Medical Genetics in Clinical Practice

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SUMMARY

Two hundred and fifty-four patients were seen in the Genetic Clinics during 1973, the first full year of activity of the Department of Human Genetics, University of Cape Town.

The current role of medical genetics in clinical practice is exemplified by an analysis and discussion of the problems presented by these individuals.

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Genetics is now an important facet of medical practice, and clinical genetic departments have been established in the majority of teaching hospitals in advanced countries.[1] Considerable development and expansion of units of this type is expected in South Africa in the near future.

The scope of medical genetics includes genetic counselling, prenatal diagnosis, and the investigation of inherited disorders in individuals or populations. Laboratory facilities for cytogenetic and biochemical investigation are an essential feature of such a genetic department.

The purpose of this article is to review the clinical activities during 1973 of the Department of Human Genetics, University of Cape Town, to present an analysis of the medical problems which have been encountered, and to discuss the application of genetics to clinical practice.

GENETIC CLINICS

Organisation

Regular genetic clinics are undertaken twice weekly at Groote Schuur Hospital and on a weekly basis at Princess Alice Orthopaedic Hospital, Cape Town. On occasion, clinics have also been conducted at other centres in South West Africa and in the Cape Province. Close liaison is maintained with the genetic clinic at the Red Cross War Memorial Children's Hospital, Cape Town, which has been functioning for several years, and support is provided by the departmental genetic laboratories. An analysis of the work of the Red Cross Hospital clinic will be presented in a companion paper.[3]

Patients are referred by colleagues in hospital, specialists or general practitioners. A key member of the department, the genetic nurse, arranges the appointments and attends the clinical sessions. The patients are registered as hospital outpatients in the usual way, and direct access to hospital services is therefore available.

Function

The practice of clinical genetics is time-consuming, since a detailed clinical and family history must be elicited before a thorough clinical examination is undertaken. The average duration of the consultation and subsequent discussion is an hour for each individual or family group. For this reason, the turnover of the genetic clinics is comparatively low.

Many patients seen in the clinics are individuals who are either affected by a heritable condition or who have a close relative with a disorder of this type. Another group consists of normal parents who have produced a child with a genetic disorder. In each instance, they pose the question 'If we have more children, will they be affected?' Before this question can be answered, a precise diagnosis must be established. Since there are over 2 000 genetic diseases, many of which are excessively rare, this is not always an easy matter. Referral to expert colleagues and sophisticated investigations may be required.

The risks of transmission or recurrence of the condition are discussed with the parents, and the possibilities of carrier detection and prenatal diagnosis are considered. A fundamental tenet of genetic counselling is that the patients or parents must make their own decisions, the genetic physician's role being to provide factual information and guidance. However, it is also his duty to ensure that the parents have a clear understanding of the situation, the magnitude of the risks involved and suitable lines of action that can be taken.

The function of genetic clinics is not confined to counselling. Patients often wish to discuss the medical prognosis and the value of various forms of treatment.[4] Since the physician conducting genetic clinics inevitably acquires specialised knowledge concerning these unusual disorders, he may well be the best person to give a prognosis or to recommend a particular line of therapy to the patient's own practitioner. Indeed, many patients are referred to the clinic for diagnosis or genetic investigation, rather than actual counselling. For these reasons, the doctor-patient relationship and interchange between medical colleagues is of paramount importance in clinical genetics.

DEPARTMENTAL FACILITIES

The efficient functioning and range of services of the genetic clinics are dependent upon laboratories and special units, which are an integral part of the Department of Human Genetics.

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Cytogenetic Laboratory

The cytogenetic laboratory provides a routine cytogenetic service and undertakes specialised investigations such as tissue culture and prenatal diagnosis. The screening of the patients of various institutions, by chromosomal and buccal smear studies, is done in the cytogenetic laboratory, which is staffed by a senior specialist, a part-time physician and 4 technicians. The investigations undertaken in the cytogenetic laboratory during 1973 have been analysed and discussed by Nelson and Beighton.[5]

Genetic Biochemistry Laboratory

Under the direction of a senior biochemist, the genetic biochemical laboratory carries out specific studies applicable to certain heritable disorders which are of practical importance in South Africa. These include Gaucher's disease, osteopetrosis and various forms of dwarfism. In addition, a long-term programme of screening of institutionalised individuals for inherited metabolic abnormalities is currently under way.

