

# PRIMARY PREVENTION OF PHYSICAL AND MENTAL HANDICAPS: GENETIC COUNSELLING AND PRENATAL DIAGNOSIS

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## OPSOMMING

Primêre voorkoming is 'n belangrike terrein vir mediese genetica en die genetiese raadgewer vertolk hierin 'n belangrike rol. Daar is egter spesifieke indikasies vir verwysing van persone na 'n genetiese raadgewer en sy span. 'n Belangrike ontwikkeling in primêre voorkoming van genetiese afwykings is die moontlikheid van voorgeboortediagnose, deur amniosentese, van veral chromosoom afwykings, neuraalbuisdefekte en sekere metaboliese toestande. Die Departement van Gesondheid en Welsyn bied gratis genetiese dienste vir die gemeenskap in Suid-Afrika aan. So 'n diens hou groot voordele in, ook vanuit die ekonomiese oogpunt gesien.

## THE ROLE OF GENETIC FACTORS IN HANDICAPS

To date there are no figures available on the number of handicapped people in the Republic of South Africa. The lack of an adequate method of assessment and the difficulty of defining the different handicaps are the major obstacles.

Handicaps, whatever their nature, have two basic causes. On the one hand the underlying cause is **genetic** where either the chromosomes or even one or several of the approximately 200 000 genes in man may be defective. Such *genetic* defects need not necessarily manifest at birth or shortly after birth — but may manifest much later in life. On the other hand the cause of a birth defect or handicap may be the result of an exogenous factor which may operate before birth (such as Rubella (German measles), thalidomide or irradiation), during birth (for example oxygen deficiency) or even after birth (such as an accident). For the purpose of this discussion, only those handicaps which are not the result of exogenous factors will be considered.

In developed countries it is estimated that 50% of the handicaps in children can be attributed to diseases or disorders of the mother

during pregnancy or to a complication during birth. In the Federal Republic of Germany this percentage is estimated to have been reduced to 25%. In the remaining cases 50% in general or 75% in Germany, the cause of handicaps is a genetic defect.

Human geneticists are further in agreement that in developed countries, at least 5% of newborns come into the world with a serious genetic or congenital defect. Of the annual 500 000 births in South Africa this would mean that 25 000 children are born with a genetic defect every year. If the 50%, or an even larger percentage, of handicaps due to external causes is added we could be dealing with approximately 50 000 — 60 000 newborns with handicaps per year.

As medical science and technology combats infections and malnutrition as causes of infant deaths, the genetic factors as cause are shifted to the foreground. So much so that the Ministry of Health in the Federal Republic of Germany has listed the following factors in the order of importance as causes of **mother and child deaths**:

- genetic
- social
- medical
- technical-organisational

In the United Kingdom an estimated one in twenty children admitted to and resident in hospitals suffer from a genetic disease, which is also the cause of infant death in one out of every ten children. It has also been reported that 40% of infant deaths in the United States of America are due to malformations and genetic-type of disorders.

## IS THERE AN INCREASE IN HANDICAPPED CHILDREN?

There is also reason to believe that genetic disorders are not only increasing relatively but also in absolute numbers. The increase in the number of handicapped persons is only partly attributed to the *genetic* causes of birth defects. In general the increase in the number of affected persons can be related to the increase in life expectancy made possible by improved medical and social care. A classical example is probably that of Down Syndrome (mongolism) for which, in the United Kingdom the life expectancy in the 1940's was about 12 years whereas today it is in the thirties. Patients with Down Syndrome who are 50 and 60 years or older are also seen frequently.

As far as the exogenous factors are concerned, it is known that im-

provement in intrapartum care has resulted in many children being born who would not otherwise have survived the birth process or perinatal period. This social and ethically unavoidable commitment of health services is thus also exercised at a price.

