Genetic services for patients with severe mental retardation

The South African situation

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Summary

In South Africa mental retardation is still ill-defined as regards the aetiology and general epidemiology.

A systematic diagnostic/genetics programme implemented at various institutions for the mentally retarded within the framework of a comprehensive genetic service is described. The progress made is reported and the contribution of genetic services to the prevention and the management of mental retardation highlighted.

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Of the nearly 23 000 patients of all population groups hospitalized for a mental condition in South Africa in 1980, some 7 000 were mentally retarded and the remaining 16 000 were diagnosed as being psychiatric patients.[1] Of the mental retardates, some 4 500 are directly provided for by central government institutions; the remaining 2 500 are cared for by subsidized private and/or licensed institutions.[1] It is estimated that at least 5 000 mental retardates of all population groups in private family care can be added to this figure.[1] The patients for whom the Department of Health and Welfare assumes responsibility are cared for in numerous psychiatric hospitals and care and rehabilitation centres (CRCs) in various regions of the RSA.

A definition of mental retardation

Through the years several criteria have been used to define mental retardation, and of these intellectual functioning has proved to be the most acceptable. According to the American Association of Mental Deficiency (AAMD), 'mental retardation refers to significantly sub-average intellectual functioning, existing concurrently with deficits in adaptive behaviour and manifest during the developmental period'.[2]

Adaptive behaviour is measured by the responsibility, independence and social skills exhibited by a subject compared with those expected for his/her age. In gauging intellectual functioning, the intelligence quotient (IQ) is quite often taken as the major criterion and is measured by a performance below two standard deviations from the mean on standardized tests. According to the Stanford-Binet Intelligence Scale an IQ of 67 is considered to be the cut-off point, and on the Wechsler Intelligence Scale for Children the cut-off point is 69. The AAMD classification of mental retardation based on IQ measurements is compared with the World Health Organization classification of 1968 (Table I).

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TABLE I. CLASSIFICATION OF MENTAL RETARDATION

Degree of retardation	IQ range AAMD	IQ range WHO
Mild	**55-69**	**52-67**
Moderate	**40-54**	**36-51**
Severe	**25-39**	**20-35**
Profound	**<25**	**<20**

Amid the international confusion of concepts relating to the classification of mental ability, the Committee of Inquiry into the Care of Mentally Deficient Persons in the RSA (1967) defined persons with mental handicaps as those with an IQ of between 0 and approximately 79, and mentally deficient persons as those with an IQ of between 0 and approximately 49.[3]

Incidence

The incidence of mental retardation is still uncertain. Estimates of the incidences in various countries range from 1,60 to 230,40/1 000 members of the population, with a mean of 23,65/1 000.[4] In the RSA the incidence of mental deficiency (IQ 0 - 49) among Whites is estimated as 4/1 000.[3] No comparable figures are available for other population groups in the RSA as yet.

Aetiology

Many causes of mental retardation are known. Statistics taken from a few selected studies[5-9] on the causes of mental retardation are compared in Table II.

In general, causes of mental retardation are classified as being environmental, genetic or multifactorial (involving genetic-environmental interaction). Most studies reveal a significant percentage of patients with an unknown cause (±40 - 50%). In general, about 50% of the cases of mental retardation can be attributed to genetic factors.[10]

In spite of the magnitude and importance of mental retardation in terms of the social, psychosocial and economic burden placed on individual families and on society, only isolated and limited investigations in the field of diagnostic/genetic studies were undertaken up to the last decade.[11]

Genetic services for mental retardates

In the early 1970s an attempt by the Genetic Services Division of the Department of Health and Welfare to establish the causes of mental retardation and reliable diagnoses from files and documentation on patients at various institutions for the mentally handicapped in the RSA met with limited success. Firstly, it transpired that virtually none of the conventional genetic diagnostic procedures and investigations had been undertaken, mainly because at