Genealogical Unit

Family studies are an inherent part of any medical genetic service. The genetic nurse and a genealogical assistant make home visits in order to obtain specimens for laboratory investigation and to construct family pedigrees.

Records and data pertaining to all patients and kindred are maintained and correlated in the genealogical unit. It is anticipated that computerisation of these records will be introduced in the near future. Precautions will be taken to ensure confidentiality.

Epidemiology Unit

Many common disorders are the result of a complex interaction between genetic and environmental factors. A programme of comparative epidemiological studies of different populations is an important activity of the departmental epidemiology unit.

THE GENETIC DEPARTMENT, 1973

During 1973 a total of 254 patients or kindred were seen in the Cape Town genetic clinics or in other hospitals (Table I). Patients examined for research purposes, referred directly for cytogenetic studies or examined in various institutions, are excluded from this analysis. Patients seen outside the Cape Province are also excluded, while those attending the Red Cross Hospital genetic clinic are described elsewhere.[3]

Patients were referred to the clinics for a variety of reasons, including counselling, diagnosis, investigation, prognostication and prenatal diagnosis. Although there was often a considerable overlap, an attempt has been made at analysis of the primary reasons for referral (Table II).

Genetic disorders fall into well-defined categories, such as chromosomal abnormalities, gene disorders and multifactorial situations. The types of conditions present in the 254 patients seen during 1973 are shown in Table III and these are further subdivided in Tables IV—VII.

TABLE I. GENETIC REFERRALS, 1973

	Ethnic group				
	White		Non-White		
Clinic	No.	%	No.	%	Total
Groote Schuur Hospital (2 clinics weekly)	113	75	37	25	150
Princess Alice Hospital (weekly clinics)	15	37	26	63	41
Other hospitals in Cape Province and SWA	15	75	5	25	20
Inpatient consultations GSH	6	18	26	82	32
Other hospitals in Cape Town	5	45	6	55	11
Total	154	61	100	39	254

TABLE II. PRIMARY REASONS FOR REFERRAL

	White	Non-White	Total
Genetic counselling	86	19	105
Diagnosis and investigation	53	60	113
Prenatal diagnosis	4	4	8
Other	11	17	28
Total	154	100	254

TABLE III. GENETIC CONSULTATIONS, 1973: PROBLEMS ENCOUNTERED

	White	Non-White	Total	%
Chromosomal problems	27	16	43	17
Gene disorders	71	65	136	54
Multifactorial problems	41	17	58	23
Miscellaneous problems	15	2	17	6
Total	154	100	254	10

TABLE IV. GENETIC CONSULTATIONS, 1973: CHROMOSOMAL PROBLEMS

	White	Non-White	Total
Chromosomal abnormality	9	3	12
Down's syndrome	9	6	15
Turner's syndrome	2	—	2
Klinefelter's syndrome	2	5	7
Other	4	2	6
Maternal ageing	1	—	1
Multiple miscarriages	—	—	—
Total	27	16	43

TABLE V. GENETIC CONSULTATIONS, 1973: GENE DISORDERS

	White	Non-White	Total
Muscular dystrophy	5	4	9
Haemophilia	1	—	1
Heritable deafness	2	—	2
Heritable blindness	6	1	7
Neurological abnormality	7	3	10
Connective tissue disorder	16	29	45
Other disorders	34	28	62
Total	71	65	136

TABLE VI. GENETIC CONSULTATIONS, 1973: MULTIFACTORIAL PROBLEMS

	White	Non-White	Total
Spina bifida-anencephaly	5	3	8
Mental deficiency	23	10	33
Epilepsy	2	—	2
Cleft lip and palate	1	—	1
Congenital talipes equinovarus	3	1	4
Congenital dislocation of the hip	—	—	—
Congenital cardiac abnormality	2	1	3
Multiple malformations	5	2	7
Total	41	17	58

TABLE VII. GENETIC CONSULTATIONS, 1973: MISCELLANEOUS PROBLEMS

	White	Non-White	Total
Fetal hazards			
Maternal rubella	2	—	2
Maternal irradiation	8	—	8
Consanguinity	2	1	3
Non-genetic malformation	3	1	4
Total	15	2	17

Cytogenetic Investigation

Cytogenetic studies were carried out on a total of 48 individuals from the series of 254 patients. These patients include the majority of those listed in Table III, together with a number with mental deficiency and multiple malformations. Chromosome investigations were also undertaken on a further 302 individuals who were referred directly to the cytogenetic laboratory.

