FRAGILE X SYNDROME: A FAMILY STUDY

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A research report submitted to the Faculty of Medicine, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the Degree of Master of Science in Medicine.

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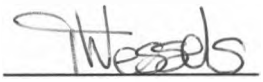
DECLARATION

I, Tina-Marié Wessels declare that this research report is my own work. It is being submitted for the degree of Master of Science in Medicine in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any other degree or examination at this or any other university.



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ABSTRACT

Fragile X syndrome is, second to Down syndrome, the commonest form of genetic mental retardation. The aim of this research project was to investigate the impact of having a child with this syndrome on the family relationships. The subjects were 21 mothers and 9 fathers of affected children. The data were collected by means of specially constructed questionnaires in interviews with 19 mothers and 8 fathers and completed by post in three cases. A control group of parents with a normal child, matched for sex and age of the affected child, family size and ethnic groups, was interviewed. The data were computerised and analyzed. The results showed that more experimental parents than controls enjoyed their child's nature, but disliked the behavioural problems. About half of the experimental parents tended not to reward good behaviour physically. However, although most of the affected children were accepted by their siblings, they had fewer friends and more problems with their peers. Some parents thought that their relationship with their spouse had improved and others thought that it had deteriorated after the affected child's birth. Most parents in both study groups would request prenatal diagnosis in subsequent pregnancies and significantly more experimental parents than controls would request a termination of pregnancy for an affected fetus. Most parents were satisfied with the health service they received. These results show that family dynamics are disturbed by the presence of a child with FMR. Counsellors and therapists working with these families should be aware of the effects of the syndrome on the family.

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LIST OF ABBREVIATIONS

bp:	Base pair (single pair of complementary nucleotides)
CCG-BP1:	Trinucleotide (CCG) binding protein
CpG island:	Cytosine rich, hypermethylated island adjacent to FMR-1
CVS:	Chorionic villus sampling
DNA:	Deoxyribonucleic acid (right-handed double helix)
DNHPD:	Department of National Health and Population Development
FMR-1:	Fragile X mental retardation-1 gene
FRAXA:	Folate sensitive fragile site associated with FMR
FMR:	Fragile X mental retardation syndrome
FMRP:	Fragile X mental retardation syndrome protein
IQ:	Intelligence quotient
kb:	1000 base pairs of DNA
mRNA:	messenger-Ribonucleic acid
NTM:	Normal transmitting male
p(CGG)n:	Nomenclature used for trinucleotide repeats
PCR:	Polymerase chain reaction
pH:	Measure of the alkalinity of a solution
PND:	Prenatal diagnosis
RNA:	Ribonucleic acid
SAIMR:	South African Institute for Medical Research
TOP:	Termination of pregnancy
Z-DNA:	DNA in the form of a left-handed double helix
60S:	One of the two subunits (60S & 40S) of the eukaryotic ribosome

CHAPTER 1

INTRODUCTION

1.1 MOTIVATION FOR THE STUDY

Fragile X syndrome (FMR) is one of the commonest genetic forms of mental retardation (second in frequency only to Down syndrome) and it is found in people of all ethnic groups (Heitz *et al.* 1992). It has a prevalence of about 1 in 1250 in males in the general population, about 1 in 500 females is a carrier, and about 1 in 5000 males is a non-penetrant carrier (Kirkilionis *et al.* 1992). It is thought to be inherited as an unusual X-linked dominant disorder with 30% of the carrier females showing some degree of mental retardation and 20% of males carrying the mutation with no phenotypic expression (Fu *et al.* 1991).

FMR also affects the physical appearance, speech and behaviour of the affected individuals. The intelligence quotient (IQ) in these affected individuals, ranges from 25 to 69 and mental incapacity seems to increase with age (Viljoen 1993). Of the female carriers, 30% are moderately mentally retarded, 18% are learning disabled, and 85% have an IQ of less than 85. The abnormal physical characteristics of affected individuals include elongated facies, large ears and macro-orchidism (Lachiewicz 1992). The language defect most often found is, perseverative language, which involves repetition of words, phrases, or topics of conversations (Sudhalter 1992). The social functioning of males with FMR is frequently characterized by autistic behaviour, attention problems, hyperactivity, impulsiveness, anxiety and self-injuring behaviour (Maes *et al.* 1992).

Being parents of a handicapped child is not a role people choose for themselves (Gargiulo 1985). The role is difficult, demanding, often confusing and demoralising. Furthermore, the birth of a disabled child may define the parents, to themselves and to others, as less capable of childbearing (Hollerbach 1979).

In adapting to the event of the birth and diagnosis of an affected child, research workers have found that the parents go through a programmed set of identifiable stages (Antley *et al.* 1984). These stages have been designated as depression, guilt, anxiety, bargaining and finally, acceptance. These stages highlight the main reactions of the parents in the process of adaptation, and all the models emphasize that no person moves through these stages discretely or sequentially (Cunningham and Davies 1985).

Parents of children with FMR might be expected to go through the same trauma, at the time of diagnosis, as families with other disabled children. However, very little research appears to have been carried out on families with a child with FMR, to explore whether this is in fact the case, or whether the relationships between the members of the family are altered by the presence of the affected child. Although prenatal diagnosis is available for at risk couples, whether they would use such a service does not seem to have been investigated.

Since FMR is one of the most common causes of mental retardation, it seems to be essential that the effects of the disorder on the various family members be studied. More appropriate services can then be provided for these families, based on the findings from such a study.

The Department of Human Genetics at the South African Institute for Medical Research (SAIMR) was conducting a molecular study on FMR. Families were therefore being ascertained and it was suggested by Prof JGR Kromberg and Dr A Krause, that a psychosocial study should be carried out simultaneously. This project appealed to me, since my own interest in FMR was stimulated by an article by Toufexis (1992) in the February 17, 1992 issue of TIME magazine entitled "The generational saga of the vicious gene" and as a genetic counselling student I am interested in the reactions of parents to their children and in assisting them in adapting to the event of the birth or diagnosis of a disabled child.

1.2 BACKGROUND TO THE STUDY

Studies on families with children with mental retardation (other than FMR) have been useful for providing a background for the present study. Cunningham and Davies (1985), Gargiulo (1985) and Turnbull and Turnbull (1986) investigated the needs of such families. They described the effects an affected child has on the siblings, on the mother and father, as well as on the marital relationship.

Byrne *et al.* (1988) and Gath (1978) reported on families with a child with Down syndrome. This group carried out a large study on children with Down syndrome, and investigated their activities, and relationships with friends, siblings, parents, as well as the families's activities. They found that 79% of mothers and their children with Down syndrome had a warm and affectionate relationship, 72% of Down syndrome children had a good relationship with their siblings and 73% had a good relationship with their friends. Gath (1978) investigated the effects the birth of a child with Down Syndrome had upon the parents, the marital relationship and the siblings and reported that 58% of parents had a good overall marital relationship and that there was no evidence that the affected child caused ill health in the normal siblings.

Very few studies on families with a child with FMR and on the dynamics of these families have been reported in the available literature. At the 1992 International FMR conference in the USA, a panel consisting of five parents discussed some of the issues of parenting an affected child (Brooks *et al.* 1992). They shared their personal experiences concerned with receiving the news of the diagnosis, the strengths of the fragile X child, the medical concerns, sibling relationships, and family planning.

Since it has been possible for FMR to be diagnosed by direct DNA analysis this technique has also been used for prenatal diagnosis of affected fetuses (Jenkins *et al.* 1992). The availability of these procedures could lead to an increased demand for prenatal diagnosis and selective abortion for the prevention of the birth of affected infants. Jenkins *et al.* (1992) have observed an increase in referrals in the USA since the introduction of the test, but the attitudes to prenatal testing for FMR in South Africa have not been explored.

1.3 THE AIMS

The aims of the study are to investigate:

1. The relationship between children with FMR and their parents, siblings and friends and the relationship between the parents of an affected child.
2. Parents' feelings about receiving the diagnosis in their child, prenatal diagnosis and selective abortion.
3. The professional help the parents used.

1.4 DESIGN OF THE STUDY

An exploratory research design was used for this study. The purpose of such a design is to explore and to build a foundation of general ideas which can be investigated later with more precise and complex methodologies (Grinnell and Stothers 1988). Due to time constraints and the need for an adequate sample the study was retrospective and spanned the years 1980 to 1996.

The first step of the study was familiarisation of the researcher with the topic. From the information obtained from a review of the literature, two interview schedules were constructed. One schedule was constructed which would be used to obtain information from the subjects with children with FMR and another (different in only some respects) to obtain information from the subjects in the control group. The subjects to whom these questions would be asked were chosen and a control group was selected. For the subjects in the Johannesburg area, the researcher and a trained research officer conducted interviews with mothers and fathers, separately, at their homes. For other subjects who lived too far to be interviewed personally, the interview schedule was used as a postal questionnaire. The data obtained from the interviews and postal questionnaires were computerised and analyzed. The results were presented, conclusions were drawn and finally results were compared with similar research available in the literature.

1.5 LIMITATIONS OF THE STUDY

There are some limitations in obtaining data from self-reports: the subjects may not be able to verbalise an answer, or admit to socially undesirable feelings or attitudes, they may misunderstand the questions, and may be unable to remember actual facts or feelings (Gochros 1988).

There are also limitations in obtaining data through an interview. When using a schedule of questions in a face to face interview, the interviewers may change the wording of questions, fail to ask a particular item, or negatively affect respondents' answers (Gochros 1988). Most interviewers record responses by summarizing them, and this practice has a high potential for error. Interviewers can also influence the respondents by non-verbal means, tone of voice, change in eye contact, or speed of questioning and by emphasis on difference words.

Postal questionnaires also have limitations (Bailey 1987): the interviewer is not present to motivate the respondent or to probe for a more specific answer, to correct misunderstandings, to observe the reactions of respondents, to ensure all questions are answered, or to obtain spontaneous answers. Low response are often found in postal surveys.

Small sample size, however, may present the main limitation on a study, since the findings may not be generalizable to larger series of families.

1.6 POTENTIAL USEFULNESS OF THE STUDY

In this study some of the psychosocial and familial aspects of the FMR will be explored and new insights on the topic obtained. These insights will provide professionals with a better understanding of the family dynamics in this situation. They should consequently be enabled to provide a more effective and appropriate counselling and support service. Also, the findings on the attitudes to prenatal diagnosis for FMR will be useful in providing genetic counsellors with a better idea of whether such a service is needed and

would be used and how it could be introduced.

In addition, this study will be useful in establishing the unmet needs of affected families for support and professional help and attempts can then be made by informed genetic counsellors to meet these needs or refer patients elsewhere for help. It would be gratifying if an outcome of the study was the initiation of a support group for affected families, should this need exist.

1.7 CLARIFICATION OF TERMS.

Certain terms used throughout this research report require clarification:

Amniocentesis

A technique for prenatal diagnosis, which involves the withdrawal of amniotic fluid and fetal cells from a pregnant uterus, and which is performed usually at 16 to 18 weeks of gestation (Connor and Ferguson-Smith 1991).

Anticipation

An increase in severity, and progressively earlier age of onset of a genetic disease in successive generations (Randall 1993).

Chorionic villus sampling (CVS)

A technique for prenatal diagnosis, which involves the obtaining of fetal tissue from the villous area of the chorion usually at 8 to 10 weeks of gestation (Connor and Ferguson-Smith 1991). In South Africa, CVS is usually performed at 10 to 12 weeks gestation.

Courtesy stigma

Stigma shared by family and friends as well as caregivers who are associated with the stigmatized (affected) individual (Cole 1993).

Dynamic mutations (Heritable unstable DNA)

A new and unusual type of DNA mutation called a trinucleotide repeat sequence. Once such sequences surpass a certain number of repeats they become highly unstable and are likely to amplify in the next generation (Randall 1993)

DNA

DNA (Deoxyribonucleic acid) is the molecule that encodes the genes responsible

for the structure and function of living organisms and allows the transmission of genetic information from generation to generation (Thompson *et al.* 1991).

Family

A dynamic system of interacting individual personalities (generally biologically related) who live together in a complex and changing society (Gargiulo 1985).

Fragile site

A non-staining region in one or both chromatids of a chromosome. In FMR this region requires certain culture conditions for its demonstration (Wolstenholme 1992). The fragile site in FMR is termed FRAXA.

Fragile X syndrome

Is the most common single recognised form of inherited mental retardation, which is characterized by an IQ typically in the range 35 to 60 and a triad of features: large everted ears, elongated facies and macro-orchidism (Hirst *et al.* 1993).

FMR-1

The fragile X mental retardation gene is the sequenced candidate gene for the FMR (Hagerman 1992).

Full mutation

The mutation which causes the FMR-1 gene to be switched off. Affected individuals have more than 200 copies of the trinucleotide repeat sequence and this is associated with mental retardation in males and in some females (Hirst *et al.* 1993).

Genetic counselling

Genetic counselling is the process by which patients or relatives at risk of a disorder that may be hereditary are advised of the consequences of the disorder, the probability of developing and transmitting it and of the ways in which the disorder may be prevented, avoided or ameliorated (Harper 1994).

Gel electrophoresis

The separation of linear DNA molecules according to size. The larger molecule will be retracted by the gel matrix (Adams *et al.* 1986).

Heterozygous (carrier) female

A female who has one Fragile X chromosome and one normal X chromosome. She may be unaffected or affected with FMR (Hagerman 1991).

Imprinting

Imprinting refers to a stable but non-genetic alteration to a chromosome that affects its subsequent function (Laird 1991).

mRNA

mRNA (messenger ribonucleic acid) is transcribed from the DNA of a gene and it directs the sequence of amino acids which are the building blocks of proteins (Klug and Cunning 1986).

Normal transmitting male

A male who carries the Fragile X mutation but is not affected by the syndrome and usually does not demonstrate the Fragile X chromosome on cytogenetic testing. These males produce obligate carrier daughters who are at high risk of having affected sons (Hagerman 1991).

Obligate carrier

A family member who, from the pattern of affected individuals within a family and what is known about the way in which a particular disorder is inherited, can be deduced to be a carrier (Parry 1993).

PCR

Polymerase chain reaction (PCR) is a technique used to amplify small amounts of DNA for diagnostic testing (Hagerman 1992).

Penetrance

Penetrance represents the percentage of individuals with the disease gene who show symptoms. If a condition is expressed in less than 100 percent of persons who carry the disease gene, it is said to have reduced penetrance (Thompson *et al.* 1991).

Pre-mutation

The first mutation in the FMR-1 gene, it is capable of rapid progression to full mutation. Individuals with this mutation have 50 to 150 copies of the trinucleotide repeat and do not show overt clinical problems (Hirst *et al.* 1993).

Prenatal diagnosis

In the context of this study prenatal diagnosis is the diagnosis of certain genetic disorders in the embryo and fetus, while it is still inside the womb (Connor and Ferguson-Smith 1991).

Psychosocial

Psychosocial refers to the interaction between characteristics of the social structure and the psychology of the individual; "the-person-in-his-situation". The situation refers to the environment of the individual and includes family, friends, employer, teacher and others (Hollis 1964).

Ribosome

A particle which is composed of RNA and protein (60S and 40S subunits) and at which translation of mRNA and protein synthesis takes place (Lawrence 1991).

Sherman paradox

The Sherman paradox is a special form of anticipation which refers to the increased risk of mental retardation in grandsons of normal transmitting males (Tarleton and Soul 1993).

Social support

Receiving practical and emotional assistance from extended family, friends, co-workers, and others in the community (Turnbull and Turnbull 1986).

Southern blotting

A method of transferring DNA from a gel to a nitrocellulose paper by means of capillary action (Adams *et al.* 1986). At present the use of nylon membranes are preferred to nitrocellulose paper.

Stigmatization

The stereotyping or labelling of an individual as deviant from the socialized expectations of normal (Cole 1993).

Syndrome

A combination of clinical features forming a recognizable entity (Harper 1994).

Trinucleotide repeat (CGG)

Three nucleotides, specifically cytosine, guanine and guanine, which occur in a repetitive fashion in the FMR-1 gene (Hagerman 1992).

X-Linked

The pattern of inheritance resulting from genes located on the X chromosome (Klug and Cunning 1986).

Xq27.3

Cytogenetic term used to describe the location of the Fragile site associated with FMR. This location is on the end of the long arm of the X chromosome (Hagerman 1992).

1.8 SUMMARY

This chapter serves as an introduction to the present study. It addresses the motivation of the study. Such a study is needed since very little research has been reported on interpersonal dynamics in families with a child with FMR. Also, since FMR is a common inherited cause of mental retardation and parenting a disabled child is a difficult and demanding task, it seemed worthwhile to study family aspects of this disorder, to see if there was anything specific in this situation that differed from that of other families with children with other disabilities or mental retardation.

Although the researcher was able to find only a few reports on the subject of family dynamics and FMR, other studies were available on families with children with Down syndrome and other types of mental retardation, and these reports were used as a background when the aims of this study were defined. The aims were broadly to study the relationship between FMR children and their family members and friends, the attitudes of parents toward prenatal diagnosis and selective abortion, and the professional help used by the affected families.

An exploratory research design was used, which served the purpose of exploring and building a foundation of general ideas. The limitations associated with the present study include inevitable errors in self-reported data obtained in both face to face interviews and postal questionnaires, and the likelihood of a sample size that could be quite small.

The potential usefulness of the findings from this study was also considered. Hopefully the findings can be used to enlighten genetic counsellors so that they can provide a more effective and appropriate counselling and support service for the affected families. Finally, this chapter also provided definitions of the terms used in the present study.

CHAPTER 2

REVIEW OF THE LITERATURE

2.1 INTRODUCTION

An excess of males among mentally disabled people has been observed in the early part of this century (Penrose 1938). With combined efforts from several researchers, FMR was described as a separate entity in 1977 to explain this observation. It is now well known that FMR is one of the commonest inherited causes of mental disability with a frequency of 1 in 1250 males. Further, FMR belongs to the newly discovered group of trinucleotide repeat disorders. These triplet repeats can lengthen in size, with longer repeat size being associated with more severe manifestation of the disorder (Sherman *et al.* 1985). In this chapter these findings will be described and discussed.

Individuals with FMR have characteristic physical features, mental retardation and behavioral problems. Since a family is a dynamic system of interacting individual personalities, having a child with such problems may have an effect on the family. However, before one can begin to comment on how disability affects the family, the family functions, the family lifecycle as well as the relationship between the family members should be understood. The literature in this regard will be presented below.

2.2 HISTORICAL BACKGROUND

Since the early part of this century, an excess of males has been noted among mentally disabled populations. In 1943, Martin and Bell report on an English family in which low intelligence was inherited as a X-linked trait and thereby explained the excess of males (Beighton and Beighton 1980). Later, in 1962, Renpenning and colleagues also reported a family who manifested X-linked mental retardation.

The association between some X-linked mental retardation and the fragile X-chromosome

was established in 1969 when Lubs reported on a three generation family with affected males and an unusual marker chromosome (fragile X-chromosome). Later in 1971 Escalante *et al.* reported on a family with X-linked mental retardation and macro-orchidism. It was only in 1977 however, when Sutherland demonstrated that the expression of the fragile site was dependent on the nature of the culture medium, that the association between X-linked mental retardation, macro-orchidism and the marker X chromosome was made. This led to the description of FMR as an entity separate from non specific X-linked mental retardation. The use of the term Martin-Bell syndrome is now reserved for the FMR, while Renpenning syndrome is used to refer to undifferentiated X-linked mental retardation (Beighton and Beighton 1980).

Continued research in the field of FMR has resulted in a better understanding of the syndrome (Hagerman 1992). It has emerged that FMR is the leading known cause, after Down syndrome, of mental retardation in boys with an incidence approaching 1 in 1000 and that the clinical picture ranges from severe mental retardation to learning disabilities, as well as depression and schizotypal features in carrier females or mildly affected females. A major breakthrough in FMR research was the isolation of the gene in 1991. Following this many of the puzzling features concerning the inheritance of the syndrome have been clarified (Hagerman 1992).