Recent research in South Africa on knowledge and attitudes regarding genetic defects which has been conducted by the Human Sciences Research Council on behalf of the Department of Health and Welfare has shown that the public is still unaware of the dangerous external factors which cause birth defects and handicapped children.

Advances in modern technology has brought with it an increased production of physical (irradiation) and chemical agents which have significantly increased the load of mutations in the population over the last century. This means that the pool of defective genetic material in the population is increasing and is passed on to successive generations. Some Western countries are concerned about this threat and special laboratories have been instituted to monitor the nature and extent of free occurring mutagenic agents in order to safeguard the genetic health of the community.

In general, public and government awareness about and government concern over handicapped children has for several reasons become increasingly evident in South Africa. State expenditure on Psychiatric Services reached the R59 million mark in 1980 — in spite of the policy that custodial care is to be replaced by a community based care system. Further State responsibilities concerning the education and training of handicapped children have escalated from R5 102 793 in 1970 to R25 544 000 for 1980. In 1977 a State Genetic Service was instituted to help cope with the growing concern over congenital and hereditary defects. During the last five years community awareness of birth defects has been widened by the formation of several parent groups for specific handicaps like neural tube defects and Down Syndrome. In 1979 alone, at least 22 articles in the mass media on congenital and hereditary defects could be accounted for as

compared to a mere 8 in 1977 and 10 in 1978.

For many years it was not uncommon to find parents *keeping* a handicapped child at home or harbouring it inconspicuously in an institution in order to avoid embarrassment. Living with the handicapped is becoming more accepted by the public, who also show an increased understanding of the causes of handicap and the potential of the handicapped child. In the social sciences, which are on the brink of major developments, psychologists and educationists are developing scientific methods which are unleashing the potential of the handicapped and making a humane life for them a reality.

Recognition of the presence of the handicapped has become firmly entrenched in society and our ethical and scientific responsibilities cannot deny the handicapped a longer life and optimal existence. Alternatively, we must direct our efforts towards a logical but human approach which is within our reach and provides a practical solution to the problem of handicap. It involves an approach more practical than the curative method which has virtually reached its limits.

With out current and existing knowledge and future consideration the most practical and rational way to overcome the growing problem of coping with the handicapped is **primary prevention**.

## PRIMARY PREVENTION

In human genetics the term primary prevention means to avoid the birth of a child with a certain handicap. Legally such an act is permissible in the Republic of South Africa. (*The Abortion and Sterilisation Act 2 of 1975*) depending on the nature of the handicap. The circumstances under which it may be performed are prescribed by the Act.

Technically, primary prevention of genetic disorders is facilitated by **genetic counselling** which could include a prenatal diagnosis.

## What is Genetic Counselling?

The object of genetic counselling is not an attempt to look for a reason to prevent a pregnancy or to recommend an abortion. It is rather a

matter of providing a distressed person or family with information about the implications of a particular risk and, if necessary, assisting with practical means of prevention where possible. In most cases it is a matter of anxious couples coming for genetic counselling only to be informed that the risk of recurrence of a handicap is relatively small or that, in some cases, a test can be performed before birth to determine whether the unborn foetus is affected or not. Should the test be positive the pregnancy can be terminated legally. In this way genetic counselling has relieved many couples of unnecessary anxiety and many could be assured that the next pregnancy would be *safe* within limits, thus relieving the fear of having further affected children.

The impression which sometimes exists that genetic counselling only aims at reducing the birth figure is a complete misconception. The contrary is true. Many parents only decide to have children after they have been informed by the genetic counsellor that there is no reason for anxiety.

More and more people are turning to genetic counselling for advice concerning the risk involved in a particular pregnancy. As the public becomes more aware of the fate of the handicapped, couples are becoming more aware of and concerned about the health of their children.

Genetic counselling aims to help these people to establish **whether** there is any cause or reason for concern. This is usually done by assessing the family history or conducting a clinical investigation on the counsellees and/or their children if they have any.

