symptom combinations for each patient and for each combination the percentage of hypothyroid patients among all patients previously shown to have that combination is calculated. If this exceeds certain predetermined limits the patient is recalled for further investigation.

By contrast, the Scottish system produces a selective diagnosis of thyroid status based on the clinical diagnostic index score and a laboratory test of thyroid function. The results are printed out for normal and abnormal patients, but an option exists for the doctor to defer recall for patients in the abnormal stream after inspection of a monthly printout which provides supplementary biochemical results and clinical information from the general practitioner. At each examination the system automatically stores the result of the discriminant functions recorded. The correlation of this information with the final diagnostic label will clearly be of interest and value to doctors in both general practice and hospital.

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Genetic Counselling

Parents make sensible use of information on the chances of a particular genetic (or part-genetic) disorder in the family recurring in future children.[1] This and an increasing demand for advice are therefore to be welcomed, since by genetic counselling, supplemented in some instances by prenatal diagnosis, we may hope gradually to reduce the number of children born with genetically determined disorders.

To estimate the risk of a recurrence the disorder must be accurately diagnosed, its mode of inheritance must be known, and a history of at least the near relatives of the patient has to be taken. Some cases may be dealt with by the family doctor and others referred to the appropriate specialist or to a specialist genetic clinic. These have now been established in most university medical centres, and they are listed in a pamphlet[2] available from the Department of Health and Social Security. When the condition is a straightforward dominant, recessive, or x-linked trait due to a mutant gene of large effect the chances may usually be given precisely. For example, the risk for each offspring of a man with a dominant trait such as classical achondroplasia, Huntington's chorea, or Marfan's syndrome is one in two. The risk to each further child of parents who have had a child with a recessive condition such as cystic fibrosis, sickle-cell anaemia, or Werdnig-Hoffmann's disease is one in four.

Counselling is less precise in conditions due to chromosome anomalies. Most are the result of an abnormality of chromosome behaviour in germ cell formation: the parents are chromosomally normal and the recurrence risk is therefore small. But when one parent has a balanced chromosome anomaly there is a relatively high risk to children. The risk of Down's syndrome, for example, is perhaps as high as one in six when a mother carries a translocation of a chromosome 21 on to one of the 13-15 group. Here the estimate of risk is made partly from knowledge of the underlying anomaly and of the genotypes of the parents and partly from empirical experience.

The conditions most often met with in genetic counselling are those such as congenital malformations of the heart or neural tube for which no single mutant gene of large effect and no chromosome anomaly are responsible. Here estimates of risk are based essentially on the empirical findings in large-scale family studies in populations similar to that to which the patient belongs. Such studies are already available in many instances for estimating risks to the later brothers and sisters of patients and in some instances also for estimating risks to their offspring. Even in the case of brothers and sisters, however, there is as yet usually not enough information to tell how the recurrence risk for, say, cleft lip and palate should be modified when parents have already had two affected children or when the mother has two brothers who also have the malformation. In these cases recourse may be had, with due caution, to theoretical considerations.

Study of the family patterns found empirically by large-scale surveys has suggested that the aetiology of many common malformations (and probably also of many other common conditions) is multifactorial with an important genetic component depending on variation at several—perhaps many—gene loci.[3] Elegant mathematical models have been applied to this hypothesis,[4] which may be used to predict risks in particular family situations. The computations are somewhat elaborate, but fortunately Dr. Charles Smith's computer programmes, which he describes on page 495, will give easily and quickly the estimate of risk in families in which there is more than one patient. Probably no hypothesis can ever perfectly fit biological reality, and so the computer estimates will need checking against the empirical findings from family surveys as they become available. These surveys should be continued among a variety of populations, and meanwhile the computer estimates will serve better than intelligent guesses.

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