Regardless of the fact that the gene responsible for FMR has been characterized and its involvement in the clinical phenotype has been described, many of the aspects of FMR are far from being fully understood.

In South Africa, Venter confirmed the first FMR cases in June 1980 (Venter *et al.* 1981). This was part of a national screening program by the Genetics services division of the Department of Health, Welfare and Pensions. The aim of the screening program was to determine whether Martin-Bell or FMR occur in South Africa and to detect as many affected families as possible. The families were selected according to three criteria: mentally retarded males with a family history of one or more affected male relatives; mentally retarded males with obvious macro-orchidism; and mentally retarded males with facial characteristics of the syndrome (Venter *et al.* 1986). By 1981 Venter *et al.* had

identified the FMR abnormality, cytogenetically, in 55 affected males and 21 carrier females from 9 families. By 1986 they had diagnosed FMR in 21 families with 74 affected males and 59 carrier females and 28 obligate carrier females. Later on, with the availability of molecular testing, Goldman *et al.* (1997) working at SAIMR, Johannesburg, conducted an extensive research project on triplet disorders in South Africa. This research project presented the first molecular evidence that FMR occurred in the South African black population. As part of this study 148 unrelated black males, with mental retardation of unknown cause, from two institutions were tested for the CGG expansion. Out of the 148, 9 males or 6.1% had FMR with the CGG full mutation. In addition to testing individuals at institutions for the mentally disabled, several referrals were made to the SAIMR laboratory, which has offered a DNA diagnostic service for the detection of the CGG expansion since 1994. From these referrals, an additional 13 white, 11 black, 4 Indian and 3 mixed ancestry individuals were identified with the CGG expansion.

2.3 CLINICAL AND GENETIC ASPECTS OF FRAGILE X SYNDROME

2.3.1 CLINICAL PRESENTATION

2.3.1.1 Physical characteristics.

FMR is associated with a variety of subtle dysmorphic features, with females being less severely affected than males (Sutherland *et al.* 1993). Patients with FMR have a normal life span with delayed milestones (Jones 1988). Although no single physical characteristic always correlates with FMR, the classical triad of features includes mental retardation, long narrow facies and macro-orchidism (Lachiewicz 1992).

The most distinctive feature of FMR is the characteristic facial appearance, with long prominent chin, long and/ or narrow face and large abnormally shaped ears (Cianchetti *et al.* 1991) (see Fig 2.1). The long narrow facies is only apparent in 60% of affected males (Gorlin *et al.* 1990). Other facial features include: prominent jaw which becomes apparent

during adolescence, midface retraction and prominent forehead with marked supra-orbital ridges. Among the affected individuals, 50% have a high arched palate and 8% have a cleft lip and palate (Gorlin *et al.* 1990). A flat occiput is apparent in 61% of FMR patients and 47% have malpositioned teeth. The length of the palpebral fissures is usually increased and the nose is broad based. Among the carrier females, especially those who are retarded, 25-40% may demonstrate some of these facial features.

Fig 2.1 Two males with FMR, of different ethnic groups, showing the abnormal facies.

Another distinctive feature of FMR is changes in the genitalia. Testicular size may be increased in FMR males before puberty but is more obviously so after puberty (Jones 1988). Macro-orchidism or enlarged testes is a finding in 75% of affected adults males but in only about 40% of affected boys (Gorlin *et al.* 1990). The testes are softer than normal, the scrotum is hyperpigmented and the penis is enlarged in over 50% of males with FMR (Gorlin *et al.* 1990). Carrier females may have high fertility, higher frequency of twinning and an increased miscarriage rate (Gorlin *et al.* 1990). Enlargement of the

ovaries has also been noted (Hagerman and Sobesky 1989). Premature ovarian failure or premature menopause (before age 40) occurs in a few heterozygotes, but research findings are contradictory. Schwartz *et al.* (1994) have conducted a multicenter obstetrical and gynaecological survey of women in FMR families. Their analysis indicated that FMR carriers are more likely to enter menopause at a significantly earlier age and experienced more gynaecological problems than non-carrier women. Partington *et al.* (1996) and Vianna-Morgante *et al.* (1996) also found premature ovarian failure in FMR carrier females. Burgess *et al.* (1996) in Australia could not confirm these findings in their study in which they compared women with the full and pre-mutation to unaffected women.

Patients with FMR can also have connective tissue changes, such as joint laxity, especially of the fingers, knees and ankles (Gorlin *et al.* 1990). Hypermobility of finger joints are seen in 88.8% of males (Cianchetti *et al.* 1991). Some patients have been found to have somewhat lax, velvety soft skin, 40% have flat feet and over 80% of FMR patients over 18 years of age have mitral valve prolapse (Cianchetti *et al.* 1991). Hyperextensible finger joints and voluntary thumb dislocation are frequent findings among impaired affected females, but are also seen in 20% or more of normal functioning carrier females (Cronister *et al.* 1991a).

Occasional abnormalities associated with FMR include ocular abnormalities and seizures. Several authors have noted a high incidence of strabismus, refractive errors and other ocular abnormalities (Maino and King 1992). Hecht (1991) has found that the association between the syndrome and seizures appears to be mostly unrecognized and that seizures are common and can begin as early as the neonatal period. Musumeci *et al.* (1992) found a significant correlation between the percentage of fragile X cells in the karyotype and the occurrence of seizures, with a high percentage of Fragile X cells correlating with high occurrence of seizures.

2.3.1.2 Cognitive profile

The most obvious symptom of FMR in males is mental retardation which varies from moderate to severe (Freund and Reiss 1991). The IQ in affected males ranges from 25-69,

with 75% of affected males however, having an IQ of less than 39 (Gorlin *et al.* 1990). Among female carriers 30% are moderately mentally retarded and 15% manifest some form of learning disability.

Several studies conclude that boys are less mentally impaired than adult male patients (Fisch *et al.* 1991, Wiegers *et al.* 1992), and that a decrease in IQ score occurs with increasing age. This decrease is particularly noticeable between the ages of 8 and 13 years. It seems that late childhood and the onset of puberty are critical periods, since if there are IQ changes they are mainly observed in that age group. IQ changes have also been noted in the general mentally retarded population but these are not as dramatic as in the FMR group. Preliminary results from a multicenter study indicate that declines in IQ scores occur in both males and females with FMR (Fisch *et al.* 1994). There appears to be no significant difference in the degree of the decrease in males as compared with females.

Mental retardation in the range found in FMR makes identification of strengths and weaknesses difficult. However, it has been demonstrated that males have more verbal strengths than weaknesses (Freund and Reiss 1991), that they have an achievement ability that exceeds their cognitive ability (Braden 1992b) and that their verbal intelligence exceeds their performance abilities (supported by psychometric tools such as the picture vocabulary and block design tests) (Fisch *et al.* 1991, Turk 1992). Affected males have strengths in long-term memory, language syntax, achievement (spelling and reading) and they have weaknesses in visual and motor skills, arithmetic and attention (Braden 1992b). They may also have difficulty with number concepts but have consistent strengths in vocabulary and early reading skills (Freund and Reiss 1991). Affected males may have greater difficulty in processing novel information than in learning school related, verbally based factual material (Turk 1992).

2.3.1.3 Language systems

The development of speech and language are almost always retarded in affected males and their defect may range from absence of speech to mild communication difficulties (Turk

1992). Fragile X boys may only utter single words until after 2 years of age, and phrases and short sentences may be delayed until 3 years of age (Hagerman 1989). Some males may be completely non-verbal and these males are usually severely retarded.

The majority of FMR males have a rather characteristic speech pattern which can be described as jocular, litany, or staccato speech (Hagerman and Sobesky 1989). A fast and fluctuating rate of talking with repetitions of sounds, words and phrases, and occasional garbled, slurred or disorganised speech in the presence of poor topic maintenance are characteristic FMR speech patterns (Turk 1992).

One of the most characteristic language deviances is perseverative language which is the repetition of words, phrases or topics of conversation (Sudhalter 1992). This language pattern may be caused by an underlying social anxiety, since FMR males have a heightened sensitivity to social gaze (Sudhalter 1992). However, deviant language was also observed when adults were not looking at children, indicating that eye contact is not the only cause for the emergence of abnormal language.

In a study done by Spinelli *et al.* (1995), word-finding difficulties were reported in 50% of patients with FMR. There is also initial evidence that these males have difficulty blocking impulsive responses and this may also be a cause of the production of perseverative language (Sudhalter 1992). Affected individuals may have difficulty inhibiting the activation of high associates, thus forcing miscomprehensions of sentences containing high associate compounds. High associate compounds are paired words, for example, birds and feathers. If an affected child is asked: "do birds see with their feathers?" The child is fooled into answering yes, because birds and feathers go together, although the answer is no.

2.3.1.4 Behavioral characteristics

The social functioning of FMR males has been extensively described and it is characterized by autistic behaviour, attention problems, hyperactivity, impulsiveness, anxiety and self-injuring behaviour (Maes *et al.* 1992).

Hyperactivity and attention deficits are behavioral problems associated with the majority of mentally retarded FMR males (Fisch 1993). Hyperactivity is often the presenting problem in an affected child, it begins early in childhood and is associated with a short attention span (Hagerman and Sobesky 1989). The child's attention jumps from one area of interest to another within minutes or seconds and the child appears disorganized and impulsive. Severely affected children with hyperactivity may go on to develop a major psychiatric disorder with a mixture of symptoms of mania and depression (Levitas 1992).

Another feature associated with the syndrome is autism. Autism can be described by the following four criteria: early age of onset, impaired social development, deviant language and stereotyped behaviour (Schopler and Dalldorf 1980). There is some confusion in the literature concerning the association of autism and FMR (Hagerman *et al* 1986b). Several researchers have demonstrated the association of autism with FMR (Eg. Hagerman *et al* 1986b, Cianchetti *et al.* 1991, Cohen *et al.* 1991, and Cohen 1992, Maes *et al.* 1992, Fisch 1993), whereas Venter *et al.* (1984) and Einfeld *et al.* (1994) were unable to substantiate these findings.

The association of autism with FMR appears to be confounded by the autistic-like behaviour seen in affected males (Fisch 1993). They may show more autistic features such as avoidance of eye contact, resistance to being touched or held, hand flapping, insisting on keeping certain objects close by, reacting strongly to changes in the environment or routine, and frequently being unaware of their surroundings or oblivious to dangerous situations (Maes *et al.* 1992). They may also repeat phrases, avoid reaching out when reached for, throw severe temper tantrums, be unable to wait for their needs to be met, and they may feel, taste or smell objects (Braden 1992a). They may also overtly turn the body away during social interaction, show repetitive motor movements characterised by anxious rubbing of the body and rocking or hand flapping (Sudhalter 1992). Fisch (1993) concluded that while autism and autistic-like behaviours are observed in mentally retarded FMR males, it is unlikely that the Fragile X abnormality is a causal factor.

The association between FMR and autism has been described in males, but this has not been systematically examined in affected females (Bolton *et al.* 1989). Only four females

with FMR and autism have been described; Hagerman *et al.* (1986a) and Bolton *et al.* (1989) each reported two affected women.

2.3.2 NORMAL TRANSMITTING MALES

The phenotype of the most severely affected individuals has been well described. In contrast, the phenotype of male and female carriers of the gene who have been considered clinically unaffected has been less well described (Dorn *et al.* 1994). The so-called carrier males have been regarded as being cognitively or mentally unaffected (Laird 1987).

Dorn *et al.* (1994) appear to have been the first to investigate the incidence of behavioral and psychiatric disorders among males who carry the Fragile X pre-mutation. They found that obsessive compulsive disorder behaviours occur with greater frequency in normal transmitting males (NTM) relative to controls, and that 46% of normal transmitting males versus 13% of controls show behaviour that meets the DSM-III-R criteria for alcohol abuse or dependence. Also, twice as many normal transmitting males as controls were reported to show verbally abusive behaviours, three times as many had been physically abusive to their spouses and four times as many had panic disorder and antisocial personality problems. Since Loesch *et al.* (1994) also found that normal transmitting males showed differences in typical facial traits when compared to normal controls, they suggested that the term "low expressing males" rather than "normal transmitting males" should be used.

Although the findings support the hypotheses that some carrier males may be mildly affected and that there may be a broad spectrum of involvement among fragile X carrier males, additional investigation is required.

2.3.3 THE FRAGILE X FEMALE

Female carriers of the FMR appear to have a broader spectrum of phenotype than males, ranging from mental retardation to learning disability to cognitively unimpaired (Miezejeski and Hinton 1992). The degree of mental retardation however, is usually less; females have milder and fewer behavioral problems and the dysmorphic features are less obvious

(Sutherland *et al.* 1993). Carrier females, with normal intelligence, but an increase in psychiatric symptoms, particularly schizophrenic disorders, have also been described.

2.3.3.1 Nature of cognitive deficits

Cronister *et al.* (1991b) estimated that obvious mental impairment, with retarded or borderline low IQ, occurs in approximately 35% of carrier females, although this figure might be as high as 55%. However, female carriers with normal IQs may have learning disabilities (Cronister *et al.* 1991b and Fisch 1993). Learning disability is a term used to identify a characteristic profile observed among individuals who possess academic performance that is marked by arithmetic disability in the presence of adequate reading and spelling (Miezejeski and Hinton 1992). FMR females with normal IQs have also been shown to have strengths and weaknesses in short-term memory (de von Flindt *et al.* 1991, Freund and Reiss 1991). The weaknesses, associated with abstract visual information, and the strengths, with meaningful visual information, are the same as those recorded for males (Freund and Reiss 1991).

Several authors have reported that there are cognitive differences between women with cytogenetic expression of the Fragile X chromosome and women with no cytogenetic expression (Brainard *et al.* 1991, Mazzocco *et al.* 1992, Hinton *et al.* 1992 and Mazzocco *et al.* 1993). The results of a study done by Hinton *et al.* (1992) showed that the women in the lower IQ maternal inheritance group (cytogenetically expressing the fragile X chromosome) did not perform as well on attentional and abstract visual spatial tests, as the other FMR women and the controls. They reported that memory skills appear to be relatively strong and visual spatial and attention skills appear to be relatively weak in cytogenetically expressing FMR women.

A similar study done by Mazzocco *et al.* (1993) also found specific deficits among cytogenetically expressing women as a group. These included: deficits in attention and visual spatial abilities and deficits in "executive function" (frontal deficits), which include planning, mental flexibility in problem solving, the ability to simultaneously consider many pieces of information when problem solving, and abstract reasoning. These deficits were

not seen among obligate carriers.

Similar differences were observed between women with the pre-mutation and women with the full mutation (Sobesky *et al.* 1994b). The latter group had problems with executive function skills and demonstrated nonverbal, spatial and memory deficits, while the women with pre-mutations did not demonstrate these cognitive deficits.

2.3.3.2 Emotional Phenotype

Emotional problems have been documented in normal IQ FMR heterozygotes (Cronister *et al.* 1991a) and these include chronic affective disorders, schizotypal features, depression and shyness in childhood (62%). Cognitively affected heterozygotes may occasionally demonstrate autism and many are shy (83%).

Psychiatric disturbance, consisting of social disability, odd communication patterns, and chronic depression have been reported to be present in a proportion of FMR females (Reiss *et al.* 1993). It was found that female carriers were more likely to show signs of long term difficulties with: social and interpersonal skills (beginning in childhood), expression and modulation of affect, unusual thought content with conceptual disorganization, and language expression (Reiss *et al.* 1989).

Several researchers have compared the heterozygous females with controls in order to assess the differences (Reiss *et al.* 1989, Sobesky *et al.* 1992, Sobesky *et al.* 1994a and Sobesky *et al.* 1994b). Sobesky *et al.* (1992) studied emotional features of FMR females, and compared those with more than 3% fragility and who are DNA positive, with other females with no fragility (also DNA positive), and with controls. Cytogenetically positive carriers are likely to have problems with depression and/or display schizotypal spectrum behaviours (Fig 2.2 shows DSM-III-R criteria for schizotypal behaviour), minimize problems and possible be more socially isolated as children and adults. They found no statistically significant differences between cytogenetically negative carriers and controls.

Five of these nine criteria are necessary for a diagnosis:	
1.	Ideas of reference: e.g., feelings of being watched, seeing meaning in events ("it was meant to be"), remarks often have personal implications.
2.	Excessive social anxiety.
3.	Odd beliefs or magical thinking.
4.	Unusual perceptual experiences (e.g., illusions).
5.	Odd or eccentric behaviour or mannerisms.
6.	No close friends or confidants.
7.	Odd speech.
8.	Inappropriate or constricted affect.
9.	Suspiciousness.

Fig 2.2 DSM-III-R criteria for schizotypal spectrum behaviours (American Psychiatric Association 1987).

Reiss *et al.* (1989) studied the paternal (inherited FMR from the father) versus maternal inheritance group (inherited FMR from the mother) and found significant differences between the two groups. All cases of positive fragility occurred in the maternal inheritance group. The maternal inheritance group have a greater magnitude of schizophrenia spectrum symptoms, social disability in adolescence, more time missed from work because of psychological problems, and higher ratings for general psychopathology than paternal inheritance or control groups.

Sobesky *et al.* (1994a) studied women who expressed the FMR chromosome cytogenetically and who displayed a full mutation on DNA. They controlled for the possible FMR developmental experience as well as the stresses of raising a child with developmental problems. Women with a full mutation display difficulties in thinking and relating affect even when cognitive deficits were controlled for. Sobesky *et al.* (1994b) found that full mutation women have elevated lie scales, which capture a tendency to endorse items that most people would recognize as "too good to be true". This suggests an unrealistic view of one's self or the failure to recognize that others would be likely to doubt the accuracy of such statements. They also stated that full mutation women display a "blinders" effect in interviews. That is, they often do not integrate past information into their current situation in responding to inquiries, for example if they are not currently depressed, they will report that they have never had symptoms of depression.

Pre-mutation women were rated as significantly more emotionally labile than women without the gene who grew up in FMR families (Sobesky *et al.* 1994a). Pre-mutation

women were different from full mutation women in that they reported themselves to be more socially sensitive and socially anxious than did full mutation women. Full mutation women were more odd in appearance and less organised in thinking than other women, and they were more gaze avoidant and more inappropriate in affect. Pre-mutation women as a group were more socially sensitive and socially anxious. The frequent occurrence of dysthymia, anxiety, cyclothymia, and phobias suggests a mood instability problem in FMR women that may be associated with the presence of the pre-mutation. However, statistical significance of the results varied depending on whether age and IQ were co-varied. All differences between FMR and control groups may be partly because of differences in intellectual ability between the groups and not directly due to the FMR-1 gene. This proposal is confirmed by the fact that there is substantial evidence to the effect that psychiatric dysfunction occurs relatively frequently in mentally retarded individuals, regardless of cause (Fisch 1993). Epidemiological studies indicate that major psychiatric disability, schizophrenia, emotional problems, depression and hyperactive chronic mood disturbances occur in many mentally retarded individuals. It seems that psychiatric disabilities appear to be confounded with mental retardation or learning disability and may not be associated specifically with FMR (Fisch 1993).

2.3.4 THE GENETICS OF FRAGILE X SYNDROME

FMR is the most common inherited cause of mental retardation (Heitz *et al.* 1992). Initial reports estimated the prevalence to be 1/2000 males with a carrier frequency of 1/1000 females (Turner and Jocobs 1983). Morton *et al.* (1995) believed the incidence to be less than 1/2197 in school age children between 11 and 16 years. More recently, Turner *et al.* 1996 reported a frequency of 1/4000 males. The syndrome is associated with a fragile site or break on the long arm of the X chromosome (Hagerman 1991) and the gene responsible for the clinical phenotype is called the Fragile X Mental Retardation-1 gene (FMR-1).