Home visits, for family studies or the collection of specimens, were made by the genetic nurse or genealogist on numerous occasions. More than 6 000 km were covered for this purpose.

DISCUSSION

The constitution of a clinical genetic unit or department depends upon local circumstances, but in general terms one or more experienced medical geneticists undertake the clinical consultations, supported by specialised cytogenetic and biochemistry laboratories.[6]

Research is an important facet of a genetic department's function, and as the field is expanding at an ever-increasing rate, the potential is virtually unlimited. However, it is likely that research in departments of this type will become increasingly concerned with genetic disease in individuals or populations, rather than with fundamental biological problems.

As genetic units are usually associated with teaching hospitals, the instruction of students and postgraduates is an important activity. The place of genetics in the medical students' curriculum varies greatly from university to university, but there is no doubt that increasing emphasis will in future be given to the clinically relevant aspects of this subject.

The scope of clinical genetics is constantly expanding and revolutionary concepts such as prenatal diagnosis by amniocentesis have now become routine procedures. A considerable proportion of the department's effort is spent in keeping abreast with new knowledge and with the establishing of new techniques which have practical value. An excellent example of this situation is provided by spina bifida and anencephaly. These related abnormalities are present in between 1/200 and 1/500 newborn children, but once an affected child has been born, the risk to subsequent siblings rises to approximately 1/20. However, during recent months methods have been developed which permit the detection of these abnormalities in early pregnancy. Amniocentesis is therefore justified in all women who have previously produced an affected child. New developments of this type inevitably enhance the potential of the department and increase the workload. There is no doubt that similar advances will occur in related fields in the near future.[7]

At present amniocentesis is most frequently undertaken for the antenatal diagnosis of Down's syndrome or mongolism. Since the prevalence of this chromosomal disorder is related to advanced maternal age, the prenatal screening of all pregnancies in 'elderly' mothers has become a routine procedure in many parts of the world. If pregnancy termination on the grounds of fetal abnormality becomes legally permissible in South Africa, it can be anticipated that there will be a considerable number of referrals for amniocentesis to exclude Down's syndrome in a fetus carried by an elderly mother. The age at which a women becomes 'elderly' is a matter for debate, but it is generally accepted that this procedure is indicated in mothers aged 40 years and over. It must be stressed that in the majority of instances the examination of the amniotic fluid will enable the medical geneticist to reassure the mother that her child will *not* be affected by Down's syndrome.

The genetic department was established in May 1972, and the total of patients referred during 1973, the first full year of activity, gives some indication of the prevalence of genetic disease in the community. It is

probable that these patients represent only the 'tip of the iceberg' and it is anticipated that with increase in genetic knowledge and interest on the part of colleagues in practice, this workload will continue to grow.

It is premature to draw any firm conclusion from the analysis of the ethnic background of patients referred to the genetics clinics in 1973. However, the excess of White over non-White referrals is probably the result of wider awareness of the significance of inherited disease among Whites, who are therefore more likely to request referral by their family physician.

The primary reason for referral was as often for diagnosis and investigation as it was for genetic counselling. This striking finding highlights the fact that there is far more to clinical genetics than the simple estimation of the chances of recurrence of a particular condition in a kindred.

During the latter months of 1973, amniocentesis for prenatal diagnosis was undertaken on 8 patients. With the new diagnostic techniques now available and the increasing appreciation of the potential value of this procedure, it is anticipated that this number will increase substantially during 1974.

When the patients' basic genetic problems are considered, it is noteworthy that the largest group of patients referred had problems due to abnormal genes. However, among those with chromosome disorders, the comparatively large number with Turner's syndrome probably reflects the orientation of one of the referring clinics. Similarly, the excessive number of individuals with inherited connective tissue disorders in the 'abnormal gene' group results from the special interest of the genetic department itself. In the 'multifactorial' group there is a notable lack of the classic genetic counselling problems of facial clefts and foot deformities.

It is evident that clinical genetics has progressed beyond the simple prediction of risks and has evolved into a complex medical speciality. It can be confidently foreseen that genetics will play an increasing part in everyday medical practice.

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