TABLE II. CAUSES OF MENTAL RETARDATION

Causes (%)	Turner[5] (1975; $N = 1000$)	Hanefeld and König[6] (1974; $N = 414$)	Angeli and Kirkman[7] (1971; $N = 645$)	Moser and Wolf[8] (1971; $N = 1359$)	Iivananien[9] (1974; $N = 338$)
Perinatal disorders		22	17	18	14
Perinatal damage	17				
Infections of CNS		8	7	6	17
Prenatal infection	7				
Postnatal infection	8				
Chromosomal abnormalities	18	13	17	19	4
Metabolic disorders		4	3	3	3
Dominant diseases	5				
Recessive diseases	11				
X-linked diseases	9				
Other genetic disorders		6	1	2	3
Malformations		6	3	10	
Injury, poisoning, etc.		1	1	2	
Cultural disintegration	3				
Indeterminate	22	40	51	40	59
	100	100	100	100	100

that stage priority was given to the provision of basic facilities, such as accommodation, and the implementation of a non-custodial care system. Secondly, the facilities, infrastructure and organization necessary for the facilitation of a systematic diagnostic/genetic programme were not available. Thirdly, there was no organizational framework for the accommodation of a comprehensive service for the mentally retarded in which genetic services should feature.

In 1971 the inclusion of a genetic service as part of the community health care system was conceived, and in 1975 an active genetic service materialized.[12,13] One of its programmes is involved with carrying out diagnostic/genetic studies on patients in the RSA with severe mental retardation.

Against this background, the Genetic Services Division of the Department of Health and Welfare undertook a diagnostic genetic programme at CRCs for the mentally retarded for the following reasons: (*i*) to determine the most efficient approach to establish the aetiology in individuals with mental retardation; (*ii*) to develop and institute a procedure for collecting data on patients to facilitate systematic genetic analyses in the future; (*iii*) to confirm, where possible, the diagnoses in cases classified as 'genetic'; (*iv*) to establish a profile of the genetic causes of mental retardation in various population groups and institutions; (*v*) to identify the genetically affected patients and at-risk family members, with a view to genetic counselling and prevention; and (*vi*) to develop a comprehensive genetic service for patients with mental retardation and their families.

In this article the philosophy and *modus operandi* of this programme are emphasized since the details and results of the ongoing cytogenetic,[14] biochemical[15] and clinical investigations will be reported on shortly.

Samples and methods

The five State-administered CRCs at which a diagnostic/genetic programme is currently in operation are the Witrand, Cullinan, Umgeni, Alexandra and Oranje CRCs. These institutions have 3 277 full-time inpatients of White descent; the age distribution of these patients is shown in Table III.

Procedures for the collection and evaluation of data

For statistical purposes a **notification form** is filled in for each patient, and contains the following items: identification particulars, particulars of natural parents, obstetrical history of mother, age at onset of mental retardation, age at diagnosis, whether the diagnosis is confirmed or probable and the status of genetic investigations. (A confirmed diagnosis is only accepted and recorded if substantiated by a written report from a laboratory or by clinical investigation.)

A family history is recorded in established or suspected cases of genetic aetiology, and a family pedigree is compiled for as far back as necessary. Sociocultural factors such as maternal alcoholism, economic status and emotional deprivation are investigated.

An initial **physical investigation** is performed and all existing data on the patient are scrutinized, and a prenatal, perinatal and postnatal history obtained to classify patients into broad aetiological categories, i.e. acquired, genetic, probably genetic or unknown.

Further diagnostic investigations such as radiography and electro-encephalography are undertaken.

A standard chromosome analysis is performed in all patients with an idiopathic malformation syndrome, as well as in

TABLE III. AGE DISTRIBUTION OF PATIENTS AT DIFFERENT CRCs IN 1980

Age distribution (yrs)	CRC				
	Witrand	Cullinan	Umgeni	Alexandra	Oranje
0-5	3	12	14	5	—
6-18	159	65	125	125	20
19-39	651	48	293	389	38
40-59	523	39	93	231	22
60 +	190	8	20	101	5
Total	1526	172	545	851	85

their siblings and parents if indicated. A cytogenetic analysis is carried out in all patients with Down syndrome or any other suspected chromosome abnormality.

Biochemical screening is performed according to indications, as well as in all patients with no other established diagnosis and whose condition is not obviously caused by environmental factors. Broad-spectrum screening tests are performed to detect defects associated with keto-acids, carbohydrates and other reducing substances, amino acids, mucopolysaccharides and organic acids and other metabolic disorders. Any abnormality is further investigated by the performance of detailed tests.

A special 'blue file' is opened for each patient, which contains at least one photograph of the patient and others recording specific abnormalities. The blue file contains a check-list of all the body systems against which abnormalities are recorded. The current status of the diagnostic genetic investigations is recorded as well as results of detailed diagnostic/genetic analyses. Files are kept in a separate filing cabinet in a room assigned to genetic services.