On the cytogenetic level, FMR is characterised by a fragile site on the X-chromosome (Sutherland 1977) (see Fig 2.3). The fragile site, Xq27.3, is only expressed when cells are cultured under specific conditions. Medium deficient in Folate or Thymidine can be

used to culture the cells in order to induce expression of the Fragile site (Tarleton and Saul 1993). However, it has been found that not all of the cells in affected individuals express the fragile site. NTMs and a significant percentage of carrier females have no detectable cytogenetic abnormality.

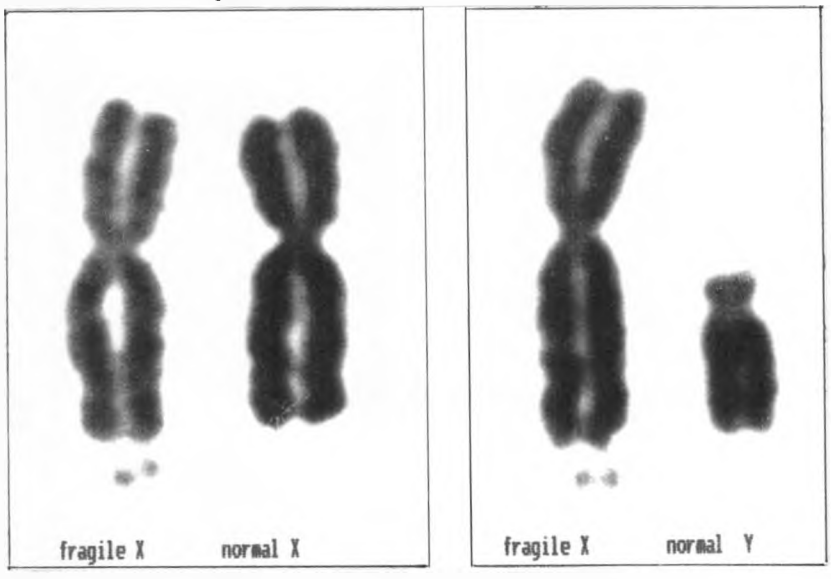

Fig 2.3 The X-chromosome showing the fragile site.

It is thought that FMR is inherited in a X-linked fashion, but the unusual segregation patterns (the existence of unaffected carrier males, and the increased risk of mental retardation in male or female offspring of daughters of these males) cannot be explained. With the discovery of the FMR-1 gene, at position Xq27.3, and the unusual DNA sequence located within the gene, the first clues to many of the mysteries of the FMR were provided (Tarleton and Saul 1993).

2.3.4.1 Molecular defect

The FMR mutation is localized to a small region on the X chromosome, Xq27.3 and the syndrome is caused by the genetic mechanism termed heritable unstable DNA (Heitz *et al.* 1992, Sutherland *et al.* 1993). The unstable DNA is found within the 5' untranslated region of the FMR-1 gene (Fu *et al.* 1991, Kremer *et al.* 1991, Verkerk *et al.* 1991 and Yu *et al.* 1991).

The first exon of the FMR-1 gene contains the triplet repeat (CGG), which lengthens in

FMR patients (see Fig 2.4). Hirst *et al.* (1993) found the stable repeats to be between 15-50, while Sutherland *et al.* (1993) found them to number between 6 and 60. The precise copy numbers which distinguish the categories of normal, pre-mutation and full mutation are not yet known. On the Fragile X chromosome the triplet repeat can exist in two states, the pre-mutation state and the full mutation state (Hirst *et al.* 1993). Hirst *et al.* (1993) found the pre-mutation state to have between 50 and 150 repeats while Sutherland *et al.* (1993) found it to have between 60 and 200 repeats.

The number of repeats of the p(CGG)n repeat correlates strongly with the clinical phenotype and/or the rate of FMR expression. NTMs and asymptomatic carrier females have between 50 and 200 p(CGG)n repeats (pre-mutation range) and are cytogenetically negative (Viljoen 1993). As soon as the repeat size is greater than 200 (full mutation range) the males are affected and cytogenetically positive, but the females can be either normal or affected. The size of the pre-mutation is a major determinant of the risk of transition from pre-mutation to full mutation and this transition appears to occur only after transmission through a female (Heitz *et al.* 1992).

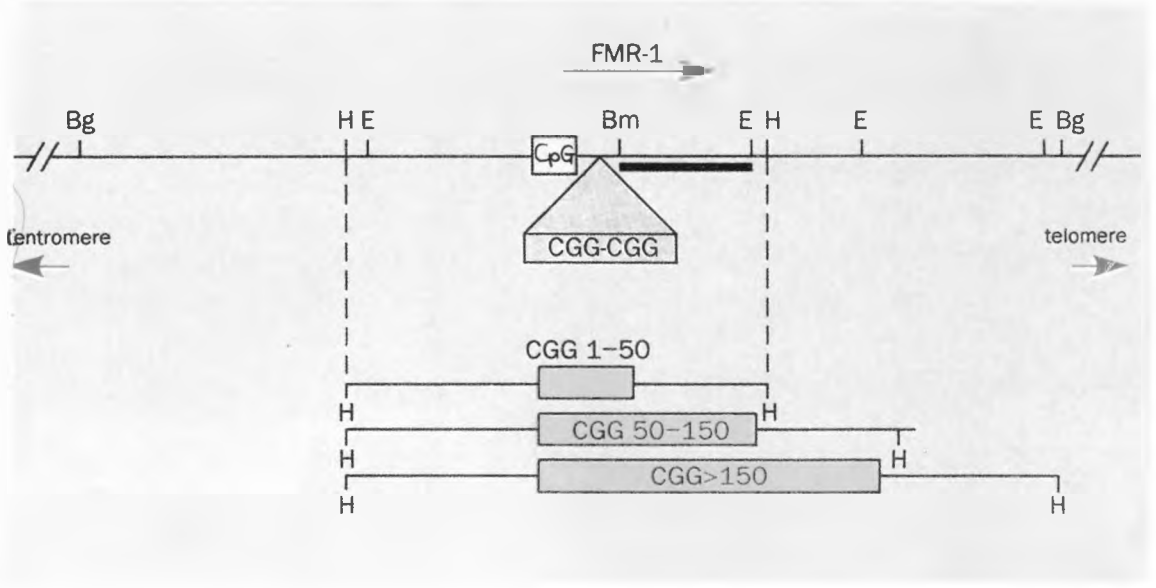

Fig 2.4 **The FMR-1 gene showing the site of the CGG repeat sequence (Hirst *et al.* 1993)**

A CpG island adjacent to the p(CGG)n repeat, has been discovered and has been shown to be associated with methylation (Heitz and *et al.* 1991 and Hori *et al.* 1993). There seems to be a correlation between the degree of amplification of the p(CGG)n repeat and the hypermethylation of the CpG island. Sutherland *et al.* (1993) found that when there are more than 200 copies of the CGG repeat the DNA becomes methylated, which then causes inactivation of the FMR-1 gene. Fu *et al.* (1991) also found that methylation of the CpG island correlates with loss of expression of the FMR-1 gene. A study done by Hagerman *et al.* (1994) showed that males with the full mutation who show unmethylated mutations have increased levels of FMR-1 and have higher cognitive functioning.

2.3.4.2 Inheritance pattern

FMR is an unusual X-linked disorder with 30% of the carrier females showing some degree of mental retardation and 20% of males carrying the mutation with no phenotypic expression (normal transmitting males) (Fu *et al.* 1991) (Sutherland *et al.* 1993). Its inheritance has been described as X-linked dominant with reduced penetrance by Tarleton *et al.* (1992), and Tarleton and Saul (1993), Viljoen (1993).

The non-Mendelian aspects of the inheritance pattern of the syndrome give it a unique place in human genetics, and the phenomenon is described as the Sherman paradox (Richards and Sutherland 1992). This paradox was first described by Sherman *et al.* (1985) who undertook a segregation analysis of 96 pedigrees of families with FMR. The Sherman paradox explains the most striking deviation from normal X-linked inheritance, the existence of NTMs. The daughters of the normal transmitting males are obligate carriers and generally have normal intelligence, but are at high risk of having affected sons. The carrier mothers of the normal transmitting males have less chance of having mentally retarded offspring than do the unaffected carrier daughters (Fu *et al.* 1991, Kirkilionis *et al.*1992 and Sutherland *et al.* 1993).

The Sherman paradox also accounts for some of the other observations: mentally retarded female carriers are more likely to have mentally retarded offspring than are intellectually normal female carriers (Hirst *et al.* 1993); the probability that a child with a fragile X-

chromosome will be mentally retarded depends on the sex and intellect of the parent transmitting the fragile X-chromosome; and, affected females receive the FMR mutation from their mothers and not their fathers (Richards and Sutherland 1992).

Since it has been observed that affected individuals receive the fragile X-chromosome only from their mothers, the question has arisen as to when the expansion of the pre-mutation to the full mutation occurs. Reyniers *et al.* (1993) suggest that the expansion of pre-mutation to full mutation occurs during maternal meiosis. Since they found that FMR male patients with the full mutation in somatic cells only have the pre-mutation in their sperm, it was suggested that the full mutation must regress to the pre-mutation in gametes of affected males. Wöhrle *et al.* (1993) suggested that carrier parents always pass on a pre-mutated FMR-1 allele to their offspring, regardless of the FMR genotype of the transmitting parent, and that the large expansion of the pre-mutated CGG repeat to full mutation takes place in a particular window of early development in the embryo, exclusively on maternally derived X chromosomes.

This phenomenon is illustrated by a family described by Hori *et al.* (1993). The authors have described a male with a full mutation (1000-1500) who had three daughters with pre-mutations (200-300bp), who then had affected children (two males and one female).

2.3.4.3 The FMR-1 protein

It remains unclear whether the amplification of the p(CGG)n repeat and hypermethylation in FMR patients is responsible for the clinical abnormalities solely by impairing the function of FMR-1 (De Bouille *et al.* 1993). It was suggested that the hypermethylation of the CpG island might down regulate adjacent genes or that there could be more than one gene affected (De Bouille *et al.* 1993).

Pieretti *et al.* (1991) have endeavoured to ascertain the levels of FMR-1 mRNA in FMR patients, carriers, and normal controls. They found that 16/20 FMR patients did not express FMR-1 in leucocytes, while normal males and females, normal members of FMR families and heterozygous females all expressed the transcript. They also found that the

fragment is completely methylated in all FMR-1 deficient patients. It is therefore possible that the lack of expression of the FMR-1 gene accounts for at least part of the FMR, although one cannot exclude the possibility that regulation of more than one gene at this location is altered owing to methylation of the region.

The involvement of the product of the FMR-1 gene in the etiology of FMR has been investigated. Researchers have found that the FMR-1 sequence is transcribed in a wide variety of tissues. According to Hanzlik *et al.* (1993), FMR-1 is expressed in human fetal brain, the spinal cord, the eye, the liver, skeletal muscle, adult jejunum and in fetal kidneys. Abitbol *et al.* (1993) found that FMR-1 mRNAs are expressed in proliferating and migrating cells of the nervous system, in the retina, and in several non-nervous tissues in 8 and 9 week-old fetuses. Hinds *et al.* (1993) demonstrated by *in situ* studies that FMR-1 is expressed during early stages of development. It has therefore been suggested that FMR-1 fulfils an important functional role during embryogenesis in numerous tissues and particularly in the central nervous system which, if disrupted, could result in developmental abnormalities (Hinds *et al.* (1993). This is consistent with FMR, which may present at a very early age as an overgrowth syndrome, accompanied by emotional, behavioral and cognitive deficits that perhaps could stem from inadequate gene expression during development.

Inadequate gene expression of FMR-1 does not only result from the presence of an amplified trinucleotide repeat. Several authors have described patients with the syndrome who lack the fragile site and the CGG repeat. For example, Gedeon *et al.* (1992) described a patient that had a deletion encompassing the CGG repeat, the entire FMR-1 gene and about 2.5 megabases of flanking sequences.

Wöhrle *et al.* (1992) presented evidence of a mentally retarded male, suspected to have FMR, with a deletion at Xq27.3. The deletion included the CpG island, the adjacent exon including the putative fragile site (CGG repeat), and at least three proximal exons of the cDNA clone. Trottier *et al.* (1994) also reported a patient with a typical FMR phenotype who had a deletion similar to that found by Wöhrle, only 100Kb smaller.

De Bouille *et al.* (1993) reported a single point mutation in the open reading frame of FMR-1, which was not found in 130 control X chromosomes, suggesting that mutations in FMR-1 can be responsible directly for FMR. The mutation was discovered in a FMR patient with very severe mental retardation and macro-orchidism, who had a repeat number within the normal range of 5-54.

These findings confirm that there are intragenic FMR-1 mutations different from the classical (CGG)n expansion and that the FMR phenotype can exist, without amplification of the CCG repeat or cytogenetic expression of the Fragile site (Gedeon *et al.* 1992).

Chiurazzi *et al.* (1994) reported 5 patients with FMR or Martin-Bell phenotype, who do not show amplification of the CGG repeat or any mutation in the FMR-1 gene. They suggested that there are other mutations that might be the cause of a Fragile X phenotype without any change in the FMR-1 gene. One explanation is that a specific protein (CCG-BP1), which binds to unmethylated CGG repeats, is part of the molecular pathway leading to the development of the FMR. Mutations in the CCG-BP1 could affect the binding to a normal size CGG repeat and cause the same phenotype as seen in patients with the CGG repeat amplification. Studies on the function of the CCG-BP1 and on the RNA binding activities of FMR-1 protein (FMRP) might clarify their involvement, if any, in the development of the Fragile X phenotype in the absence of mutations in the FMR-1 gene.

Further studies revealed that FMRP is a RNA-binding protein of unknown function (Eberhart *et al.* 1996). Khandjian *et al.* (1996) found that FMRP binds to the ribosomal 60S subunit and they therefore proposed that FMR may result from altered translation of transcripts which normally bind to FMRP. Eberhart *et al.* (1996) confirmed these finding when they found that the FMRP contained nuclear localization and export signals.

2.3.4.4 Proposed mechanisms of inheritance of fragile X syndrome

(i) Methylation

Several researchers have investigated the association of methylation with FMR, specifically

the methylation status of the CpG island, which is proximal to the p(CCG)n repeat. Hori *et al.* (1993) reported that the degree of methylation in the CpG island correlates with the increased sizes of the unstable DNA sequence. When the DNA sequence is less than about 600bp, the methylation status of the CpG island is normal, but amplification of the sequence beyond this size results in hypermethylation. Oberlé *et al.* (1991) found that the CpG island is totally methylated in most Fragile X males, methylated only on the inactive X chromosome in females and unmethylated in normal transmitting males.

Exactly when the abnormal methylation occurs is not known, but it may happen early in embryogenesis. This suggestion is supported by the finding that in chorionic villi the full mutation is, in general, methylated, whereas the normal inactive X is in general unmethylated at the CpG island (Heitz *et al.* 1992 and Hori *et al.* (1993).

Although there is a positive correlation between the degree of amplification of the p(CCG)n repeat and methylation of the CpG island, the relationship of methylation to the fragile X genotypes and instability is not clear. Some of the possible hypotheses include: methylation may have a role in the expression of genotypes by inhibiting expression of FMR-1 (Hori *et al.* 1993); methylation in the CpG island may be a consequence of amplification of the CCG repeat, as amplification produces many additional targets for methylation; and methylation may alter the DNA structure (abnormal conformation, Z-DNA) around the FMR region, which in turn affects the DNA replication processes (Oberlé *et al.* 1991, Heitz *et al.* 1992 and Hori *et al.* 1993).

(ii) Founder effect

FMR is one of the most common human genetic diseases (Richards *et al.* 1992). Since FMR patients generally do not reproduce the FMR-1 mutation would be expected to gradually disappear out of the population. A high mutation rate has been proposed to explain its high frequency (Buyle *et al.* 1993 and Smits *et al.* 1993).

Haldane's theory (there should be a balance between the loss of deleterious X-linked genes because of impaired reproduction, and the gain of cases because of new mutations) also

favours the fact that many new mutations must continuously arise (Buyle *et al.*. 1993). However, several authors found no evidence for the presence of new mutations in FMR families (Chakravarti 1992, Richards *et al.* 1992, Buyle *et al.* 1993 and Smits *et al.* 1993).

Because FMR is characterised by these two apparently contradictory properties, reduced reproductive fitness with high frequency of the mutation, and no new mutations, it has been suggested that FMR mutations are the result of a founder effect (Chakravarti 1992). Richards *et al.* (1992) suggested a founder effect in American and Australian populations and Buyle *et al.* (1993) suggested a founder effect within the Belgian-Dutch population.

The possible existence of a founder effect suggests that a few ancestral mutations are responsible for most of the patients with FMR today (Buyle *et al.* 1993). It also implies a high frequency of the pre-mutation in the general population.

A possible explanation for the founder effect and high frequency of pre-mutations is discussed by Chakravarti (1992). It is suggested that there are four types of alleles at the fragile X locus: N-normal, S-stable insert, Z-unstable insert and L-full mutation. The N allele may have mutated to allele S which is old and polymorphic. This suggests that many individuals carry this silent pre-mutation which constantly occurs but is rarely observed because it is not associated with any abnormal phenotype. Allele S then converts to Z at a rate of 1.1% per generation and the L allele arises only from Z via the female germ-line at the remarkably high rate of 74%. The conversions of S to Z and Z to L are very common with an average age of less than 2 generations and are routinely observed in families. So the fragile X mutation is not a single step change but a multistep process. This model explains the high frequency of the FMR mutation, the founder effect and the absence of new mutations.

2.3.5. DIAGNOSTIC TESTING FOR FRAGILE X SYNDROME

2.3.5.1 Cytogenetic methods

FMR is associated with a folate sensitive fragile site, called FRAXA, on the X-chromosome at position q27.3 (Wang *et al.* 1993). There are two other fragile sites close to FRAXA, one at position Xq27.2 (FRAXE) and the other at position Xq28 (FRAXF), which are not associated with the syndrome (Sutherland *et al.* 1993).

The detection of the fragile site on the X-chromosome is the basis for cytogenetic laboratory diagnosis (Viljoen 1993). The fragile site is not spontaneously expressed on the X chromosome and is only evident in chromosomes obtained from cells grown in a folate deficient medium at an elevated pH for up to 26 hours. The folate deficient medium leads to a relative deficiency of either thymidine or deoxycytidine at the time of DNA synthesis and ultimately results in the expression of the fragile site (Sutherland *et al.*. 1993).

Being able to induce the fragile site, does not guarantee the diagnosis of FMR. It was shown that not all patients with FMR express the fragile site cytogenetically. Literature reports reveal that FRAXA is only expressed in 5 to 50% of lymphocytes of affected males and in less than 15% of obligate carrier females (Viljoen 1993). Individuals with a copy number of fewer than 200 p(CGG)n repeats do not express the fragile site cytogenetically (Sutherland *et al.* 1993). This means that the normal transmitting males and mentally normal carrier females can not be identified using the cytogenetic method.

Jenkins *et al.* (1992) in the USA reported false negative findings (13 of 250 cases) with the cytogenetic test. The authors suggested that the use of multiple fragile site induction systems, the number of cells analyzed, the number of flasks analyzed and, the type of culture medium were critical for the prevention of false negatives.

Although the cytogenetic test is not very reliable and is also labour intensive, it should not be ruled out completely (Wang *et al.* 1993). It is still good practice to do routine

karyotyping as part of the diagnostic work-up, since other significant chromosome causes of mental disability can be detected (Sutherland *et al.* 1993).

2.3.5.2. Molecular methods

Direct DNA analysis of the fragile X mutation has become available with the isolation of DNA probes that detect the unstable DNA sequence containing the CGG repeat (Oostra *et al.* 1993). The number of these repeats as well as the methylation pattern of the adjacent CpG island can be determined using molecular genetic techniques.