Where a significant risk for occurrence or recurrence of a particular handicap exists, the genetic counsellor can explain the risk figures as well as the medical and social implications. For most people the initial encounter with a handicap in the family is a traumatic experience until they have learnt to cope with the situation.

**To summarise the genetic counsellor can do the following:**

— listen to the problem of the counsellees;

- assess the situation by taking a family history and making a diagnosis of any affected individual;
- explain the risk of occurrence or recurrence of a particular handicap;
- explain the medical and social implications;
- draw some blood for a chromosome analysis or a special blood test if necessary;
- refer the patient for appropriate treatment and most often psychosocial support;
- help the couple to come to a realistic decision and above all start to help them to cope with the situation.

### Genetic sisters

Very often genetic counselling is performed in the presence of a multidisciplinary team because the complexity and implications of coping with a handicapped child in the family demands this approach. In this context the genetic nurse has a particularly important function. She is a nurse specially trained to deal with all aspects of a community based comprehensive genetic service. In summary, she serves as a referral point in the community and most often makes the initial assessment of the need or situation. Where indicated the counselees are referred or accompanied to a genetic counselling clinic for further assistance. One of the functions of the genetic sister is to co-ordinate facilities. After the genetic counselling session, when the couple may be distressed and in need of support in order to cope with the situation, this support can be provided by the nurse. Follow-up of certain patients is done routinely to ensure that they have understood the counselling and to assess any further needs. Psychosocial support is offered.

### When is genetic counselling necessary?

Due to limited facilities it would be impossible to provide genetic counselling to all prospective couples. This is also not necessary. Prospective couples and high risk families should refer to the following indications for genetic counselling to determine whether they qualify:

- A family history of a particular handicap, disease or malformation, such as porphyria, diabetes, blindness, deafness, epilepsy, premature coronary thrombosis and any other congenital defect.
- An affected child in the family with a diagnosed genetic disorder such as cystic fibrosis or Down Syndrome.
- A child with one or more congenital malformation, such as cleft lip and palate, deformities of hands and feet for example extra digits, malformed ears and other abnormalities.
- Severe or moderate mental retardation.
- Malformations suggesting a specific syndrome associated with abnormal chromosomes.
- Signs and symptoms suggesting a metabolic disease such as:
  - failure to thrive;
  - unusual odour;
  - skin and hair changes;
  - abnormalities of the eye (cataracts or corneal clouding);
  - neurological disorders.
- Individuals with
  - ambiguous external genitalia;
  - particularly short stature;
  - lack of secondary sex development;
  - sterility.
- Repeated spontaneous abortions or a previous stillbirth.
- Possible harmful factors during pregnancy, such as:
  - irradiation;
  - smoking;
  - alcohol;
  - infection (for example Rubella)
  - unprescribed medicines;
  - advanced maternal age (over 40)
- When related individuals wish to marry.

The number of known diseases and defects which have a genetic origin is increasing every day. In 1960 only 700 inherited disorders were catalogued, whereas today nearly 3 000 single gene disorders are known. This excludes the multitude of chromosomal defects and those spontaneous congenital defects and diseases in general which are partly of genetic origin.

It is significant that abnormal inherited blood fat levels are associ-

ated with coronary thrombosis and premature heart problems which is one of the major killers in society. Then there are certain *soft* signs like specific learning problems, such as dyslexia, which are in many cases inherited, adding another dimension even to this type of problem.

### Prenatal diagnosis of genetic defects

Prenatal diagnosis refers to a method of determining at about 14 to 18 weeks of gestation whether the unborn baby has a specific genetic disorder or not. This method has become a powerful instrument in practical genetic counselling. Several techniques are available:

**Sonography** (a harmless ultrasound method by which a *picture* can be obtained of the foetus in the uterus and obvious morphological malformations detected), or

**Amniocentesis** which is used most widely. The technique is virtually painless and involves drawing about 10cc of amniotic fluid which contains cells derived from the foetus and on which the necessary tests are performed. Amniocentesis is performed at 14-16 weeks of pregnancy.