At least one specially trained genetics nurse of the Department of Health and Welfare regional office is responsible for the genetics programme at any CRC. In liaison with the superintendent and health personnel of the CRC this nurse arranges for genetic examinations and tests, follows up families for genealogical data and maintains the filing system. A contact person on the establishment of the CRC assists the genetics nurse. Depending on the outcome of the work-up, auxiliary personnel such as social workers are mobilized to provide psychosocial support; this is seen as being an essential step in the development and provision of a comprehensive genetics service.

Results and discussion

Because of the limitation of available diagnostic/genetic facilities at the different CRCs, the full spectrum of investigations on all patients still needs to be completed. The number of individual investigations performed so far are listed in Table IV.

Chromosome investigations performed so far reveal that 18,1% of the patients have a chromosomal abnormality. Detailed results of the different chromosomal abnormalities are reported elsewhere.[14] Biochemical analyses performed to date reveal that about 1% of the patients have a known biochemical/metabolic defect. The individual defects found are also reported separately.[15] Physical investigations are at various stages of completion, and details will be published at a later stage.

A systematic approach to the provision of a comprehensive genetic service has been established at three centres, the Witrand, Oranje and the Cullinan CRCs. This system comprises formal lines of communication between the genetics sister, the contact person at the CRC and the psychosocial supportive services (Fig. 1).