The length of the CGG triplet can be detected by Southern blot analysis or the polymerase chain reaction (PCR) (Sutherland *et al.* 1993). Southern blot analysis involves the digestion of the DNA with different restriction enzymes and separating the fragments by gel electrophoresis (Oostra *et al.* 1993). For the status of the CpG island, several probes can be used to detect its abnormal methylation.

The size of the CGG repeat and the presence of abnormal methylation appears to determine the phenotype (Oostra *et al.* 1993). A normal phenotype is predicted for male and female subjects with a pre-mutation. Males with a full mutation and abnormal methylation always show the fragile X phenotype with mental retardation. Unfortunately, insufficient data are available to predict the phenotype of females with a full mutation, but from the data available the risk of showing mental retardation for females with a full mutation is between 50-75%.

Smits *et al.* (1994) have calculated the specificity and sensitivity surrounding the CGG trinucleotide repeat length by analysing the CGG repeat length in 106 males and 73 females. Sensitivity is the proportion of mentally retarded carriers who were classified correctly by the presence of a full mutation. Specificity is the proportion of mentally normal carriers who were classified correctly by the presence of a pre-mutation. They concluded that 100% of males who carry a full mutation will be mentally impaired but it remains impossible to predict accurately whether and to which degree a female fetus with a full mutation will be affected. However, a female with a mutation of pre-mutation size

will have less than a 1% chance of being mentally impaired.

2.3.5.3 Prenatal diagnosis

Prenatal diagnosis of FMR is performed on amniocytes (collected by means of amniocentesis), chorionic villus cells (collected by chorionic villus sampling) or fetal blood (obtained via peripheral umbilical blood sampling) (Howard-Peebles 1992).

Before direct DNA analysis became available in 1991 the only way to do prenatal diagnosis was by using cytogenetic techniques. As discussed in section 2.3.5.1 this is not a very accurate method for prenatal diagnosis. Direct DNA and PCR studies of the FMR mutation, FMR-1, have revolutionized testing (Jenkins *et al.* 1992). The DNA test is quicker and more reliable. It is expected that false positive and negative diagnoses will be rare and therefore the reliability of prenatal diagnosis for Fragile X diagnosis will be high.

Molecular prenatal diagnosis of FMR is complicated by several factors. The most important factors are when and how the extension from pre- to full mutation occurs (Oostra *et al.* 1993), and methylation of the full mutation and X inactivation in the female fetus may not occur or may be incomplete in chorionic villus cells, at the 8-10 week stage of pregnancy (Shapiro and Wilmot 1992). However, with the combining of PCR and Southern blotting the molecular status of any individual can be inferred accurately, except for the mental status of full mutation females carriers (Castellví-Bel *et al.* 1995).

Another complicating situation is when a mother with a pre-mutation carries a female fetus. It is difficult to predict the intellectual ability of the fetus since, there is a 50% risk of mild mental handicap of females with the full mutation (Bonthron and Strain 1993). Since, the number of CGG repeats can be heterogeneous, distinguishing the normal transmitting males from affected males and unaffected carrier females from affected females can be difficult simply because the number of CGG repeats can overlap due to heterogeneity (Shapiro and Wilmot 1992).

2.3.6 SCREENING FOR FRAGILE X SYNDROME

FMR screening at a population level is a public health activity and must be evaluated by the community as it impacts on the general population. A questionnaire on screening was completed by the attenders of the third international FMR conference (Meadows and Sherman 1992). The questionnaire was completed by 28% of the attenders of which 75% thought there was a need for mass screening and 46% thought woman considering pregnancy should be screened. The biggest concerns regarding implementing a screening program were: lack of specific treatment, stigmatisation of affected individuals, confidentiality and lack of understanding.

Meadows and Sherman (1992) outlined issues that should be considered prior to implementing any screening program. These issues include the following:

1. Does the disorder have a significant impact on the affected individuals and their families? In response to this issue, the seriousness of the FMR is related to the level of mental retardation in the affected individual and the risk of transmitting the gene.
2. The test must be accurate and an inexpensive method of quality control must be available. With regard to FMR a choice has to be made for the most accurate and cost effective screening test.
3. The feasibility of undertaking a screening program must be assessed. Feasibility depends on the acceptability of the program by the people who will be screened, the possible number of cases identified and the ability to follow-up such cases, the cost effectiveness of the program, and the target population to be screened (pregnant women, newborns, school-aged children, women of reproductive age, only mentally retarded males or the whole population).
4. Who has access to results ? This is an important issue because positive results affect all the family members and not only the affected individuals. A number of individuals in the USA have lost their health coverage or have not been able to obtain new coverage because of their status as a FMR gene carrier.
5. Funding for the screening program.

Screening programmes have been implemented in New York (Nolin *et al.* 1991) and in New South Wales, Australia (Turner *et al.* 1992). The goal of these programs was to identify FMR individuals, to inform their extended families, and to reduce the number of pregnancies which produce an infant with FMR. Since cytogenetic screening is costly and time consuming, a two-step program, of physical screening of males with mental retardation of unknown cause, followed by a selective cytogenetic screening, was implemented in New York by Nolin *et al.* (1991). In this way it was possible to increase the efficiency, and reduce the cost of the program.

The physical screening of males with mental retardation of unknown cause was done by assessment of 10 characteristics: family history of developmental disabilities, ear length of more than 7cm, increased testicular volume, inner canthal distance of less than 3.5cm, calluses on hand or forearm, long and narrow face, high arched palate, prominent ears, hyperactivity, and avoidance of eye contact (Nolin *et al.* 1991). Each positive characteristic was given a score of 1 with a total score of 10. Patients with a score of more than 4 were selected for cytogenetic testing as well as individuals with macro-orchidism or who had a family history of mental retardation. The FMR checklist developed by Hagerman is also based on the same principle (Hagerman *et al.* 1991). The characteristics Hagerman assessed included: mental retardation, hyperactivity, short attention span, tactile defensiveness, hand flapping, hand biting, poor eye contact, perseverative speech, hyperextensible joints, large or prominent ears, large testicles, simian crease or sydney line, and family history of mental retardation.

The largest screening endeavour is Turner's project in New South Wales (Turner *et al.* 1992). The clinical assessment done was similar to Hagerman *et al.* (1991) and Nolin *et al.* (1991) and was documented using a five trait scale. The male patients scored from 0-2 points on each specific item depending on severity, with a maximum of 10 points and a minimum of 0. The five traits that were assessed included: family history of mental retardation, characteristic personality, large or prominent ears, long face and characteristic body habitus. Turner found that no individuals with a score of 1-4 were FMR positive (0/220), 19.3% of individuals with a score of 5-7 were FMR positive (18/93) and 75% of individuals with a score of 8-10 were FMR positive (24/32).

Thus utilizing a clinical score will identify those at highest risk for the FMR (Turner *et al.* 1992). Screening young boys is more difficult because some physical manifestations, such as macro-orchidism and long face, may not be present prepubertally. Behaviour can often be more helpful in prepubertal males than their appearance. Macro-orchidism and family history of mental retardation is predictive of FMR according to Nolin *et al.* (1991). However these authors agree that some positive males may have been missed, specifically those with few phenotypic manifestations.

2.4 PSYCHOSOCIAL ASPECTS PERTAINING TO THE FRAGILE X SYNDROME

2.4.1 INTRODUCTION

People choose to have children for various reasons including culmination and fulfilment of marriage (Gargiulo 1985). Children may represent a way for the parents to fulfil their own dreams of accomplishment and achievement. The parents may see the child as an extension of themselves, and they may live their lives vicariously through the life of the child. The child is a means of affirming the parents' success and ability to be parents and for some, the child is a step towards immortality.

The birth of a child with a problem, could define the parents to themselves and to others as less capable of childbearing (Hollerbach 1979). Pride in the child's accomplishments and the ability of the child to carry out the parents' hopes and dreams may be impossible in such a case (Hollerbach 1979). The child becomes an exception to the normal rules of growth and development and the rewards of parenthood may be diminished (Gargiulo 1985). With the dream of the perfect child destroyed, the parents are often left with guilt and self-recrimination.

However, the birth of an affected child may successfully satisfy other motivations of childbearing (Hollerbach 1979). The desire to feel essential and protect another human being may be enhanced. Having children may be a way of avoiding loneliness and could satisfy altruistic motivations for parenthood, since parental self-sacrifice for the child will

produce feelings of virtue and self-worth. A parent may gain a sense of creativity and accomplishment from meeting the challenge of rearing an affected child. It may also signify to the parents a test of their religious faith.

There are two approaches regarding how a handicap in a child affects the parents (Lea 1990). The more common approach holds that the diagnosis of mental disability in an infant or child is seen as an emotionally crippling experience from which families do not recover. By contrast, it has been argued that the problems facing parents of mentally disabled children are not special problems, but are, in fact, the problems facing all parents (Lea 1990). The difference between raising a handicapped child and a normal child lies mainly in the length of time for which difficulties extend, and the fact that a number of problems often occur simultaneously. This approach holds that parents are capable of coping with and making a satisfactory adjustment to the diagnosis of handicap in the child, to the point where they may live happy and fulfilled lives.

2.4.2 THE MOURNING PROCESS

In an attempt to explain how parents adjust to the birth of an affected child, the reactions to dying (bereavement or the grief process) as described by Kübler-Ross (1970) can be applied (Gargiulo 1985). The birth of a handicapped child can be seen as symbolic of the death of the ideal child and may precipitate a grief reaction similar to that associated with the loss of a loved one.

The state of the parents, upon receiving the news of the handicap, is that of persons who have suffered multiple losses and who perceive the prospect of continued loss (Antley *et al.* 1984). At stake is the anticipated health and intelligence of their child. In addition, the loss and disappointment is heightened by the implication that parents may personally be abnormal, since they have produced a child with a disability. According to Antley *et al.* (1984:76),

> "With the diagnosis, a new dimension to personal self and family self has to be confronted, one which is perceived as deficient and defective, and for which no previous allowance in self and family concepts had existed. Out of the disappointment, a conflict emerges between idealized self and family, and perceived

> self and family. The personal and family adjustment necessary to integrate and bring back into equilibrium the ideal self and the self is the grief process."

The stages in the grief process reflect the predominant reactions in the process of adaptation to the news of the handicap, and all the models emphasize that no person moves through the stages discretely or sequentially (Cunningham and Davis 1985). Commonly, people move between stages and there is often reversal. Also both parents do not necessarily go through these stages together (Gargiulo 1985).

Several authors have described the grief process. Although the authors have termed phases differently, they generally highlight the same reactions. Antley *et al.* (1984) suggested that the grief process comprises five phases: shock, denial-anxiety, guilt, bargaining and acceptance. Cunningham and Davis (1985) describe three stages: the shock, the reaction, and the adaptation. Gargiulo (1985) outlined four phases: the primary, secondary, tertiary and adaptation phases.

The first phase according to Antley *et al.* (1984) and Cunningham and Davis (1985) is the shock phase. The initial response of the parents, when confronted with the unexpected diagnosis, is that of overwhelming shock and disbelief. It is characterised by a period of irrational behaviour, excessive crying and feelings of numbness and helplessness (Gargiulo 1985). It may last for hours or even days and since it involves massive anxiety, threat, or possibly guilt it may be associated with low self-confidence (Cunningham and Davis 1985).

During the next phase, the denial-anxiety phase (according to Antley *et al.* 1984) parents fear that if they acknowledge and accept all of the facts, they will become overwhelmed with anxiety and will not be able to cope (Antley *et al.*. 1984). Denial and refusal to recognize the disability, provides a temporary solution to the inability or reluctance of the parents to understand what is happening (Cunningham and Davis 1985). Parents may deny the impact of the disability by expressing lack of emotional upset, which could result in them becoming too co-operative too quickly (Gargiulo 1985).

The guilt phase tends to occur along with feelings of anger and depression during the

period when denial is lessening (Antley and co-worker (1984). Guilt can be seen as an attempt to hold on to the previously held hopes for a normal child while indicating some acceptance of abnormality. The parents may believe that somehow they caused their child's handicap or that the handicap is a punishment for past wrongdoings (Gargiulo 1985). Shopping behaviour is common during this stage and is precipitated by parental guilt. Shopping behaviour occurs when parents visit the same professional or a number of different professionals or clinics, in such a manner that one visit follows another without resolution of a resolvable problem (Gargiulo 1985). The parent hopes to prove that the professionals are, not only wrong, but also responsible for the child's handicapping condition.

Gargiulo's (1985) primary phase can be compared to the shock and denial-anxiety phases described by Antley *et al.* (1984). During this phase the parents experience feelings of shock, denial, grief, depression, and withdrawal. Grief and depression occur because of disappointment and concern about the future. Expressing their grief allows the parent to progress from the state of initial shock and disbelief to that of awareness of the disappointment. Depression occurs as a consequence of the grieving and is followed by withdrawal, where the parent severs him or herself from social contact with others.

The secondary phase described by Gargiulo (1985), is comparable to both the guilt phase of Antley *et al.* (1984) and the reaction phase described by Cunningham and Davis (1985). It is characterised by ambivalence, guilt, anger, shame and embarrassment. Parents may experience ambivalent feelings and some parents may wish the child was dead. Often parents express feelings of anger. Parents may ask, why me? or their anger may be directed towards the doctors (often the bearers of the bad news), teachers and therapists of the child (for disrupting their lives). Parents may be embarrassed or ashamed of the child's handicap and avoid situations where the child's differences are accentuated or commented upon (Clarke 1982). Hospitals, doctors, clinics and even everyday shopping trips may become an ordeal of embarrassment for the parent. This could result in social withdrawal and consequently, social isolation.

When entering the bargaining phase, parents are beginning to accept the diagnosis, while

attempting to partially restore the child to normality by making sacrifices (Antley *et al.* 1984). Their hope is to retain a portion of the normal child that they had expected. The tertiary phase according to Gargiulo (1985) is similar to this phase.

Finally the parents enter the acceptance phase (Antley *et al.* 1984, Gargiulo 1985, Cunningham and Davis 1985). When this phase becomes predominant parents begin to ask such questions as "what can be done?" and "how can we help?" (Cunningham and Davis 1985). Parents begin to organize, seek help, establish new routines, plan resources and learn new skills. Adaptation and reorganization is a gradual process requiring varying lengths of time and a reduction in the feelings of anxiety and other intense emotional reactions (Gargiulo 1985). The parents gradually become more comfortable with their situation.

The grief process as described above, is the long-standing traditional view of parents' reactions to the news of disability in their child (Bruce *et al.* 1994). The process results in the successful completion of the task of mourning. The emphasis on completion of the task however, has given little consideration to the unique life-span features of parenting an impaired child. The impact of later experiences in raising a child with a disability may be underestimated, since the extent and nature of the disability is only fully realised when the child fails to reach critical developmental milestones.

According to Olshansky (1962), most parents who have a mentally disabled child suffer chronic sorrow throughout their lives. The intensity of this sorrow varies from person to person, from situation to situation and from one family to another. The author emphasized that chronic sorrow is a "natural and understandable response to a tragic fact". All the parental reactions reported in the literature such as anger, guilt and denial may be intertwined with chronic sorrow but the chronic sorrow does not prevent the parents from deriving satisfaction and joy from the child's achievements. Release from chronic sorrow may be obtainable only through death.

Bruce *et al.* (1994) conducted a preliminary study to investigate the nature of the grief of parents of children with intellectual disability. The participants in the study comprised 58

mother-father dyads divided into 3 cohorts: cohort 1 were parents whose children were 0-4 years of age, cohort 2 parents whose children were 5-10 years of age, and cohort 3 parents whose children were 11-21 years of age. Their study concluded that grieving is an ongoing feature of rearing a child with intellectual disability and is more intense for mothers than for fathers. They hypothesised that it is unlikely for the parents to resolve their grief and that grief-like reactions are triggered continuously, since the source of grief remains because normal children may represent constant reminders of the loss in terms of discrepancies.

2.4.3 DISABILITY AND THE FAMILY

In some families, having an exceptional child is a major tragedy, in others it is a crisis but one that can be resolved, for others it is not considered a problem in itself but rather one element in a daily struggle for survival (Gargiulo 1985).

Many of the problems in families with an exceptional child are essentially no different from difficulties found in any family (Gargiulo 1985). A family is a dynamic system of interacting individual personalities so whatever affects the individual affects the family. Families vary from one another, and when assessing the effect that a handicapped son or daughter has on the family one needs to understand how the family changes over time, what the interaction between the members are and what the functions of a family are. In the next few sections these aspects will be discussed, using a few key reviews on the subject.

2.4.3.1 Family life cycle

Families experience change as their members are born, grow up, leave home, retire and pass away (Turnbull and Turnbull 1986). A child with a disability affects and is affected by the other changes that occur in the family. The needs of a family with a young disabled child are not the same as that of a family with an adolescent child with a disability. Furthermore the family's attitudes and values about the exceptionality change over time.

It is therefore important to understand how families change throughout their life cycles and how these changes affect their needs and attitudes towards the child with a disability (Turnbull and Turnbull 1986).

The exact number and character of life cycle stages varies according to the persons who described them, some authors have suggested there are as many as 24 stages and some as few as 6 (Turnbull and Turnbull 1986). One author's view of the life cycle stages (comprising eight stages) will be considered here (Williams 1989). Williams's (1989) stages are as follows: Phase I, the beginning family (married couple without children); Phase II, childbearing family (oldest child up to 30 months); Phase III, families with pre-school children (oldest child 30 months to 6 years); Phase IV, families with school children (oldest child 6 to 13 years); Phase V, families with teenagers (oldest child 13 to 20 years); Phase VI, families as launching centres (first child gone to last child leaving home); Phase VII, families in the middle years (empty nest to retirement); and Phase VIII, ageing families (retirement to death of both spouses). During each stage of the life cycle, the family's lifestyle may be considered relatively stable and each member is engaged in a series of developmental tasks related to that period of life (Turnbull and Turnbull 1986). The transition between the stages is a potential time of difficulty for the family and may involve anxiety (Williams 1989).

Although all families may experience anxiety in moving from one stage of the cycle to the next, a child with a disability may put additional stress on the family. For example families moving from phase III to IV, have to make decisions about the type of school, and travel arrangements for their child. For parents with a handicapped child this is frequently a period of great searching (Cunningham and Davis 1985). These parents may be faced with many more issues than other parents, for example: should the child go to a special school, and if the child does, will there be a stigma attached and will the other siblings cope with the situation.

According to Gargiulo (1985) the life cycle is unfulfilled or arrested when there is a child with a severe impairment. The child with a disability will assume the social role of the youngest child, regardless of his or her birth order. It is therefore speculated that the

family with a child with a disability impedes movement through the life cycle as well as preventing family members from reaching the final stages.

2.4.3.2 Family interaction

To understand how families function it is useful to consider the family as a unit consisting of many interactions or subsystems (Cunningham and Davis 1985). These subsystems have emotional boundaries to restrict emotional interchange between what is within and what lies outside (Williams 1989).

A family consists of four major subsystems (Turnbull and Turnbull 1986); The marital subsystem (husband and wife interactions), the parental subsystem (parent and child interactions), the sibling subsystem (child and child interactions) and the extrafamilial subsystem (family's interactions with extended family and friends).

(i) Marital subsystem (husband and wife interactions)

The marital subsystem consists of interactions between husbands and wives (Turnbull and Turnbull 1986). Since both husband and wife have needs and roles as marital partners, the presence of a child with an exceptionality can have an impact on their relationship and interaction.