A large number of genetic disorders can be determined prenatally by amniocentesis. These are:
 

- all the known chromosomal defects;
- about thirty metabolic defects, for example Tay Sachs disease;
- certain neural tube defects or the *open* type, such as spina bifida.

Most international surveys show that 3-5% of the amniocenteses performed, result in a termination of pregnancy based on the diagnosis of a defect in the foetus. Thus at least 95% of the patients which underwent a prenatal diagnosis could be assured of a *safe* pregnancy which in many cases would not even have been considered in the light of uncertainty and unfounded fear of having an affected baby.

### Limitations of prenatal diagnosis

Although prenatal diagnosis of severe handicaps is probably the biggest advance medical science has

experienced in the last two decades, especially in the field of primary prevention, it must be stressed that amniocentesis, as a method of prenatal diagnosis, cannot be performed at liberty. There are several limitations:

- first of all, the process of amniocentesis necessitates close collaboration between a maternity clinic and the genetic counselling clinic. Genetic counselling should precede amniocentesis. Care is taken that the counsellors are properly prepared for the process, including the understanding and acceptance that a termination of pregnancy is implicated should the prenatal diagnosis be positive. It does happen that a mother suddenly declines from having an abortion regardless of the result of prenatal diagnosis. It further means that the prenatal diagnosis can only be done to test for those handicaps for which an abortion is justified;
- an amniocentesis is an expensive and highly specialised procedure and facilities extremely limited. This necessitates that amniocentesis can only be done in selected cases and only where it is really indicated;
- the physical process of an amniocentesis does involve some risk to the mother and child, such as causing or inducing an abortion. This risk is however less than 1% but implies that the reason for doing an amniocentesis must at least involve a risk greater than 1%;
- as the public becomes more and more aware of the need for prenatal diagnosis, more people appear to be under the impression that any disorder or malformation can be detected before birth. The converse is true. On the one hand only those disorders and malformations for which a prenatal test is known, and there are not all that many, can be tested for. (The genetic counsellor should be consulted about available tests). By the same token no prenatal test can guarantee a mother a perfectly normal baby. There is no prenatal test for the majority of genetic disorders and even if an

amniocentesis has been performed to exclude a specific disorder, the baby still runs the same risk as any other to be affected by another disorder;

- technically the laboratory procedure for the diagnosis cannot be guaranteed. In about 4% of amniocenteses the amniotic fluid obtained for diagnostic purposes is not adequate and the process has to be repeated. Each repeat means that the pregnancy is further advanced which complicates a therapeutic abortion and increases the risk for the mother.

### **Indications for prenatal diagnosis**

A prenatal diagnosis is only advisable when a risk for a defined handicap exists and provided the handicap can be detected in the amniotic fluid or -cells, the blood of the foetus or from the morphology of the foetus. Routine prenatal diagnoses have shown that there are basically six categories of indications for prenatal diagnosis. By far the most important is advanced maternal age.

#### **Advanced maternal age**

It is now generally known that the risk of a baby having a genetic defect increases with the age of the mother. From the age of about 35 the risk for a handicap due to a chromosomal defect starts increasing, so much so that between the age of 38 and 40 there is a 1 in 60 risk of the child being affected and above the age of 45 the risk is nearing 1 in 25. This incidence makes it imperative that all pregnant mothers who are 40 or over should have a prenatal test done.

#### **A previous child with a chromosomal defect**

The best known example of a genetic disorder of this type is Down Syndrome (mongolism). In 96% of the cases of Down Syndrome the cause is a third chromosome No. 21. A normal person has altogether 46 chromosomes occurring in 23 pairs in each cell of the body. The risk for a second affected child with an

extra chromosome No. 21 (Trisomy 21) is about 1,5 % higher than that of the normal population. It has been shown that the recurrence risk is somewhat higher in women younger than 25 years of age.

