is little point in asking about diseases not obviously related to the patient's, whether they are hereditary or not. A routine question about common familial diseases like allergy, diabetes, cancer, heart disease, etc.,

is irrelevant unless this is a possible diagnosis for the patient. The question should be "Does anyone else in the family have anything like this?"

The second requirement of a family history is a record of the patient's parents and siblings, including the ages and sexes of normal as well as abnormal sibs, and any relevant diseases. Unless the family history is positive, it is usually unnecessary to record other relatives. If the history is positive, the mode of relationship should be clearly indicated, and the same information taken for each sibship with an affected member as for the patient's sibship. The age and sex of siblings is required because absence of the disease in a sibling below the age of onset is of no significance, and absence of a sex-linked disease in sisters of a patient is also expected. Also, a positive history may assume exaggerated significance if the normal family members are omitted. This information should be recorded routinely at the time of interview, and included in a published case report. It is unfortunately true that, in most reports of family histories in the medical literature, the omission of essential information makes genetic analysis of the data not only worthless but misleading.

The third and last item in a good family history, is a statement about the presence or absence of parental consanguinity, especially if a possible diagnosis is a rare recessive disease. If the parents are related, the mode of relationship should be outlined in detail. Parental consanguinity may be of suggestive value in establishing the diagnosis, in determining genetic risks, and in defining pathological and genetic entities in a disease that is heterogeneous. In modern populations parental consanguinity is rare, even in many recessive diseases, but a routine question on consanguinity may be justified by the exceptional cases in which a positive answer is helpful in arriving at the correct diagnosis.