A number of researchers have postulated that the presence of a defective child in the family will have an effect on the parent's marital relationship, however, research findings are contradictory (Lea 1990). On the one hand, certain studies report that the child constitutes a negative influence on the parents' marital relationship. Gath (1985) reported on the destructive effects a child with Down syndrome has on the marital relationship. Interviews were conducted with 30 couples who had children with Down syndrome and a control group, 18 months after the birth of the child. Of the 30 marriages three had broken down and six were most unhappy with open discord, hostility and lack of interest in the welfare of the partner, while none of the marriages in the control group had broken down during the same period. By the time the children with Down syndrome were 8 to

9 years of age, there had been no further marital breakdown. With this in mind, there seems to be evidence that it is the initial emotional trauma rather that the wear and tear of looking after the child that is so devastating to the marital relationship.

The presence of a handicapped child may precipitate tension or conflict between husband and wife (Gargiulo 1985). The parents may blame one another and this can take its toll on the stability of the marriage. It appears that typical family controversies over caretaking demands, disagreements about discipline and management, future needs and expectations are accentuated by the child' special needs, since they take place in the context of higher uncertainty and demands (Cunningham and Davis 1985). Marital relationships are vulnerable to the problems of day-to-day care and the increasing burden on family resources as children grow older.

Turnbull and Turnbull (1986) state that the number of desertions and divorces in families with exceptional children far exceeds that found in the general populations and suicide and alcoholism occur more frequently in families with disabled children. The child is held responsible for the poor quality of the parents' marriage and the child may become a negative bond, binding together the parents in an unhappy marriage. To dissolve the marriage could be unthinkable.

On the other hand, reduction in marital stability is not necessarily an inevitable consequence of having an impaired child, the stress that accompanies the parenting can bring spouses closer together and strengthen the marriage (Gargiulo 1985).

According to Cunningham and Davis (1985) there does not seem to be hard evidence that the incidence of marital break-up and family disharmony is higher in families with handicapped children. The incidence of marital break-up varies with such factors as the age of the child and the nature of the child's handicap. Studies indicate that marital satisfaction decreases over time in all kinds of families, not just in those with handicapped children. Whether there is a disproportional decrease in relation to the increasing demands made by the child's handicap is not yet known. However, separation and disharmony are more likely when there have been marital difficulties prior to the birth of the affected

child.

At present, it remains largely unclear as to what factors cause a marital relationship to deteriorate or improve, and more rigorous research is needed to understand the complex interplay of the factors involved (Lea 1990).

(ii) Parental subsystem (parent and child interactions)

The parental subsystem is composed of interactions between parents and their children (Turnbull and Turnbull 1986). In a family, parents assume certain roles which can change over time. The presence of a child with an exceptionality has an impact on parent roles, and fathers and mothers can be affected in different ways.

Traditionally the male parent's role is seen as instrumental; involved with finance, education and vocation; and the female parent role is seen as expressive, involving affection, physical care, and self-definition (Turnbull and Turnbull 1986). In families with an exceptional child, fathers may be assuming a role that increasingly focuses on the expressive needs of their child and mothers on the instrumental needs. Parents may be beginning to share more of the same roles when caring for their child with an exceptionality.

The fathers of children with intellectual impairments are generally more involved with care activities than fathers of ordinary children (Cunningham and Davis 1985). There is some indication, however that fathers are less likely to spend time with the child, the more developmentally delayed the child is. There is some evidence that fathers may be less aware than mothers of the degree of strain the child's demands make on the family and may also have a less optimistic view than mothers of the child's current and future achievements. Fathers appear more likely to take on an assertive role and fight for family rights and express demands when dealing with services.

Cunningham and Davis (1985) report that fathers are more affected by a disability in the child and take longer to adjust than mothers. It is suggested that this is because men are

more achievement orientated and more concerned with the achievements and independence of their children. It is also suggested that the birth of a child with an impairment is a greater shock to the role structure and self-esteem of fathers, because it is largely based on socio-cultural values such as manhood, independence, competitiveness and achievement.

The initial impact on the fathers is greater if the child with a problem is a boy, and on mothers it is greater if the affected child is a girl (Turnbull and Turnbull 1986). Fathers are more concerned about the community stigma that their family may face. Stigma may be accentuated by the sex of the child. A father may feel greater stigma over a sixteen year old son just learning how to throw a ball than a sixteen year old daughter learning the same activity. Fathers may be disappointed that they were not able to share what they considered "male hobbies" with their sons.

On the other hand mothers shoulder the main day-to-day care and are more likely to experience both physical and emotional strain (Cunningham and Davis 1985). It is suggested that this is due to mothers being more inward looking and concerned with the emotional wellbeing of the family, as well as the fact that they spend so much time with the child. One frequently noted difficulty is the feeling of isolation (Cunningham and Davis 1985). This relates to the social restriction placed on mothers and is associated with younger children and with the severity of demands made by the child with special needs.

Since mothers are mostly the ones who care for the handicapped child, physical and mental health has been assessed in such mothers (Clarke 1982). Physical symptoms such as frequent colds, lethargy and a general feeling of being run-down, and also more chronic conditions including bronchitis, rheumatism and back pain were reported. Mothers also experienced some form of mental ill-health in terms of being nervy, on edge or depressed. It was found that fathers suffered less than their wives from ill-health, and their level of mental ill-health was similar to that of the general male population.

(iii) Sibling subsystem (child-child interactions)

The sibling subsystem is composed of interactions between brothers and/or sisters in the

family and the child with an exceptionality (Turnbull and Turnbull 1986). The child's impact upon the siblings has not been fully explored, understood or recognised. Siblings may find it difficult to express their feelings or the parents may be less sensitive to the needs of the other children when focusing on the needs of the child with a disability.

Normal sibs tend to mimic and adopt the feelings and behaviours expressed by their parents (Gargiulo 1985). The father's reaction in particular has been shown to greatly influence the overall family demeanour. Hence the parents' attitudes are crucial to sibling adjustment. Many times the non-handicapped siblings suffer from neglect or a lack of attention as both parents become overly involved with the special needs of the exceptional child, however brothers and sisters need attention in their own right. The non-handicapped sibs are affected more by their perception of how the parents treat them in comparison to the handicapped sibs than they are by the reality of the condition itself.

Research on siblings, which relies on questioning the parents, will be influenced by the parents' hopes for their children and their perception of what has been 'given up' for the child with special needs. The parents often report more negative consequences on the normal siblings than do the siblings themselves (Cunningham and Davis 1985). Siblings are usually unaware of what might have been and report the positive factors.

Besides feeling a sense of being neglected by their parents, siblings may also have other negative experiences like resentment and guilt, fear that they too might be exceptional, shame and embarrassment (Turnbull and Turnbull 1986). The time, energy, affection, money and other family resources that are given to the child with an exceptionality can create resentful feelings for siblings.

Sibs are often expected to take the responsibility of helping with physical and caretaking needs of their affected brother or sister (Turnbull and Turnbull 1986). An elder sister may be placed in a caretaking role, which can limit her opportunities for personal development and extending social relationships (Cunningham and Davis 1985). Some evidence suggests that this can also result in emotional disturbance, which appears to be more likely in the case of severe physical or behavioral difficulties. In some instances sibs experience a need

to overachieve in an effort to compensate for their brother's or sister's disability, especially in two child families and particularly when the sibling is a son (Turnbull and Turnbull 1986). Some sibs feel a great deal of stigma at school and a reluctance to bring friends into their home. Siblings can also experience difficulties from the reactions of friends and other children, such as teasing or harsh comments about the brother or sister (Cunningham and Davis 1985). It appears that this has only a temporary effect. Sibs have expressed concern and worry regarding their future responsibilities for their brother or sister (Turnbull and Turnbull 1986).

Despite an increased risk for emotional problems and increased demand for caretaking, siblings can also experience some positive outcomes (Turnbull and Turnbull 1986). A study done by Grossman found that sibs can benefit, from having an exceptional sib, by developing more tolerance and compassion, a greater understanding of other people and an appreciation of life that is far beyond their years, increased awareness of prejudice and its consequences, and a greater appreciation of their own health and intelligence (Turnbull and Turnbull 1986). Sibs who become more tolerant and accepting of differences gain positive effects in their socialization.

For many siblings, knowledge about the impairment is important, because they may fear that they will catch the disability or that there is future risk to their own children (Cunningham and Davis 1985). Several studies indicate that many siblings are rather ignorant of the details of causes, and that they do not raise these issues with their parents. Generally the more understandable and/or more socially acceptable the special need, the less the anxiety is felt by the siblings, and indeed by all the family members. However the social acceptability of the handicap will be influenced by both cultural and societal values and the personal values of the family. For example, where families value intellectual performance, learning difficulties may be less acceptable, and they may find it more difficult to adjust.

(iv) Extrafamilial subsystems (family and extended family interactions)

The extrafamilial subsystems are composed of family and/or individual interactions with

extended family, friends, neighbours, and professionals (Turnbull and Turnbull 1986). This subsystem can make a major contribution to the progress of the child with an exceptionality, and also provides parents with a network of support.

The extended family members may have many of the same problems that people in general have regarding exceptionality (Turnbull and Turnbull 1986). Lack of information and experience may create attitudes of fear, mistrust, or condescension. They may also have to deal with their own feelings of grief, shock, anger, or disappointment at the same time that they are expected to provide support for the family. These relatives can be a source of various kinds of support in many families, although they often do not know how to fill many of the roles they fulfil in a family without an exceptional child. The additional challenge for the parents is in introducing the new family members to exceptionality. Many of the extended family members' close friends or neighbours will not be able to provide support to the child and the family unless some of their needs for knowledge, experience, and skills can be met. Addressing some of the needs of the family's extrafamilial subsystem is a strategy for helping children and for supporting families.

2.4.3.3 Family functions

Families need to perform certain tasks to meet the needs of their members (Turnbull and Turnbull 1986). The presence of a family member with an exceptionality can impact on each of the areas of family functioning.

(i) Economic needs

Families need to earn a living and make decisions on how the family's money will be spent (Turnbull and Turnbull 1986). Having a child with a disability can create special economic needs by increasing the family's expenses and decreasing its income.

Having a family member with a disability can create financial hardship, since the child's special needs can include costly medical bills, expensive equipment, or structural adaptations at home (Turnbull and Turnbull 1986). Similarly some family members may

have to sacrifice their careers, or take lower paying jobs to care for the child, thereby decreasing the income.

However, not all exceptional children necessarily have a negative effect on the family's income (Turnbull and Turnbull 1986). In fact, in some situations the child may even cost the family less because he or she may not be requesting such expensive items as a new video recorder, personal computer or car.

(ii) Domestic and health care needs

A basic function of families is to meet the physical and health needs of the members (Turnbull and Turnbull 1986). This includes the day-to-day tasks of living for example cooking, cleaning, laundry, and obtaining medical care when needed.

The domestic and health care needs for a child with a disability can create stress for the parents (Turnbull and Turnbull 1986). A family's needs vary depending on the type, degree and severity of the disability. For example a child with deafness and a child with severe mental retardation will make different demands. When the parents are too busy meeting the child's needs, they may overlook their own needs and may experience exhaustion. However, just because an exceptional child can create a problem does not necessarily mean they always do. There are many positive contributions that they can make to family functioning, for example they can help with housekeeping, yard work, laundry or the needs of younger siblings.

(iii) Recreation needs

An important function of the family is that it serves as an outlet where its members can relax and be themselves (Turnbull and Turnbull 1986). This function is sometimes decreased by the presence of family member with a disability.

It has been reported that some families find it difficult to enjoy family outings such as trips to the beach, picnics, or trips to the swimming pool or cinema (Turnbull and Turnbull

1986). Again, having a child with special needs does not necessarily mean that family recreation will be diminished, it can also have a positive effect on the family's ability to rest and recreate as illustrated by this quotation:

> "One example that comes to mind is our acquisition of a cabin or summer house, as we call it. Our favourite vacations used to be finding a cabin in the wooded area away from civilization. It was always difficult to take Jennie because we had to cart cribs and other paraphernalia, not knowing what we would find wherever we settled ourselves. We therefore decided that it would be much easier for us if we had our own cabin already stocked with the equipment we all wanted. After diligent searching, we found a cabin in woods an hour from our home. It is now one of the main forces that keeps us a united family and is a great source of inspiration and joy to all of us. In a sense, we have to thank Jennie for making it more difficult to travel and for prompting us to find our own cabin." (Turnbull and Turnbull 1986:72-73)

(iv) Socialization needs

Families are the basis from which individuals learn to interact with others (Turnbull and Turnbull 1986). In turn socialization is vital in determining the overall quality of life for most individuals.

Many families with exceptional children experience stress in attempting to meet socialization needs (Turnbull and Turnbull 1986). Children with disabilities, regardless of the disability, may have significant social handicaps.

The lack of socialization options for families can be caused by specific skill deficits (lack of mobility or verbal skills) or could be attributed to the fact that community members, neighbours, and relatives have negative attitudes towards persons with a disability (Turnbull and Turnbull 1986). Furthermore the socializing opportunities of the parents are also affected because of difficulties in finding someone to stay with the child when parents go out. On the positive side however, parent support programs have offered families the opportunity for forming friendships, which in many cases have lasted long after their children has left the program.

2.4.4 FACTORS AFFECTING THE FAMILY'S RESPONSES TO A DISABILITY

2.4.4.1 Family size and form

Larger families tend to be less distressed by the presence of a child with an exceptionality (Cunningham and Davis 1985). The reasons for this may be that there are more people available to assist with the handicapped child, or that a larger number of normal children creates a greater atmosphere of normality, or that there are a larger number of siblings that may be able to absorb the parents' expectations for achievement.

2.4.4.2 Cultural background

The cultural background of a family lays a foundation of values and perspectives of the world that help the family define who they are (Turnbull and Turnbull 1986). These values and perspectives play an important role in shaping a family's reaction to an exceptionality. Some cultural lifestyles may accept a handicap more easily than others and may assist the family to cope with the implications of a handicapped child (Turnbull and Turnbull 1986).

The country of origin helps define the cultural background of a family. In their study, Aminidav and Weller (1995) have shown that country of origin may affect attitudes toward mental retardation. Their results showed that Israeli Jews of Western descent had a greater understanding of the causes of illness than those of Yemenite or Iraqi descent. The Western group saw illness more scientifically, as caused by viruses and infections, whereas the other group viewed illness in a more traditional way, as emanating from spirits, the evil eye and fate. Aminidav and Weller (1995) also compared the attitudes of three Jewish groups (one of Western descent and two of Eastern descent) to mental retardation. They found that those of Western descent had a more accurate and wider knowledge of mental retardation than the groups of Eastern descent.

Since cultural values influence a family understanding of mental retardation and understanding of mental retardation plays a role in shaping reactions to a child with a disability, it could be assumed that cultural values will play a role in family coping and adjustment to a child with a disability.

2.4.4.3 Socio-economic status

Socio-economic status includes income, level of education of the family members, and social status implied by the occupations of the wage-earners (Turnbull and Turnbull 1986). Certain authors regard socio-economic status as a critical demographic characteristic when considering families of handicapped children (Lea 1990).

A few researchers have examined the influence of socio-economic status on the family's ability to cope with the impact of the handicapped child (Lea 1990). Some research indicates that families with a low income experience greater stress than high-income families. It could be argued that since low income families do not have the ability to pay for services and do not have a high level of education, which are both definite resources, they are expected to experience greater stress than the families with high socio-economic status (Turnbull and Turnbull 1986). However, a high socio-economic status does not automatically guarantee better coping, since families of low socio-economic status can have other resources, which include large families and extensive support networks. Kromberg *et al.* (1993) reported on a study of Down syndrome in the black South African population of the Southern Transvaal. They found that the mothers of children with Down syndrome had significantly increased levels of psychosomatic symptoms compared with controls with normal children, which suggested they were stressed. They concluded that, in many respects black families appear to have the same sorts of psychosocial and emotional experiences as families described in the literature (Byrne *et al.* in Manchester in 1988).

A second aspect that is of interest with respect to socio-economic status is the association of this status with a parent's acceptance or rejection of the handicapped child (Lea 1990). Few studies have been undertaken on this aspect and, most researchers have merely

involved themselves in speculation. Some have postulated that there is less of a stigma related to mental handicap among lower socio-economic groups, since people within these groups suffer a multiplicity of stigmata. Consequently, the impact of the handicap will be reduced and a greater acceptance is predicted. Families with high socio-economic status may consider having a child with mental disability a severe disappointment because such families are very achievement orientated (Turnbull and Turnbull 1986). However, it may not be possible to generalise and there may be families in both categories who accept or reject their children for a multiplicity of interacting reasons.

2.4.4.4 Religion

Studies indicate that deep religious conviction influences parental adjustment to the mentally handicapped child, particularly with regard to how parents interpret and understand the presence of handicap in their family (Lea 1990). Parents may interpret the event in either positive or negative way that is as a blessing or punishment from God. Parents who believe that a handicapped child is part of a divine plan or a special gift, may find it easier to accept the child (Levitz 1993). Some couples seek a religious explanation for the handicap, others merely derive strength and hope from their religion (Lea 1990).

2.4.4.5 Social support

The availability of social support is assumed to be beneficial to families with children with disabilities (Lea 1990). Distinction should be made between formal (or public) and informal (or intimate) sources of support. Formal sources of support include the general public, medical professionals, and social services, while informal support included spouse, siblings, family and friends. It was found that social support may not be of benefit to parents in all cases. Certain parents reported that various people had given support when it was not wanted, or had given the wrong kind or support. Therefore, we should not assume that social support necessarily has a positive effect.

2.4.4.6 News of handicap.

There is no good way of telling parents that their child is mentally disabled, but there must be ways of not adding to the suffering that is already considerable (Clarke 1982). The whole experience of learning about the diagnosis is extremely difficult, often painful and always a severe shock to the parents. It is complicated by the timing, the circumstances, the attitudes of the person who gives the news and how it is done. If the initial experience of being told the diagnosis is unsatisfactory, the parents may not be able to come to terms with their shock and feelings about the diagnosis.

A high rate of parental dissatisfaction about how they were told of the diagnosis has been reported (Cunningham and Davis 1985). Complaints include: the withholding of the news by professionals and/or denying the parents' concerns; unsympathetic ways of giving the information; lack of privacy and/or time to take in the information. In some cases however, where the parents have suspected that the child is mentally handicapped, it brings great relief to know the diagnosis (Clarke 1982).

Parents want to know the truth about the disability (Clarke 1982). If they sense deceit it could generate bitterness and resentment which may result in the parents rejecting further help. Alternatively, one could suppose that if the parents are feeling that a stigma is attached to having a child with a handicap, that they might question their competence in coping with the child's condition (Cunningham and Davis 1985).

2.4.4.7 Coping resources of parents

Coping can be defined as active efforts to master, reduce or tolerate the demands created by stress (Weiten 1992). Individual family members may vary in the particular strategies they adopt to deal with stress. Olson 1983 has described different categories of coping styles: passive appraisal (ignoring a problem in the hope that it will go away); reframing (changing the way one thinks about a problem, in order to solve it and/or make it seem less stressful); spiritual support (deriving comfort and guidance from one's spiritual beliefs); social support (receiving practical and emotional assistance from friends and

family); and professional support (receiving assistance from professionals and human service agencies) (cited in Turnbull and Turnbull 1986).

2.4.4.8 Characteristics of the handicapped child.

The primary characteristics identified as influencing the degree of stress parents experience and the ability to cope include the child's age, diagnosed condition, physical appearance, degree of retardation, number of associated handicaps and level of social skills (Lea 1990). Kromberg *et al.* (1987), in a study of 37 mothers of albino infants, found that more mothers of albinos infants than mothers in the control group did not like their child's appearance and they seemed more upset and reluctant to breast-feed and hold their infants close. This did however improve after a time lapse of three months. In essence, it would seem that the closer the child approximates normality in terms of appearance, IQ, and social behaviour, the less stress the parents experience.

The extent to which the child is different from his peers is related to stigma (Cole 1993). The child, as well as the parents, bear a stigma and this may influence the ability of affected individuals and parents to effectively adjust to their social environment.