#### **When a parent is a carrier of a balanced chromosome translocation**

In rare cases a person can have a rearrangement of his chromosomes (translocation) without showing any clinical signs and symptoms of a handicap. However, if the translocation is a *Down's type*, the offspring of such a person will have a 10% to 15% risk of having a chromosome defect which has the same clinical features as the previously mentioned Trisomy 21 or Down Syndrome.

There are also other syndromes arising from the same mechanism although these are very few. In the case of Down Syndrome only 2-3% of the cases can be attributed to a translocation. In the remaining 96% of the cases the cause is the spontaneous occurrence of an extra chromosome 21 which occurs in 1 in every 600 births.

#### **When the mother is an obligate carrier of a serious genetic disorder**

The disorders of Haemophilia and Duchenne muscular dystrophy are the best examples where a mother can be a carrier for a single gene disorder without being affected. Each of her sons, however, has a 50% chance of manifesting the disorder. This mode of genetic transmission is called sex-linked or X-linked inheritance (since the defective gene occurs specifically on the X-chromosome (sex chromosome) in man.

Although these and many other sex-linked defects can rarely be tested for prenatally, one can test for the sex of the baby. If it is a boy he will have a 50% chance of being affected if it is known that his mother is a carrier. In some practices this is considered adequate reasons to proceed with an abortion — but a serious religious/ethical consideration comes into play in

these cases. A prenatal diagnosis in these cases is made on a 50% risk possibility that the child will be normal, i.e. there is a 50% chance that one will be aborting a perfectly normal son!

With the modern methods of managing some of these sex-linked disorders, especially Haemophilia, one has to exercise the greatest caution when resorting to prenatal diagnosis for prevention of these disorders.

### Both parents a carrier

Over and above the X-linked genetic disorders, there are 600 known genetic disorders where a person can be a carrier of a defective gene without manifesting the particular disorder (called recessive genes which are situated on any chromosome other than the sex chromosomes). When, however, two parents happen to be carriers for the same defective gene then there is a 25% risk of any child inheriting the defective gene from both parents in which case the child will manifest the handicap. Examples of genetic defects exhibiting this mode of inheritance include cystic fibrosis, Tay Sachs disease and many others.

Approximately 50 metabolic defects with this mode of inheritance can at present be determined prenatally.

### Neural Tube Defects

Approximately two births in every thousand are associated with a neural tube (spinal column) defect, for example spina bifida or hydrocephalus. Unlike the classical inherited single gene defects which have either a dominant, recessive or X-linked mode of inheritance, neural tube defects are called multi-factorial which means that several genes in conjunction with environmental factors (mostly unknown) are responsible for the disorder. The risk of recurrence is consequently relatively small. However, with each affected child in a particular family the risk for the next baby being affected increases. After the first affected child the risk for the second is 3-5% and 8-10% for the third affected and so on.

With neural tube defects of the

open type, that is when the skin covering the spinal column is ruptured, the spinal fluid of the foetus leaks into the surrounding amniotic fluid.

By determining the level of a substance known as alpha-fetoprotein in the amniotic fluid one can determine whether the foetus is affected or not.

Fortunately, there is now a test by which a foetal open neural tube defect can be determined by testing the mother's blood serum. This of course opens a completely new avenue of screening for neural tube defects in pregnant mothers.

### PSYCHOSOCIAL ASPECTS

A wide variety of psychosocial processes are centred around the occurrence of a handicap in a family. Experience has shown that these psychosocial processes can be divided into distinct phases.

- A reaction of **shock** and disbelief.
- **Pre-comprehension phase of chronic sorrow.** This is a normal reaction to the impact of learning that a serious handicap has occurred in the family. A feeling of inadequacy — bordering on failure — is often associated with this response. Impressions of faulty genetic material in the family and the possibility of stigmatisation and being ridiculed are evoked.
- During the **non-acceptance phase shopping around** at all possible facilities, grasping at the last straw of possible sympathy and a defiance of the realities is often seen. It is here that psychosocial support of the distressed family is invaluable.