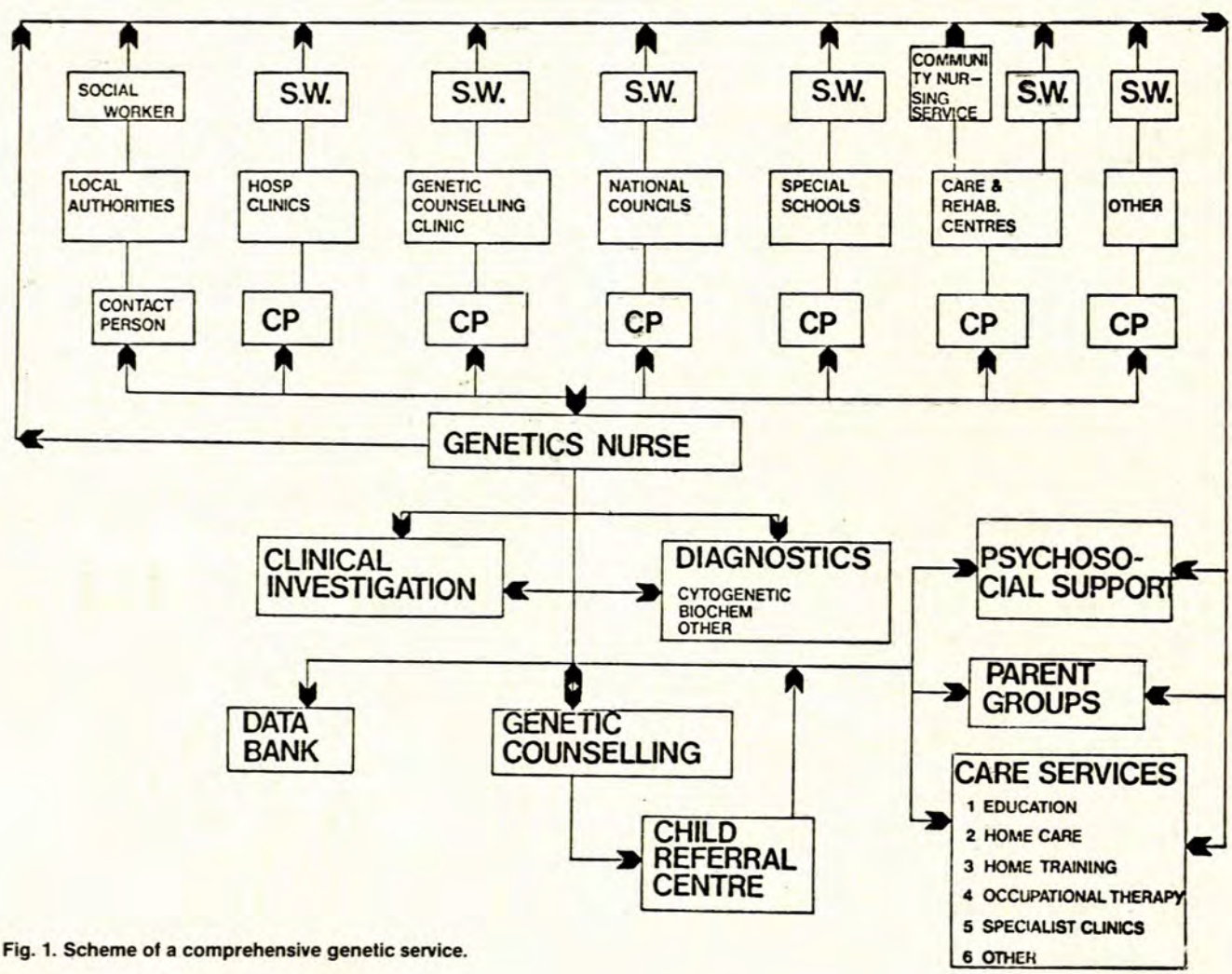

Fig. 1. Scheme of a comprehensive genetic service.

TABLE IV. INVESTIGATIONS/PROCEDURES COMPLETED AND THE NUMBER INDICATING ABNORMALITY

Investigations/procedures	No. completed	No. abnormal	%
Chromosome analyses	**2054**	**371**	**18,1**
Biochemical analyses	**2655**	**26**	**0,9**
'Blue files' completed	**3317**	—	—
Physical examination initiated	**1323**	—	—
Notifications	**2791**	—	—

As the programme progressed the need for a supportive service and an extended genetic and auxiliary service emerged; this necessitated the co-ordination of available resources. Although not complete, this rudimentary system could be integrated into other services to comprise an extended comprehensive service system for the mentally retarded which would include: child development, vocational services, residential services and central and supportive services.[16]

Prevention of mental retardation

Besides the importance of establishing diagnoses and the causes of mental retardation in specific individuals, the element of prevention has sometimes been questioned. Nevertheless, the basis of prevention resides in identifying at-risk family members, especially if the patient concerned is young.

Through his contributions to human biology and genetics and his research in mental retardation, Penrose[17] uncovered the manifold possibilities for the prevention of mental retardation. According to Wald,[18] the classic model of prevention includes three types of activities (Table V).

TABLE V. TYPES OF PREVENTIVE ACTION

Type	Action
Primary*	**Prevention of the development of diseases by the removal of the causative factor or by changing the resistance of the organism**
Secondary	**Prevention of the development of symptoms in an organism affected by the pathological process**
Tertiary	**Prompt, effective treatment leading to the disappearance of symptoms and the prevention of long-lasting handicap**

* Prevention of an at-risk pregnancy or termination of pregnancy is considered part of primary prevention.

TABLE VI. AETIOLOGICAL FACTORS AND PREVENTIVE MEASURES IN LOW-GRADE MENTAL RETARDATION

Factors	Estimated incidence (%)	Preventive measures possible
Factors acting before conception		
Genetic		
Chromosomal	**15 - 20**	**Prenatal diagnosis, genetic counselling**
Single gene		
Structural	**1 - 2**	**Genetic counselling, fetoscopy, ultrasound**
Metabolic	**2 - 4**	**Prenatal diagnosis, preventive therapy**
Multifactorial	**2 - 4**	**Genetic counselling, prenatal diagnosis**
Prenatal factors		
Infections and parasite invasions	**2 - 3**	**Immunization, treatment of mother**
Chemical influences	**?**	**Environmental control**
Alcohol	**0 - 0,1**	**Prenatal care**
Nutritional factors	**?**	**Proper nutrition**
Physical factors	**?**	**Environmental measures**
Immunological factors	**0,5 - 1**	**Desensitization, exchange transfusion**
Endocrinological disorders in the mother	**?**	**Specific treatment**
Placental disorders	**?**	**?**
Intra-uterine hypoxia	**?**	**?**
Perinatal factors		
Asphyxia	**2 - 4**	**Improvement of obstetric paediatric care**
Birth injury	**2 - 3**	
Prematurity	**8 - 12**	
Postnatal factors		
Infections	**2,5 - 5,5**	**Vaccination, prompt treatment**
Injuries	**0,5 - 1,5**	**Environmental measures, proper treatment**
Chemical factors	**0,1 - 0,5**	**Environmental measures, proper treatment**
Nutritional factors	**?**	**Adequate nutrition**
Deprivation factors	**?**	**Stimulation**
Other	**?**	

The primary and secondary modes of prevention are effective and feasible in the prevention of genetic disorders. Wald[18] tabulated the preventive measures possible in the different aetiological categories of low-grade mental retardation (Table VI).