(i) Sex

It has been suggested that parents are less stressed by having a daughter with special needs, than a son (Cunningham and Davis 1985). This may be due to traditional sex stereotypes influencing aspirations, with girls being more dependent than boys. Similarly, fathers tend to be more affected by having a handicapped son than by a daughter. This may be because fathers are more achievement oriented and concerned about their children's achievements, especially those of their sons. Equally it is suggested that conditions with marked physical appearance can be more distressing for parents of girls than boys. Changing social attitudes to sex and appearance will presumably influence such reactions.

(ii) Age

Age is often cited as important (Cunningham and Davis 1985). As the affected child gets older he or she will want more freedom, which will increase the amount of supervisory time needed and entail decisions about how much freedom to give, which will be dependent upon the local environment. For both sexes, the onset of puberty is likely to cause some stress with different consequences for boys and girls.

The effects of the age of the mentally handicapped child upon level of stress are controversial (Byrne and Cunningham 1985). There are some suggestions that there are events throughout the child's life which precipitate stress, these include the initial diagnosis, siblings overtaking the mentally handicapped child in ability, consideration of school placement, onset of puberty, discussion about guardianship and residential care. Whereas other suggestions include that it may be more relevant to consider stages in the family's life cycle, and events within the cycle, as contributors to stress.

(iii) Level of intellectual impairment

The level of intellectual impairment is often assumed to be highly related to stress in families (Cunningham and Davis 1985). The degree of stress experienced by families is related to the demands made by the child upon the family resources and the family's attitude to cognitive abilities. For example, the increased need for physical care and the medical/health problems, may reduce the time that individual members and the family have as a whole for other activities. Such increased needs may also influence employment opportunities by restricting both mother and father and thereby reducing the financial resources.

(iv) Unpredictability

Unpredictability of the child's behaviour is amongst the most common causes of stress (Cunningham and Davis 1985). If the parents cannot anticipate the child's behaviour or needs, they will be extremely anxious and be unable to establish routines and organize the

running of the family. Anxiety and satisfaction with parenting have also been linked with the level of the child's social responsiveness. Whilst this has been mainly demonstrated with young children with intellectual impairment, it is also seen in children who are withdrawn, and who do not express their feelings and concerns. Many parents testify to the frustration of not being able to get children to talk to them about the reasons for their behaviour. They describe feelings of being rejected or shut out by the child and of not experiencing affectionate reactions.

2.5 GENETIC COUNSELLING

Genetic counselling is a process of communication between a counsellor and the persons who seek genetic counselling. Essentially there are three aspects to counselling: the scientific aspects (includes genetic mechanisms and recurrence risks); medical aspects (includes diagnosis and genetic heterogeneity); and psychological aspects (understanding and appreciation of the psychological effects) (Emery 1984). The Ad Hoc Committee on genetic counselling of The American Society of Human Genetics, coined a definition of genetic counselling which includes all the issues that should be covered during genetic counselling (Fraser 1974). The definition is as follows:

" Genetic counselling is a communication process which deals with the human problems associated with the occurrence, or the risk of occurrence, of a genetic disorder in a family. This process involves an attempt by one or more appropriately trained persons to help the individual or family (1) to comprehend the medical facts, including the diagnosis, the probable course of the disorder, and the available management; (2) to appreciate the way heredity contributes to the disorder, and the risk of recurrence in specified relatives; (3) to understand the options for dealing with the risk of recurrence; (4) to choose the course of action which seems appropriate to them in view of their risk and the family goals and act in accordance with that decision; (5) to make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder"

Genetic counselling is essential in families with children with FMR. The families should be informed about the inheritance pattern, diagnostic testing and prenatal diagnosis (Silverman *et al.* 1992). Further, FMR is a complex disorder with several non-Mendelian characteristics which the family also needs to understand in order for them to make appropriate decisions. Some of these aspects include:

1. The daughters of normal transmitting males are obligate carries and are at high risk

of having affected sons. Mothers of normal transmitting males are at low risk of having affected children.

2. The degree of mental retardation in affected offspring depends on the sex and mental ability of the carrier parent.

3. Mentally retarded carrier females are at higher risk of having affected children than are carrier females with normal intelligence.

4. Affected females receive their fragile X gene from their mothers and not their fathers.

5. The fragile site is usually only seen, cytogenetically, in 10-40% of retarded males, less frequently in retarded females, in only a proportion of asymptomatic carrier females and almost never in asymptomatic carrier males.

6. DNA diagnosis is based on the abnormally methylated CpG island in Xq27.3 as well as on the increase in size of the CGG fragment. It has been shown that the chorionic villi are unmethylated, therefore one should be very careful in predicting whether a pre-mutation found in a CVS accurately reflects the mutation pattern in fetal tissue.

7. Up to 5% of individuals in fragile-X families are mutation mosaics (Hirst *et al.* 1993). In these individuals some cells carry the pre-mutation and others carry the full mutation, so that they show multiple DNA fragments or a heterogeneous smear of fragments.

Support to families, however needs to involve more than just providing the information regarding the genetic aspects and testing options (Silverman *et al.* 1992). Individual concerns should be validated and the emotional impact of the diagnosis should be acknowledged. When a child is diagnosed, the parents are grieving over the "loss" of their normal child and they are emotionally charged with feelings of guilt and loss of self esteem (Emery 1984). The information which needs to be communicated to the families, regarding FMR, should be done keeping these psychosocial issues in mind.

2.6 SUMMARY

In this chapter a review of the literature relevant to the present research was presented. An overview of the clinical, genetic and psychosocial aspects pertaining to FMR was given.

The clinical presentation of FMR includes the classic triad of features (mental retardation, long narrow facies and macro-orchidism), characteristic delay in the development of speech and language (repetition of words, phrases or topics of conversation) and behavioral characteristics such as autistic like features (avoidance of eye contact and resistance to being touched or held). The normal transmitting males and carrier females are less severely affected, with normal IQ females showing learning disabilities. Only 35% of carrier females show obvious mental impairment. Furthermore emotional problems have been documented in normal IQ females which included chronic affective disorders, schizotypal features and depression.

FMR appears to be a X-linked dominant disorder with reduced penetrance. The gene (FMR-1) is on the X-chromosome at position Xq27.3. The molecular defect is an unstable triplet repeat within the 5' untranslated region of exon 1 in the FMR-1 gene. The triplet can lengthen in size ranging from normal (0-50 repeats) to pre-mutation (50-150 repeats) to full mutation (more than 200 repeats). The unusual aspects of the inheritance of FMR were described by Sherman are known as the Sherman paradox. This paradox explains the striking deviations from normal X-linked inheritance: the existence of normal transmitting males; the fact that mentally retarded female carriers are more likely to have mentally retarded offspring; that the probability that a child will be mentally retarded depends on the sex and intellect of the parent transmitting the fragile X chromosome; and that affected females receive the FMR-1 gene from their mothers and not their fathers.

The FMR-1 protein and its involvement in the etiology of the disorder was briefly mentioned as well as some of the proposed mechanisms of the inheritance of the syndrome (methylation and founder effect). The methods of diagnostic testing for FMR were discussed. It was established that cytogenetic testing (demonstration of the fragile X chromosome) was not always reliable and that DNA methods (demonstration of the length of the CGG triplet and abnormal methylation) were much more accurate. Furthermore, FMR can be diagnosed prenatally by amniocentesis, CVS and fetal blood sampling. However, care should be taken in the case of CVS, since methylation may be incomplete at that stage of embryogenesis. Aspects of a screening program were discussed.

The second part of the chapter was devoted to the psychosocial aspects pertaining to FMR. Firstly, the mourning process was described. The grief reactions that are triggered by the birth or diagnosis of a child with a disability can be described as denial, anger, guilt, bargaining and acceptance. One of the aims of the present research was to investigate the parents' feelings upon receiving the diagnosis and it was therefore important to include this section.

The remaining parts of the chapter covered aspects concerning disability and the family. The family life cycle was described, and the changes families experience as their members are born, grow up, leave home and finally retire were discussed. A child with a disability may pose extra strain on the family as they pass from one stage to another compared to normal families. The interactions between the husband and wife, the parents and the children, the children among themselves and the family and extended family were described. As one of the aims of the present research was to investigate the relationship between the children and the relevant people in their lives an understanding of the literature on relationships within families was necessary. Family functioning, as well as some of the factors which affect a family's response to a disability were discussed. Families need to perform certain tasks to meet the needs of the members and a child with a disability can impact on each of the areas (economic, domestic and health care, recreation and socialization needs). Factors such as the family size and religion were shown to be important when assessing the impact of a child with a disability on the family. Finally, the chapter ended with a section on genetic counselling.

CHAPTER 3

METHODOLOGY AND PROCEDURE

3.1 INTRODUCTION

The purpose of this chapter is to describe the nature of the methodologies and procedures used in the present research. The ascertainment and selection of the two groups of subjects and the setting and scope of the research will be described. A specially constructed questionnaire was used to obtain the data and the details of its construction will be given. Finally, the details of the testing of the questionnaire through a pilot study, and the collection and analysis of the data will be reported.

3.2 ASCERTAINMENT AND SELECTION OF SUBJECTS

The subjects for the present study were the mothers and fathers of one or more children with FMR. There were two groups of subjects in the study: the experimental group, consisting of families with a child with FMR and the control group, consisting of families with children who did not have FMR.

The experimental subjects were ascertained from two sources; the cytogenetics and molecular laboratories of the department of Human Genetics at the South African Institute of Medical Research (SAIMR) where samples from FMR patients are processed, and Genetic services of the Department of National Health and Population Development (DNHPD) where the names and addresses of all the individuals with FMR, obtained after the screening program by Venter *et al.* (1986) were recorded.

1) Department of Human Genetics, SAIMR

Addresses and names of individuals from 39 families referred for FMR testing and their files were extracted (15 from the cytogenetics and 24 from the molecular laboratory). These files were examined and six patients were rejected as they were too old (born before

1950) and their parents were unlikely to be living. A further patient, with a family history, tested negative for FMR and three individuals requested carrier testing with negative results, and they had no affected child. The remaining sample consisted of patients confirmed with a diagnosis of FMR from 29 families. Two of the families lived too far away for a home visit (Welkom and Pietermaritzburg) and a postal questionnaire was sent to them with no reply. Current addresses for a further seven patients were not available. The final sample was therefore 20 families, whose parents were contacted, and 19 mothers and 8 fathers agreed to participate.

2) Genetic services, DNHPD

For reasons of confidentiality the Department of National Health and Population Development did not allow the researcher access to the addresses of their patients with FMR. However, the staff of the Department agreed to send the questionnaires (see Appendix C, D, E, G, with an introductory letter of their own (see Appendix B), to these patients. The 84 patients from DNHPD were sent postal questionnaires. Only two families returned questionnaires, two were completed by mothers and one by a father. Of the remaining 80 questionnaires 28 were returned (address unknown) and the remaining 52 families did not respond for reasons unknown.

The control group was obtained by house to house visiting in urban suburbs in Pretoria and Johannesburg. These suburbs were similar to those where many of the experimental subjects lived. Matched controls were selected. The criteria for matching were: the control parents should have a child of the same sex and age (within 4 years) of the affected child, the number of children in the family should be similar to the experimental family and they should be of the same ethnic group. When a suitable matched control family was identified they were interviewed with a slightly modified version of the questionnaire. Altogether 21 control mothers and 9 fathers were interviewed.

3.3 SETTING AND SCOPE OF THE STUDY

The setting for this study was the Gauteng region (mainly Johannesburg and Pretoria), since the subjects were interviewed personally and generally in their own homes, which

had to be accessible. All the subjects lived in urban areas. However, subjects from other areas were included, using postal questionnaires as an attempt to enlarge the sample size. Since FMR does not occur more commonly in a specific ethnic group, subjects from all population groups were included.

The study was based in the Department of Human Genetics, SAIMR and the School of Pathology, University of the Witwatersrand, where the researcher was a student and where the necessary infrastructure was available.

The majority of the subjects in the present study was obtained from the records (39 families) held at the Department of Human Genetics at the SAIMR and WITS from 1990 to 1996. Three further subjects were obtained form the records (84 patients) held at Genetic services of DNHPD from 1980 to 1986. These records were obtained by Dr P Venter during a national FMR survey of males in institution in South Africa. These records initially provided a reasonable large sample size (123 cases).

3.4 RESEARCH TOOL

The research tool used was a schedule of questions which was used both in interviews and as a postal questionnaire for inaccessible subjects. The advantages of using the administered questionnaire are that a higher response rate is usually obtained, and the meaning of difficult questions can be explained (Grinnell 1988).

3.5 CONSTRUCTION OF THE SCHEDULE

The researcher was unable to find a schedule which addressed all the aims of the present study, and so an interview schedule was specially constructed. A schedule consisting of a total of 64 items (schedule A) was used for the experimental group. This schedule was modified and reduced to 51 relevant items for use with the control group (schedule B). Both forms of the schedule as well as the introductory and cover letters that accompanied the schedules appear in Appendices G and J.

Schedule A was divided into four sections: 1) Personal details of parents (Eg. age, marital status) 2) Details of the child with FMR in the family (Eg.age, sex, birth-order), 3) the effects of the child on the family, in terms of his relationship with his parents, siblings and friends, and the effects on the marital relationship and 4) the support services provided. The items were selected by using the experience of the genetic counsellors in the Department of Human Genetics at the University of the Witwatersrand who had counselled affected families, as well as reported studies on Down syndrome and the family (Gath 1978 and Byrne *et al.* 1988).

The modified Schedule B, was divided into three sections: 1) Personal details (Eg. age, marital status) 2) Details of the child in the family (Eg. age, sex, birth-order), and 3) the effects of the child on the family, in terms of his relationship with his parents, siblings and friends, and the effects on the marital relationship.

3.5.1. SECTION ONE

Section one of schedules A and B was constructed to gain information on the biographical data of the sample. It contained items on the sex [item 1] and age of the informant [2], marital status [3], religion [4], ethnic group [5], education [6], occupation [7], income [7] and living arrangements [8].

3.5.2. SECTION TWO

Section two of schedule A was constructed to gain information on the child or children with FMR in the family: how many children were affected, their sex and birth order [9], the type of school the child attended [10,11], the characteristics of FMR in the affected child [12] and the child's favourite activities [13,14].

For the control group (schedule B) irrelevant items were omitted and only information on the sex and birth order of the children in the family [9], and favourite activities of the children were required [10, 11].

3.5.3. SECTION THREE

This section of the schedule was divided into four subsections: Section 3.1 was constructed to gain information on how the child with FMR and the matched control child relate to their friends and siblings. Friendships were evaluated by assessing: how many friends the children had [item 15 experimental group; item 12 control group]; who the friends were [16; 13]; and how the parents perceived these relationships [17,18; 14,15] . Information on the relationship between the children and their siblings was gathered by items on how they interacted [19,20,21; 16,17], whether there were problems [22,23,24; 18,19,20] and whether the other siblings felt excluded [25; 21].

Subsection 3.2 of the schedule included items on the parents' relationships with their children. The aspects evaluated included: discipline [26,27,28,29; 22,23,24,25], feelings towards the child [30,31,32; 26,27,28], responsibilities for physical caretaking [33,34,35,36; 29,30,31,32] and family activities [37,38; 33,34].

The next subsection, 3.3, was constructed to obtain information on the effects of having a child with FMR on the parents. The first few items explored how the parents felt after the diagnosis was made (only for the experimental group) [39,40,41,42]. These items were followed by questions on the effects [43; 35] on parents' ambition [45; 37], time for themselves [44; 36], their family planning [46; 38], and attitudes towards prenatal diagnosis and selective abortion [47,48; 39,40]. The last item [49] in this section, for the experimental group only, was "what advice would you give other parents who are in a similar position (having a child with FMR) to the one you were in?"

Section 3.4 contained items on the effects of a having a child with FMR (or matched control in the case of the control group) on the parents' marital relationship. The issues covered included: causes of friction [50,51,52; 41,42,43], satisfaction with help received from the partner [54; 45], satisfaction with the amount of time spent alone [53; 44], how the relationship is viewed [55; 46], and how the relationship has changed since the birth (or diagnosis) of the affected child [56,57; 47,48].

3.5.4. SECTION FOUR

The last section (only schedule A) required information on the professional help provided, who diagnosed the child [58,59,60], whether genetic counselling was received [61], and opinions about a support group [62,63].

One last open-ended item was added for both groups, and subjects were asked to add any comments or thoughts [64; 49].

3.6 THE PILOT STUDY

The completed interview schedule was pretested through a pilot study. The pilot study was conducted to exclude any unforeseen problems, to test the instrument for ambiguous or misleading questions and to test the length and time it took to complete.

The interview schedule was given to 10 subjects at the cytogenetics unit of the SAIMR; three males (one married with a child) and seven females (one single mother, five single and one married women) in their child-bearing years. They were asked to complete the questionnaire themselves and to comment on whether the questions were suitable and easily understood and how long it took to complete the questionnaire.

The pilot study subjects took between 30 and 40 minutes to complete the questionnaire and all had some problems in answering certain items of the questionnaire. The schedule was therefore revised by changing the wording of these questions and adding further items. For example [items 14 in shedule A and 11 in shedule B]: " what does your child like playing ?" was changed to "what **games** does your child like playing ?". Provision was made for **"unsure"** in asking parents whether other siblings knew of the diagnosis, and the item on which aspects parents liked and disliked about the child was changed to two separate questions, "do you like any particular aspects about your child ?" and "do you dislike any particular aspects about your child ?".

The revised schedule with informed consent sheet was submitted to the Committee for

Research on Human Subjects (Medical) of the University of the Witwatersrand for approval. The project was subsequently unconditionally approved by the committee (approval number: M 940716). A protocol of the study also had to be submitted to the Postgraduate Committee of the University of the Witwatersrand, the Committee approved the protocol. The letters of approval from the two committees appear in Appendix A.

3.7 COLLECTION OF DATA

The data were collected by interviewing the experimental and control group subjects with schedules A and B in face to face interviews either in their own homes or at the SAIMR (in one case). The 88 subjects from DNHPD and two from SAIMR were sent schedule A in the post, and were requested to complete and return it.

The data from the subjects identified from the SAIMR's files (with the exception of two families) were collected either by the writer alone or by the writer and Sr E Zwane, a research officer in the Department of Human Genetics. Sr Zwane was asked to participate because it was felt that some of the subjects would communicate more openly and effectively if they were allowed to speak in their own language. The writer was present when Sr Zwane conducted the first interview to ensure that she understood what the writer wanted from each item.

Data were collected from the subjects identified from the DNHPD's files by means of postal questionnaires. Only three subjects returned their completed questionnaires, one from Durban and two from Cape Town. Also, two subjects identified from the SAIMR records who lived in Welkom and Pietermaritzburg were sent questionnaires, but did not respond.

3.8 ANALYZING THE DATA

The completed schedules were coded so that the subjects' names were not on their answer sheets. The information obtained from the schedules and the returned postal questionnaires was then computerised. The computer program DBase III was used for this purpose. There was no need to code any of the responses (except for one item), since the data were

entered using words and most of the items were open-ended. For ease of analysis the responses to item 12 in shedule A, which referred to how often the affected children demonstrate various characteristics common in FMR, were coded in terms of a three point scale: often (scored 2), sometimes (scored 1) and never (scored 0). The minimum a child could score was 0 and the maximum was 28, and the higher the score the more features of FXS were present in the child. The scores were grouped into mild (0-4; 5-9), moderate (10-14; 15-19), and severe (20-24; 25-28) with two subgroups in each group.