The supporting team of the genetic counsellor, that is the genetic nurse, social worker and psychosocialist help the shattered family to grasp the realities of the situation. In particular the cause and mechanisms giving rise to the handicap are explained in much detail as well as the possible practical implications of the disorder. The socio-economic effect of a handicap on a family and the affected person have far-reaching consequences.

Gradually the **phase of com-**

**prehension and acceptance** of the handicap is entered. In some cases this phase is never reached, usually with unfortunate consequences. The extent to which the family copes with the situation depends on many factors of which the type and severity of the handicap is the most important. Secondly, the effect of the handicap on the socio-economic status of the family is a decisive factor. Above all, the integrity and maintenance of the psychosocial stability of the family and the affected individual will greatly determine to what extent the family will be able to cope.

Every family or affected person goes through these stages to a different degree. The need for a sophisticated, experienced and highly specialised psychosocial support service is still a great need in this country. In the meantime, parent groups have mushroomed to fill the gap by providing fellowship and helping each other to cope.

### COST AND BENEFIT

In some respects it is inhumane to even equate a life to an economic value. In planning health services for the community, however, this issue is an important factor in determining priorities in state expenditure.

More and more women in the advanced age group are demanding prenatal diagnosis as a routine investigation. Unfortunately, existing facilities are far from adequate to cope with the demand for prenatal diagnoses in spite of the obvious benefits entailed. Serious efforts are, however, being made by the Department of Health and Welfare to contend with the demand which is at least ten times greater than the services which the present facilities can provide.

The cost to maintain a child with a severe mental handicap such as Down Syndrome in a State institution amounts to R4 000 per annum (excluding medicines which are needed regularly). Not all children with Down Syndrome are severely mentally retarded. If a life expectancy of 30 years is reached, which is not unusual, the total cost is at least R120 000 per person. In con-

trast the cost to the state of a chromosome investigation following amniocentesis is R43,00. If all pregnancies of mothers of 40 years and older were screened for a chromosome defect then at least one in every fifty investigations would reveal an affected child. The cost of fifty investigations amounts to R2 150. The monetary saving by screening could thus be more than R100 000 for every prenatal diagnosis of Down Syndrome. In South Africa an estimated 1 000 children with Down Syndrome are born annually. Health administrators have the arduous task of weighing up the benefits of a national prevention programme for Down Syndrome against the odds of combating malnutrition or providing spectacles to the indigent.

Health authorities in developed countries such as the Federal Republic of Germany have recently

accepted genetic services as an integral part of community health. A complete shift of emphasis in the priorities for health care programmes, especially primary prevention of specific handicaps, has taken place.

### **WHO DO YOU CONTACT FOR FURTHER INFORMATION?**

Genetic counselling clinics are available in the major centres. The fieldworkers of the genetic services of the Department of Health and Welfare are genetic sisters, trained to provide help and advice to families affected by genetic/hereditary disorders and birth defects. They can be contacted at the regional offices of the Department and serve as a central referral point in the community for all genetic aspects of health. This is a free service to the whole community.

## **DEPARTMENT OF HEALTH AND WELFARE**

### **Head Office**

Genetic Services, Department of Health and Welfare, Private Bag X63, Pretoria 0001. Tel (012) 482640 x 70 or 32.

### **Regional Offices**

The Regional Director of Health Services

Private Bag X19, Bellville 7530 — Tel. (021) 978151

P.O. Box 441, Bloemfontein 9300 — Tel. (051) 72194

Private Bag X54318, Durban 4000 — Tel. (031) 319381

P.O. Box 8623, Johannesburg 2000 — Tel. (011) 8362238

Private Bag X9395, Pietersburg 0700 — Tel. (01521) 6541

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