Primary prevention

With the advent of amniocentesis prenatal diagnosis became almost 100% accurate, and this has greatly enhanced the value of genetic counselling in certain conditions.

In contrast with the traditional method of genetic counselling based on the classic risk figures of 25% or 50% for single gene defects or empirical risks for multifactorial or chromosomal defects, all of the chromosomal abnormalities, over 60 metabolic disorders and a few multifactorial defects (e.g. neural tube defects) can be accurately diagnosed before birth.[19] These and other techniques of prenatal diagnosis afford practical means for the primary prevention of mental retardation.

In 1974 Turner[5] stated that Renpenning's syndrome is the most common of the X-linked hereditary disorders (incidence 9%) causing mental retardation, and that approximately one-third of the X-linked conditions may be prevented by genetic counselling. Another relatively common X-linked mental retardation condition is the Martin-Bell syndrome which can be diagnosed by the detection of a fragile site on the X chromosome,[20] even in most female carriers. With the prospect of prenatal diagnosis the primary prevention of this condition does not seem remote.

If all pregnant women over 35 years of age and those in families at risk for Down syndrome were to undergo amniocentesis, which is economically and practically feasible and in fact the case in several countries, the incidence of Down syndrome could be reduced by 20 - 25%.[21,22] If all pregnant women had access to amniocentesis and decided on termination of pregnancy if Down syndrome was detected, the incidence of the latter among newborns could be reduced by another 20%,[22] although such a step would not be practically feasible. Where Down syndrome is the leading cause of major mental retardation[23] prevention of some of these cases could have a significant impact on the prevalence of mental retardation.

Carrier detection for genetic defects

Carrier detection via population screening is a means of identifying heterozygous carriers of deleterious genes for diseases causing mental retardation. It would, however, be illogical to try to test for all testable genetic disorders. Detection programmes must be limited to specific families and specific population groups at risk for specific genetic diseases. The detection of carriers for Tay-Sachs disease among Ashkenazic Jews is an excellent prototype for a population screening programme for the prevention of mental retardation.[24]

Newborn screening and treatment of metabolic disorders

Early diagnosis and treatment is a means of attaining secondary prevention of mental retardation, the detection of phenylketonuria having been the model for this procedure.[25] With minimal added effort and expense other amino acid metabolic disorders and hypothyroidism can be added to a routine screening programme for newborns.[26]

Several ways of treating hereditary metabolic disorders leading to mental retardation are known: replacement of missing product, reduction of excess substrate, reduction of excess metabolite, replacement of missing enzyme, replacement of missing co-enzyme, replacement of defective gene, intra-uterine therapy and organ transplantation.[27]

Avoidance and control of infections during pregnancy

As shown earlier (Table VI), the incidence of mental retardation caused by infection (prenatal and postnatal) varies from 5% to 8%. Appropriate immunization and the early diagnosis of infections in the mother or child followed by prompt treatment therefore seem to be feasible means by which some cases of mental retardation can be prevented.[28]

Antenatal and neonatal care

Since environmentally induced mental retardation can be accounted for by perinatal, pre- and postnatal events in approximately 10 - 20% of cases (Table VI), adequate prenatal, perinatal, obstetric and gynaecological measures should prevent a significant percentage of cases of mental retardation. Schmid *et al.*[29] established that perinatal damage accounted for 32% of cases of mental deficiency in which trisomy 21 had been excluded. Surveys conducted in South Africa have indicated the gross ignorance of the role of adverse factors during pregnancy and the scope for simple self-help preventive measures which remains (H.M. Esterhuysen — Human Sciences Research Council findings, 1979-1980). The need for promoting education of the general population with the aim of preventing infant mortality and morbidity (including mental retardation) is self-evident.

Surveillance of mental retardation

The expected number of individuals with mental retardation, the number officially accounted for, and the number of individuals involved in diagnostic/genetic services indicate that there is still ample room for the extended implementation of genetic services.

There are numerous homes and institutions for the mentally retarded other than those mentioned earlier which could equally share in the benefits of a comprehensive genetic service. Although some of the components of the service are sophisticated and limited according to availability of means and facilities, an effort could be made to institute some of the basic procedures (such as systematic record-keeping of patients' genetic data) until the comprehensive genetic service has reached its full potential.

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