The data were analyzed by means of content analysis. This can be defined as the "classification of the parts of a text into content categories" (Rosenthal and Rosnow 1991:158). The responses from the experimental group and the control group were compared, where appropriate and relevant. A t-test was used to determine whether the average age of the children in the experimental group was significantly different from that of the control children. Chi-square tests (2x2 and IxJ contingency tables) were used for selected responses to determine whether any of the differences obtained between the experimental and control subjects were significant (Steyn *et al.* 1989). A confidence interval of 5% was taken as significant. The results obtained were compared wherever possible with those from similar studies found in the literature.

3.9 SUMMARY

In this chapter the research methodology and procedure of the present study were described. The sample for the present study consisted of an experimental group, of families with a child with FMR, and a control group of families with normal children. The subjects (mothers and fathers) were ascertained from the records of both the Department of Human Genetics, SAIMR, and the Genetic Services of the DNHPD. A matched control group was selected by matching for the ethnic group, age, sex and number of children in the family.

Since the subjects were interviewed personally where possible and they needed to be accessible, the setting for this study was the Gauteng region. However, a few subjects from other areas ???????? were included by means of postal questionnaires, in an attempt

to enlarge the sample size.

The researcher and/or a research officer in the Department of Human Genetics conducted all the interviews with the control and experimental subjects. A specially constructed administered schedule, consisting of four sections in the case of the experimental group and three sections in the case of the control group, was used for this purpose. This schedule also served as a postal questionnaire for those subjects who lived far away.

The information obtained from the interviews and the postal questionnaires was analyzed by using the computer program Dbase III and the method of content analysis. For the statistical analysis the chi-square test was used to identify significant differences, in selected items, between the experimental and control groups. Finally, the results obtained were compared to similar studies in the available literature.

CHAPTER 4

RESULTS

4.1 INTRODUCTION

The information obtained from the schedules completed by the experimental and control subjects was analyzed using the computer program Dbase III. Chi-square tests (2x2 contingency tables and IxJ contingency tables) were used to test for significant differences between the control and experimental groups. The results obtained from the analysis of the data are recorded in this chapter.

The composition of the two study groups is described first, then the biographical data, including the details regarding the children in each family are presented for all the participating subjects. The findings on the relationships between the children and their sibs, friends, and the children and their parents, the effects of having an affected child on the parents and on the marital relationship, and finally the results on the help the parents received are reported.

4.2 COMPOSITION OF THE EXPERIMENTAL AND CONTROL GROUPS

The experimental group consisted of 30 subjects from 22 families. Interviews were conducted with 27 subjects, while postal questionnaires were completed by three further subjects. The age range of the 30 subjects (parents of children with FMR) was between 28 and 69 years of age, with an average age of 44 years. There were 21 female and nine male subjects and among these 30 subjects there were eight couples in whom mother and father were both interviewed (see Fig 4.1).

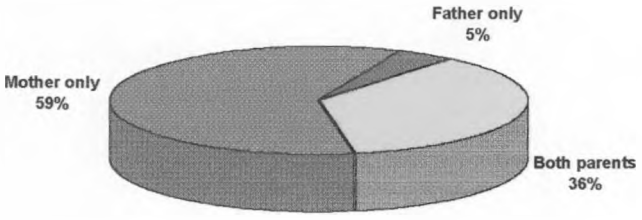

Fig 4.1 The number of Mothers and Fathers of FMR children interviewed in 22 families.

Altogether 11 of the 22 families had one affected male child, one family had one affected female child, six families had two affected sons, and four families had an affected son and daughter (see Fig 4.2).

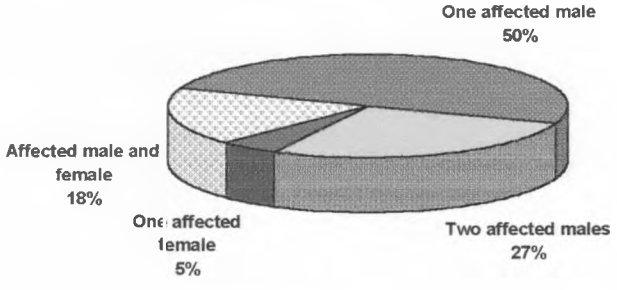

Fig 4.2 Sex of children affected with FMR in 22 families.

The control group subjects (parents of normal children) were matched with the subjects of the experimental group. The matching criteria included: ethnic group; sex of the index and control child; age of the index and control child (within four years of each other ie two years older or two years younger); and the number of children in the experimental and control families should be as similar as possible. The groups were closely matched for ethnic group, the only exception being that of an Indian family who was matched with a black family due to logistical problems. Matching for the sex of the child was perfect, and the groups were closely matched for age of the index children (average age 15.7 and 16.7 in experimental and controls respectively. Matching for family size was 93%, the exceptions being two control families who had only two children while the two matching experimental families had three or more children each. The details about the experimental families and the matched control families appear in Appendix L.

The control group and the experimental group were the same size with 30 subjects in each, 21 mothers and nine fathers, from 22 families. Interviews were conducted with both the parents in eight families and only one parent in the remaining 14 families. The age range of the 30 parents in the control group was between 29 and 60 years of age, with an average age of 43 years.

4.3 BIOGRAPHICAL DATA

4.3.1 INTRODUCTION

The first part of the schedule was concerned with the personal details of the subjects. The aim was to obtain information on their marital status, religion, ethnic group, and socio-economic status.

4.3.2 MARITAL STATUS

The majority of the subjects (21, 70%) in the experimental group were married (one woman had remarried after her first husband, the father of her son and daughter with FMR, passed away; three were single; three separated; two subjects were divorced and one widowed. Most (27, 90%) of the subjects in the control group were also married, but one female subject was divorced, one was single and one was living with a partner. There was, also one control woman who remarried after her first husband passed away. The difference between the number of married subjects in the experimental and control groups was not significant ($\chi^2 = 3.56$ $p > 0.5$)

4.3.3 RELIGION

The majority of the subjects in the experimental group were of the Christian faith (20, 67%), with most of this group being either Methodist (seven, 23%) or Catholic (four, 13%). The control subjects were also mostly Christians (29, 97%) with many being from the Dutch Reformed Church (57%), Reformed (18%), Protestant (18%), or Catholic

Church (3%). Although more control subjects were of Christian faith compared to the experimental group, the difference was not significant ($\chi^2 = 3.56$ p > 0.5). The details are shown in Table 4.1.

Table 4.1. Religion in the 30 subjects from the experimental and control groups.

RELIGION	*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*
Christian	20	66.8%	29	97%
Jewish	3	10%	0	-
Zion	2	6.7%	1	3%
Worldwide Church of God	1	3.3%	0	-
Muslim	1	3.3%	0	-
Jehovah's Witness	1	3.3%	0	-
None	1	3.3%	0	-
Atheist	1	3.3%	0	-
Total	**30**	**100%**	**30**	**100%**

4.3.4 ETHNIC GROUP

The majority of the subjects in both groups were Caucasoids of European extraction (21, 70%), five (17%) were of African origin, three (10%) were so-called Coloured and only one (3%) subject was of Indian origin.

4.3.5 LEVEL OF EDUCATION

Most of the subjects of the experimental group had attended school and there was only one subject who had no education at all. In general the control group had a slightly higher level of education than the experimental group. A larger number of control subjects had a tertiary education (15, 50%) than experimental subjects (7, 23%), however this was not significant ($\chi^2 = 3.52$ p > 0.5). There were no control subjects who did not have an education (see Fig 4.3).

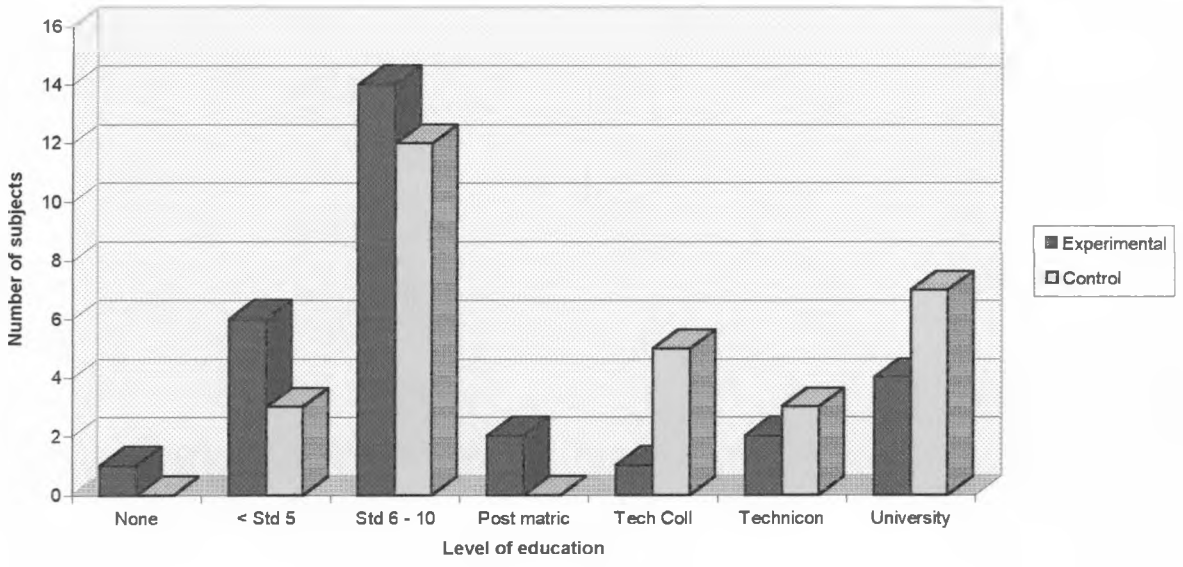

Fig 4.3 Level of education of the 30 subjects of the experimental and control groups.

4.3.6 SOCIO-ECONOMIC STATUS

The type of living accommodation and the subjects' level of income per annum were recorded to provide insight into the socio-economic status of the families. In the experimental group, 14 (64%) families lived in their own houses, one lived in a rented house and one lived in a rented apartment. There were four families who lived with their parents, one lived in a house provided by the husband's company and one lived at her place of employment (domestic worker). Similarly, the majority of the control families, 16 (73%) lived in their own houses while six (27%) occupied rented houses.

The largest single group of the experimental subjects (12, 40%) had no income. Of this group three subjects were unemployed (one male and two females), seven were housewives and two were on pension (one male and one female). While seven control subjects (all females) had no income, five were housewives and two were unemployed. The control subjects had a slightly higher income than the experimental subjects, thought not significant, and 12 controls earned over R48 000-00/anum compared to eight experimental subjects.

4.3.7 SUMMARY

Table 4.2 Summary of the characteristics of the subjects

SUMMARY	*Subjects*	
	Exp group	*Cnt group*
Total number of subjects	30	30
Females	13 (59%)	13 (59%)
Males	1 (5%)	1 (5%)
Couples	8 (36%)	8 (36%)
Age in years		
Average	44	43
Range	28 - 69	29 - 60
Children		
One affected male	11 (60%)	
Two affected males	6 (27%)	
Affected male and female	4 (18%)	
Affected females	1 (5%)	
Married	21 (70%)*	27 (90%)*
Religion - Christian	20 (67%)	29 (97%)
Ethnic group		
Caucasoid (European)	21 (70%)	21 (70%)
Black	5 (17%)	6 (20%)
Coloured	3 (10%)	3 (10%)
Indian	1 (3%)	0
Level of education		
Matric	14 (47%)	12 (40%)
Tertiary education	9 (30%)**	15 (50%)**
Socio-economic status		
House owners	14 (64%)	16 (73%)

* $\chi 2 = 3.56$ $p > 0.5$
** $\chi 2 = 3.52$ $p > 0.5$

The main characteristics of the subjects in the experimental and control groups are summarised in Table 4.2. As may be seen from this table the two groups were very similar in most respects. None of the differences between them were significant, although the groups were somewhat dissimilar with regard to marital status, religion and tertiary education.

4.4 DETAILS OF THE SUBJECTS' CHILDREN

4.4.1 INTRODUCTION

Information was obtained on the number, sex and status (affected or normal) of the children in the families included in the two study groups. Details were also collected regarding the type of school attended, or the type of employment of the individuals with FMR. Further, the features of the condition that occurred in the affected children were recorded. Finally, information on the activities and games of the experimental and control children was sought.

4.4.2. COMPOSITION OF THE GROUP OF AFFECTED AND CONTROL INDIVIDUALS

In the 22 families in the experimental group there were 31 individuals with FMR, 25 (81%) were male and six (16%) were female. The control group was selected so that the sex of the matched control child was the same as that of the oldest child with FMR in the experimental family (the parents with more than one affected child only reported on the first-born child with FMR).

In the 22 experimental families, 10 (45%) families had two children affected with FMR and 12 had only one affected child. Although birth order was not one of the matching criteria, when selecting the control group, the two groups of children were fairly similar in birth position (see Fig 4.4).

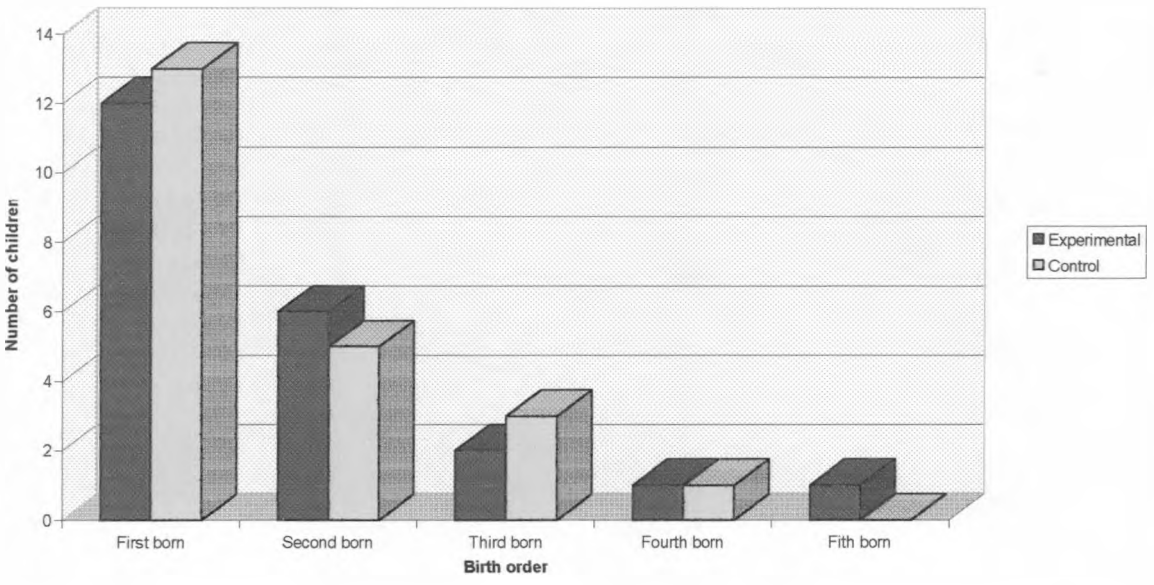

Fig 4.4 The birth position of the 22 children with FMR and their matched controls.

The age range of the individuals diagnosed with FMR was 3 to 44 years, with the largest single group being children between 5 and 9 years of age (six, 27%). The age of the affected child (only the first-born in families with more than one affected individual) was one of the matching criteria in selecting the control group. Since it was difficult to meet the exact requirements of the matching the age of the control children was matched within a four year range (two years older or younger) of the experimental child's age. The age range of the controls was smaller (5 - 27 years) but a quarter of control children (6, 27%) were 5 - 9 years of age. The average age of the children in the experimental group (only the first-born child in the family) was 16.7 years whereas the average age of the children in the control group was 15.7 years. This difference is not significant ($t = 0.41$).

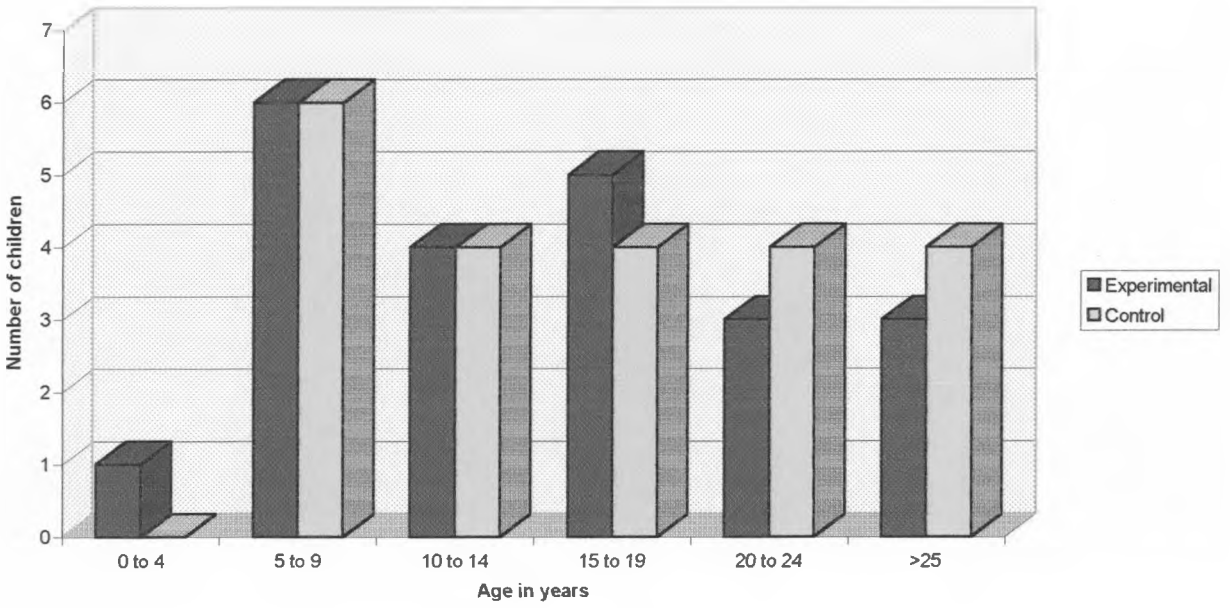

Fig 4.5 The ages of the children in the experimental and control groups.

4.4.3 OCCUPATION OF THE INDIVIDUALS WITH FMR

The majority (27 or 90%) of the 31 individuals with FMR were scholars at the time of the study, and only four (11%) had completed school and were working. Of the 31 individuals, 25 (83%) had attended or were attending a special school, four (13%) had not attended school (three were too young and the other did not provide a reason, but he was working), one was in a special class in a normal school, and one was in a normal class in a normal school. Three of the four adults (75%) with FMR that were working were in sheltered employment and one was in normal employment (he was working in his father's business).

Table 4.3 shows a summary of the characteristics of the two groups of children and from this table one can see that the two groups are matched fairly well. None of the differences were found to be significant.

Table 4.3 Summary of the characteristics of the two groups of matched children in the 22 matched project families

SUMMARY	*Children*	
	Exp group	*Control group*
Total number of children		
Females	3 (14%)	3 (14%)
Males	19 (86%)	19 (86%)
Total	**22***	**22***
Age in years		
Average	16.7	15.7
Range	3 - 44	5 - 27
Total	**22**	**22**
Birth order		
First born	12	13
Second born	6	5
Other	4	4
Total	**22**	**22**
Type of schooling		
Special school	16	1
Special class	1	0
Normal class	1	18
None	1	0
Too young	3	3
Total	**22**	**22**

* In the experimental group there were 31 children with FMR, but only the first-born child in each family (22 children) was matched with a normal control child.

4.4.4 CHARACTERISTICS OF THE FMR IN AFFECTED CHILDREN

The parents were asked to describe their child with FMR by reporting on selected characteristics found commonly in affected children. These characteristics included: speech (incomplete sentences, rapid speech rate, perseveration), socialising (difficulties,

shyness, avoidance of eye contact) and behaviourial problems (hyperactivity, hand-biting, hand-flapping, tactile defensiveness, emotional outbursts, rocking, short attention span, and self-mutilation). This information was not collected from the controls.

