Genetic disease

Genetic disorders place considerable health and economic burdens not only on affected people and their families but also on the community. As more environmental diseases are successfully controlled those that are wholly or partly genetically determined are becoming more important.

Despite a general fall in perinatal mortality rate the incidence of lethal malformations in newborn infants remains constant. Between 2-5% of all liveborn infants have genetic disorders or congenital malformations. These disorders have been estimated to account for one third of admissions to paediatric wards, and they contribute appreciably to paediatric mortality.

Many common diseases in adult life also have a considerable genetic predisposition, including coronary heart disease, diabetes, and cancer.

Though diseases of wholly genetic origin are often individually rare, they are numerous and therefore important. Genetic disorders are incurable and often severe. A few are amenable to treatment, but most are not, so that emphasis is often placed on prevention of either recurrence within an affected family or complications in a person who is already affected.

Increasing awareness, both within the medical profession and in the general population, of the genetic contribution to disease has led to an increasing demand for clinical genetic services. Some aspects of genetics are well established and do not require referral to a specialised genetics clinic—for example, the provision of amniocentesis to exclude Down’s syndrome in pregnancies at risk because of advanced maternal age. Other aspects are less well understood by non-geneticists—for example, the role of molecular biology in clinical practice, which is an area of rapidly advancing technology requiring the specialised facilities of a genetics centre.

Aims of genetic counselling

Genetic counselling covers more than estimating risks and extends beyond the person who presents to the whole family in changing situations over many years. The role of clinical geneticists is to establish an accurate diagnosis on which to base counselling and then to provide information about prognosis and follow up, the risk of developing or transmitting the disorder, and the ways in which this may be prevented or ameliorated. Throughout, the family require support in adjusting to the implications of genetic disease and the consequent decisions that have to be made.
Diagnosis

An accurate diagnosis is the first essential requirement for genetic counselling. This may not always be straightforward as genetic disease is often variable in its presentation and different members of a family with the same disorder may present to different specialties with diverse manifestations of the condition. Conversely, disorders which are clinically similar may follow different inheritance patterns in different families.

The person requesting genetic counselling may not be the one affected, and the diagnosis may need to be confirmed by examining the affected relative or reviewing their hospital records.

Without a defined diagnosis appropriate genetic advice may be given if the pattern of affected subjects within a family points to a particular mode of inheritance.

Drawing a pedigree

Constructing a family tree is the best way to record genetic information. The main symbols used are shown in the upper box. It is important to record full names (including maiden names) and dates of birth on the pedigree. Specific questions should be asked about abortions, stillbirths, infant deaths, multiple marriages, and consanguinity as this information may not always be volunteered. It is also useful to record details of the medical care of relevant family members.

Estimation of risk

Estimation of genetic risk depends on the pattern of inheritance of a disorder and applies both to the risk of developing and of transmitting a particular disorder. In some disorders specific tests to identify carriers are available.

Mendelian disorders due to mutant genes generally carry high risks of recurrence whereas chromosomal disorders generally have low risks. For many common conditions there is no clearly defined pattern of inheritance, and empirical figures for the risk of recurrence are given, based on information derived from family or population studies.

Transmitting information

Interpretation of risk varies depending on the severity of the disorder, its prognosis, and the availability of treatment or palliation. All of these aspects need to be discussed with the family.
The risk of transmitting a disorder, the severity of the disorder, and the availability of prenatal diagnosis all influence the decisions of couples about pregnancy, as do their moral and religious convictions. Contraception or sterilisation may be considered, and alternative options may include insemination by a donor, ovum donation, or adoption.

It is important that the counselling process is not directive and that couples can reach their own decisions armed with the necessary information.

**Psychological aspects**

The diagnosis of genetic disease causes considerable emotional stress, and to be effective the counselling process must provide psychological support in addition to information. Recognition of the impact of genetic disease and the various stages of the process of coping allows counselling to be pursued at an appropriate pace for each couple. Some knowledge of the couples’ educational, social, and religious backgrounds is important as these influence their reactions and decision making.

Counselling must be unhurried and undertaken in a quiet environment. The counsellor needs to spend sufficient time with the couple to establish mutual rapport, so that personal feelings can be freely discussed and questions asked and dealt with sensitively; several counselling sessions, either in the clinic or at the patient’s home may be necessary to achieve this.

**Departments of clinical genetics**

Departments of clinical genetics tend to be based regionally in main teaching centres and often have academic as well as NHS staff. The clinical team includes various health care professionals.

**Associated laboratory services**

Specialist laboratory services form an integral part in providing clinical genetic services. The laboratories are usually based in regional or supraregional centres and provide services in biochemical genetics, cytogenetics, and DNA analysis.

**Clinical use of genetic registers**

Clinical use of genetic registers is aimed primarily at ascertaining as completely as possible all people at risk of developing or transmitting a particular disorder so that appropriate counselling can be offered. A register approach permits long term follow up of family members, which is important for children at risk, who will not need investigation or counselling for many years. Registers are particularly useful for disorders that are amenable to DNA analysis in which advances are of clinical importance and families need regular counselling with new information. Disorders suited to a register approach include dominant disorders with late onset, such as Huntington’s chorea and myotonic dystrophy, and X linked disorders, such as Duchenne and Becker’s muscular dystrophy. Registers can also provide data on the incidence and natural course of diseases and the effect of counselling and preventive programmes.

Genetic registers are held on computer and are subject to the Data Protection Act. No one is included in the register without having given informed consent.

Dr Helen M Kingston, MD, is consultant clinical geneticist at St Mary’s Hospital, Manchester.