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The Computer and Thyroid Disease

Practical help can now be given by computers in the screening, diagnosis, and follow-up of some forms of thyroid disease—either in terms of the patient's thyroid status or of the pathological abnormality in the gland. The computer enables diagnostic information to be assessed in terms of probabilities based on similar data already culled from large numbers of patients known to have the disease in question. Stored information can be instantly retrieved.

Computer techniques in medicine must rely on the accuracy with which clinical information can be measured and arranged in order of its diagnostic value. This may be done by calculating the discriminatory value of symptoms and signs after recording their incidence in the normal population and in a similar group with proved disease. A positive or negative numerical weighting can be applied to each clinical feature to produce the maximum separation between normal and abnormal patients. This approach, known as discriminant function analysis,[1 2] has been used to produce diagnostic indices for hyperthyroidism[3-5] and hypothyroidism[6] by workers in Glasgow, Aberdeen, and Newcastle, and has been adopted by many other thyroid clinics and general practitioners.

Careful collation of clinical and biochemical information from one patient may not lead to a clear diagnosis. Nevertheless, the problem is simplified when the significance of particular symptom and sign combinations is known in a population for whom objective evidence of the disease process has been obtained—for example, by a histopathological diagnosis. A computerized model for the differential diagnosis of the lesions responsible for non-toxic goitre in Glasgow[7] has shown that the conditional probability theory[8-13] can be successfully applied in the derivation of a calculated diagnosis. From a population of 155 patients with either Hashimoto's disease, simple goitre, or thyroid cancer the observed incidence of 30 items or characters from the clinical and laboratory assessment was recorded in the form of a probability matrix. The matrix was introduced into the memory of a digital computer and used to produce an accurate differential diagnosis in a new group of patients with non-toxic goitre. These authors emphasized the need for careful planning and selection of the patients from which the probability matrices are constructed. Serious diagnostic errors may result if the characteristics of the population which provides the basic reference data differ greatly from the population which is studied.

The concept of conditional probablity has also been applied to the diagnosis of hypothyroidism and hyperthyroidism, using several clinical and laboratory criteria of thyroid function.[14] The computed diagnosis agreed with the retrospective clinical diagnosis in 96% of 268 test cases, despite incomplete patient profiles in some instances. Further study of the diagnostic process in difficult cases led to a modified programme[15 16] which successfully identified cases of "masked hyperthyroidism." It also takes account of drugs which may influence the laboratory tests and automatically incorporates the probability values for the symptoms of new patients when the diagnosis is eventually proved. Thyroid investigation units can now construct distribution curves for most tests, based on many observations from normal and abnormal members of the local population. A programme in Arkansas[17] uses knowledge about the continuous distribution of thyroid function tests in the locality. Shifts in the mean values and changes in the precision of individual tests which may result from changes in laboratory methods, environmental iodine levels, or the dietary habits of the community can be monitored constantly and the diagnostic criteria adjusted.

Measurement of symptoms and signs in a diagnostic index and the ability to carry out analyses on large numbers of blood samples with automated laboratory equipment have allowed the development of computer-based systems of aftercare for patients with thyroid disease in Scotland[18-21] and Birmingham.[22-23] The Birmingham system, which is confined to the surveillance of radioiodine-treated patients, obtains clinical information from patients by a postal questionnaire requiring "Yes/No" answers. The Scottish follow-up is life-long for patients who have received any form of therapy for thyrotoxicosis and all patients on thyroxine replacement therapy. The computer arranges a consultation between the patient and her general practitioner, who sends the computer an unprocessed hypothyroid diagnostic index[6] consisting of eight symptoms and six signs, each with positive or negative weightings and a blood sample. In Birmingham the nine-question clinical document allows 511 possible symptom combinations to be derived from the patient's response. The computer determines the number of

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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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