Table 4.4 shows the number of children in the six scoring groups. In 31 cases the child was assessed by the mother only and in 10 cases the child was evaluated by both parents. From the table it is clear that half (16 or 52%) of the children (when only the mothers' responses were considered) had a low moderate score between 10 and 14. Only one child had a high score of 24. Mostly the two parents assessed their child similarly, however two couples responses differed to such an extent that the child was seen by the mother to be mildly affected (score 5 and 7 respectively) and by the father as moderately affected (score 13 and 16 respectively). The commonest characteristics reported were short attention span (nine subjects reported this often and 15 sometimes), followed by emotional outbursts (nine parents reported often and 14 sometimes) and shyness (10 reported often and 12 sometimes). These were followed by perseveration, rapid speech rate, avoiding eye contact, hyperactivity, hand-biting, hand-flapping, speaking without completing sentences, self-mutilation, tactile defensiveness and rocking.

Table 4.4 Number of characteristics in FMR children as assessed by their parents.

SCORE		*Number of children*					
		*Assessed by Mother only**		*Assessed by both parents*			
				*Mothers***		*Fathers***	
		No	*%*	*No*	*%*	*No*	*%*
0-4	Mild	2	6%	1	10%	1	10%
5-9		9	29%	4	40%	3	30%
10-14	Moderate	16	52%	3	30%	4	40%
15-19		3	10%	2	20%	2	20%
20-24	Severe	0	-	0	-	0	-
25-28		1	3%	0	-	0	-
Total		**31**	**100%**	**10**	**100%**	**10**	**100%**

* Including mothers from couples who both assessed the child.
** Two couples had two children affected.

4.4.5. THE CHILDREN'S FAVOURITE ACTIVITIES AND GAMES

Many of the children in both groups enjoyed physical activities such as kicking a ball or running around and playing football (11, 36% in the experimental group and 18, 60% in the control group). Although more parents of the children in the control group reported this, the difference was not significant ($\chi^2 = 1.87$ $p > 0.5$). A few mothers in the control group reported that their children liked going to movies (two cases) or reading (two cases) whereas this was not reported by the parents in the experimental group, although a few children with FMR liked watching television (4, 19%). No subjects in the control group reported that their children enjoyed helping their parents, whereas three (14%) experimental parents reported this behaviour. Four mothers and two fathers with normal children but only one experimental parent reported that their children played computer or television games.

4.5 RELATIONSHIPS BETWEEN THE CHILDREN AND THEIR SIBLINGS AND FRIENDS

4.5.1 THE INDEX CHILDREN AND THEIR SIBLINGS

In both the experimental and control groups, most parents reported that the index children related well to their siblings (see Table 4.5). However, a few more parents (eight, 28%) of children with FMR reported that their children's relationship with the other siblings was bad or very bad, than did the parents of normal children (only two mothers), but the differences was not significant ($\chi^2 = 3.28$ p > 0.5).

Table 4.5 Relationship between the index children and their siblings according to their parents*.

RELATIONSHIP WITH SIBLINGS	*Individual subjects**				*Couples***			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Very good	7	25%	4	14%	1	2	1	1
Good	8	29%	13	46%	2	2	4	2
Moderate	4	14%	9	32%	2	1	2	4
Bad	2	7%	1	4%	1	1	0	0
Very bad	6	21%	1	4%	1	1	0	0
Did not answer	1	4%	0	-	0	0	0	0
Total	**28**	**100%**	**28**	**100%**	**7**	**7**	**7**	**7**

* Including both mothers and fathers
** One couple in the experimental group and control group had only one child

Some examples of the comments made by the parents in the experimental group include: "they are very close and he (affected) takes his younger brother (also affected) under his wing, he is very caring towards him" (respondent was a mother); "he (affected) bullies his younger brother (affected), he hurts him, he bites and scratches him terribly" (mother); "she (affected) is very jealous of her brother (affected), she ignores him and shows no

affection towards him" (mother of affected son and daughter); "my normal son is very protective over him (affected), he told me that he will have to find a good job so that he can look after his brother" (mother); "his sister can do more than he (affected) can, I think she gets frustrated with him" (father). Control parents'comments included: "they are very close, they do fight a bit but they love each other a lot" (father); "he is very protective over his sister, they can give each other a hard time, he will usually be the first to give in if she nags enough" (father); "very bad, they fight a lot, he cannot even look at her" (mother).

Experimental subjects were asked whether the siblings knew of the diagnosis of FMR and how this affected the relationship between the index child and the sibs. In the majority of cases (14 or 67%) the siblings were aware of the diagnosis of FMR, in three (14%) cases they were not aware, and in four (19%) the parents were unsure whether they knew it or not. The responses of parents who reported that the siblings were aware of the diagnosis, included: "my son is aware his brother has mental retardation, and he is now teaching him everyday after school so that he can also go to a normal school" (father); "he knows it is genetic and understands that J has limitations" (mother).

In 12 families (55%) felt that knowledge of the diagnosis of FMR had affected the sibling relationship either positively or negatively, and some of their responses included: since the siblings know the children are special they are more tolerant of them; the siblings are more protective; and four parents stated that the siblings are impatient with the affected child. There was one mother who reported that her daughter went through a resentful stage towards her affected brother because she was worried that one day when she has children they might also be affected.

Parents were asked whether there were any problems in the sibling relationship. Although the majority of subjects (18, 64% experimental and 25, 89% control) in both groups stated that there were no problems, fewer control group parents (three, 11%) reported problems compared to parents in the experimental group (10, 36%). However, this was not a significant difference ($\chi^2 = 3.61$ $p > 0.5$)

The following examples were given by the experimental group parents who described problems: "my son gets impatient with her (affected) and pushes her away" (mother); "J bullies S, they get on better when they are by themselves, they fight when they are together" (father with both sons affected); "he has a different way of doing things, and he has difficulty fitting in with the household, he wants to go back to boarding school after a few days at home" (mother). Examples given by the control parents included: "they don't get along any more since she went to high school" (mother); "he is very rough with his younger brother, he hits him when they fight" (mother).

Parents were asked whether they thought the other siblings felt left out or jealous in any way of the index child. The majority of parents in both the experimental (21, 75%) and control group (25, 85%) did not think the other siblings felt excluded. However, four parents in the experimental group did feel this was the case: "my normal son complains that his brother gets more attention" (mother); "the children with FMR get a lot of attention and she doesn't understand" (mother). Three control parents felt similar: "I think my daughter did feel left out because she stuttered and started biting her nails" (mother); "sometimes I think they do, because he is brilliant and a top student, the others are jealous of him" (mother); "because he is in a school mainly for white children, he has some learning difficulties" (mother of a child of coloured origin).

4.5.2 THE CHILDREN AND THEIR RELATIONSHIPS WITH THEIR FRIENDS

The relationship between the children (experimental and controls) and their friends was assessed by asking the subjects to comment on the number of friends the children had, who the friends were and how they related to each other. All the parents in the control group reported that their children had friends compared to only 23 (77%) in the experimental group. Six parents of children with FMR thought that their children had no friends whereas no control parents reported this, and this difference was significant ($\chi^2 = 4.83$, $p < 0.05$). Table 4.6 shows these results.

Table 4.6 The number of friends of the children in the experimental and control groups.

NUMBER OF FRIENDS	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Many	9	30%	11	37%	0	1	5	2
Few	14	47%	19	63%	4	6	3	6
None	6	20%	0	-	4	1	0	0
Don't know	1	3%	0	-	0	0	0	0
Total	**30**	**100%**	**30**	**100%**	**8**	**8**	**8**	**8**

The experimental group parents reported that the friends of their affected children were school friends (14, 47%) or neighbours (7, 23%). While control parents' children had friends at school, university and work.

Significantly more parents with FMR children than controls rated the relationship with their friends as problematic ($\chi^2 = 9.40$, $p < 0.005$). And significantly more parents of normal children than children with FMR rated the relationship with their friends as "good" ($\chi^2 = 7.47$, $p < 0.01$). See table 4.7 for details.

Table 4.7 The children's relationships with their friends.

RELATIONSHIP WITH FRIENDS	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Very good	0	-	6	20%	2	0	3	1
Good	10	33%	16	53%	0	3	5	3
Moderate	6	20%	6	20%	1	2	0	4
Some problems	10	33%	2	19%	6	3	0	0
Not good	3	10%	0	-	0	0	0	0
Don't know	1	3%	0	-	0	0	0	0
Total	**30**	**100%**	**30**	**100%**	**8**	**8**	**8**	**8**

The parents in the experimental group described some of the relationships of their affected children: "he feels inadequate among normal peers" (mother); "he fights when he cannot express himself, he gets rid of his frustrations by hitting and biting" (mother); "he doesn't get involved with other children, he will only play by himself" (mother); "she can be overbearing and gets too exited and frightens the friends away" (mother); and "the normal children are cruel, they tease and laugh at him, especially his ears" (mother).

The control parents stated: "rather shy, doesn't make friends easily" (father); "good, there are always children here to play" (mother); "they look up to him, they see him as a leader" (mother); "boys like to fight sometimes" (mother).

4.5.3 SUMMARY

In this section the relationship between the index children, their siblings and friends was evaluated from the parents' perspective. Although more experimental than control parents reported that the relationship between the children and the other siblings in the family was bad, this was only a trend and the difference was not significant. The experimental subjects reported that there were problems in the sibling relationship which included not communicating, bullying and fighting.

In 67% of cases the siblings of children with FMR were aware of the diagnosis. More than half the parents (55%) thought that this did affect the sibling relationship. While some siblings were more tolerant and protective over the affected children, others were resentful and impatient. Most parents (21, 75% experimental and 25, 87% controls) thought that the normal sibs did not feel excluded.

Significantly more parents in the control group reported that their children had friends compared to experimental parents ($\chi^2 = 4.83$, $p < 0.05$). The friends of both groups were mostly from school or neighbours. Significantly more control parents reported a good relationship between their children and their friends compared to parents with children with FMR ($\chi^2 = 7.47$ $p < 0.01$) and significantly more parents with children with FMR compared with parents in the control group, reported that there were some

problems in the relationship between the children and their friends ($\chi^2 = 9.40$ p < 0.005).

These findings suggest that the relationships of affected individuals with their peers may be influenced by the nature of their condition. An individual with FMR, may experience marked problems in relating to extrafamilial individuals, while their relationships with their siblings may be affected to a lesser extent.

4.6 THE CHILDREN AND THEIR PARENTS

4.6.1 INTRODUCTION

Data were collected on the relationship between the individuals with FMR and their parents and compared with the data on the controls and their parents. Issues addressed included: management and discipline, aspects parents liked and disliked about their children, child care responsibilities and family activities.

4.6.2 MANAGEMENT OF THE CHILDREN

Over half of the parents (16, 53%) in the experimental group stated that they had management concerns, compared with about a quarter (8, 26%) of controls (see Table 4.8). However, this difference was not significant ($\chi^2 = 3.4$, p > 0.5).

Table 4.8 Management concerns among parents.

CONCERNS	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
No concerns	14	47%	22	73%	4	5	6	7
Some concerns	12	40%	7	23%	3	1	2	1
Many concerns	4	13%	1	3%	1	2	0	0
Total	**30**	**100%**	**30**	**100%**	**8**	**8**	**8**	**8**

The concerns were different for the subjects in each group: many of the experimental

group worried about the long term, while the control parents worried about short term problems. The parents of children with FMR reported concerns related to finding an appropriate school for the child, the child's inattentiveness, the future, financial problems, and the child's dependence on the mother. The concerns the control subjects mentioned included: the child's quick temper, the influence of friends, lack of confidence, reading difficulties at school, difficulties in asserting discipline, spoiling the child, not taking education seriously, and wasting money.

The method used by the parents to discipline their children, in both groups, was most often verbal (26, 87% experimental group and 28, 93% control group). Other methods used included time out (sending the child to his/her room or to stand in the 'naughty' corner), threats, withdrawal of privileges or not allowing the child to watch a favourite television program or to play with a favourite toy. The comparisons between the experimental and control couples revealed that the experimental mothers (7/8) used physical punishment more than the experimental fathers did, while control fathers (6/8) were more likely to use such punishment than control mothers. This is only a trend which cannot be tested statistically because of the small sample size. For details, see table 4.9.

Table 4.9 Disciplinary methods used by the parents in the experimental and control groups.*

DISCIPLINE	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Verbal	26	87%	28	93%	8	6	7	8
Physical punishment	16	53%	16	53%	7	3	2	6
Time out	12	40%	7	23%	4	4	3	2
Withdrawal of privileges	12	40%	12	40%	4	4	3	3
Threats	10	33%	14	47%	4	2	4	4
Other	3#	10%	5##	17%	1	2	2	1
No confrontation	3	10%	0	-	0	1	0	0

* Several subjects gave more than one response.
\# Talking calmly, telling the child to "chase the devil on his shoulder away", and withholding a meal from the child.
\## Talking calmly (3), "the look", and a family discussion every week to sort out differences.

All the parents stated they rewarded good behaviour and all did this verbally. Three experimental parents also praised good behaviour by giving the child special privileges, whereas parents in the control group did not use this method. Significantly more parents in the control group reported that they praised good behaviour physically by hugs and kisses (14, 47%) than did the parents in the experimental group (4, 13%) ($\chi^2 = 5.10$, $p < 0.05$).

4.6.3 FEELINGS TOWARDS THE CHILDREN

Parents were asked which aspects they liked and disliked about their children and whether they treated the affected or normal control child differently to the other children in the family.

All the parents (except one) in the experimental group, could think of something about their child with FMR that they liked. The exception was a widowed black father with a grown-up son. There were 14 (47%) parents who enjoyed their children's happy and loving nature, compared to seven (23%) parents (all mothers) in the control group. Similarly, more experimental parents (8, 27%) reported that they enjoyed their children's caring and thoughtful nature compared to the parents (3, 10%) of control children. When these two categories were combined the differences between the two achieved significance ($\chi^2 = 7.38$, $p < 0.01$).

The experimental parents reported other aspects they liked about their children, such as helpfulness, obedience, and a good memory. Control parents liked their children's obedience, responsibility, strong personality, goals, ambition, honesty and intelligence.

Parents were asked to report on the aspects they disliked about their children. The parents in the two groups provided very different responses. Several parents in the experimental group reported that they disliked their children's bad tempers (10, 36%), the fact that their children were difficult to control (5, 17%) and destructive (4, 13%), whereas a few parents in the control group reported that they disliked their children's laziness (5, 17%) and moodiness (4, 13%). More parents in the experimental group reported a dislike for

behaviourial aspects than the parents in the control group. This achieved significance when the responses for temper, difficult to control and destructiveness were combined ($\chi^2 = 15.44$, $p < 0.001$).

More than half of the parents in both groups reported that they did not treat their index children differently to their other children (16, 57% experimental and 15, 53% control). However 10 (35%) experimental and 13 (46%) control parents thought they did and some of their responses included: "I try not to, but they are treated different because they are different children" (experimental mother); "I treat him with cottonwool gloves, I am more tolerant with him than with his sister" (experimental mother); "he is the first born, I was much more attentive with him, I am more relaxed with the second one, he is almost neglected" (experimental father); "I have more patience with her" (control mother).

4.6.4 PARENTAL CHILD-CARE RESPONSIBILITIES

The child care responsibilities assigned to each parent were investigated by the following question: "who is responsible for the physical caregiving, who plays with the children and who is responsible for taking the children for therapy or doctor's visits?"

In most cases, as expected, for both the experimental and control groups, the mothers (22, 73% in both groups) were responsible for physical caregiving, such as feeding, washing and dressing of the children. Mothers in the experimental group received help in 16/22 cases (72%), and when they did, it was mostly from their husbands and/or the child's siblings. Mothers in the control group also reported receiving help (20/22 cases or 90%), mostly from their husbands (see Table 4.10).

Table 4.10 Physical caregiving and sources of help.

PHYSICAL CAREGIVING	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Mother (no help)	6	20%	2	7%	1	1	0	1
Mother (received help)	16	53%	20	67%	6	6	8	7
from: siblings	8		4		3	2	3	1
Husband	9		15		6	4	7	6
Domestic worker	4		1		0	1	0	0
Grandmother	3		2		2	2	1	0
No response*	5	17%	8	26%	1	1	0	0
Siblings	2	7%	0	-	0	0	0	0
Father	1	3%	0	-	0	0	0	0
Total	**30**	**100%**	**30**	**100%**	**8**	**8**	**8**	**8**

* The "No response" included parents, with grown-up individuals, who did not respond and those who said their children perform tasks on their own.

Again in the majority of cases when asked who played with the child most of the time, the experimental mothers (17, 57%) stated that they played with their children most of the time. The results comparing partner's perceptions within the couples were interesting: mothers tended to report that they played with the children mostly, whereas fathers in both groups tended to report that they themselves played with the children most (see Table 4.11).

Table 4.11 Persons who played with the children in the experimental and control groups most of the time.

PLAYED WITH CHILDREN	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Mother	17	57%	11	36%	7	4	3	3
Siblings	15	50%	5	17%	4	2	2	0
Father	13	43%	13	43%	5	6	3	5
Friends	5	17%	8	27%	1	0	0	1
Others*	6	20%	3	10%	2	3	1	2

* eg. cousins, grandparents

Similarly, experimental (13, 43%) and control (20, 67%) mothers were also mostly responsible for taking the children to the doctor. The results comparing partners' responses showed that experimental parents were more likely than control parents to go together with the children. Very few fathers (one experimental and two controls) took their children to the medical practitioner alone. However, the samples are too small for statistical testing.

4.6.5 FAMILY ACTIVITIES

In most cases, the parents reported that they had family outings with their index children (23, 77% experimental subjects and 27, 90% control subjects). However, although the samples are too small to test statistically slightly more parents (seven) in the experimental group compared to the parents in the control group (three) did not include the index child. Only one couple, with two affected boys, reported that their behavioral problems makes it "a nightmare to go out". The activities included visiting friends and relatives, going shopping, going out to dinner, going to the zoo and going on holiday.

4.6.6 SUMMARY

To evaluate the relationship between the children and their parents, several aspects were

investigated. Although it was found that more parents of children with FMR than controls had concerns about management the difference was not significant. The concerns expressed by the experimental parents were finding an appropriate school for the child, finances and the child's future.

In disciplining the children all the parents reported using verbal methods, and praising good behaviour. However, significantly more control parents rewarded good behaviour by physical contact such as hugs and kisses than did experimental parents ($\chi^2 = 5.10$, $p < 0.05$).

All the parents (except for one experimental father) could think of something about their children that they liked. Remarkably, significantly more parents in the experimental group than controls reported that they liked their children's happy, loving nature, caring and thoughtfulness ($\chi^2 = 7.38$, $p < 0.01$). Further, significantly more ($\chi^2 = 15.44$, $p < 0.001$) experimental parents disliked their children's tempers, the fact that they were difficult to control, and their destructiveness.

The mothers in both groups were mostly responsible for the physical caregiving of the children. Although more siblings in the experimental group compared to the control group played with the children, the difference was not significant. The results comparing the small group of couples' responses showed that more experimental parents took the child to the doctor together, compared to the control group, in which the mothers went alone. Finally, all the children were usually included in family activities.

4.7 THE EFFECTS OF THE INDEX CHILD ON THE PARENTS

4.7.1 INTRODUCTION

Information was collected on how the index child affected the parents, how the experimental parents felt when they noticed their child had a problem, and when they received the final diagnosis. All the subjects were questioned about their changing ambitions, how much of their time the child demanded, and future childbearing decisions.

4.7.2 THE PARENTS' FEELINGS BEFORE AND AFTER THE DIAGNOSIS

The parents of children with FMR were asked when they first noticed that their children were different. The results are shown in Table 4.12. From the table, it is clear that most parents (21, or 70%) noticed a problem when the children were in their preschool years. One father said that he and his wife noticed that their affected daughter was delayed, especially in her speech development. A couple reported that the husbands' mother pointed out that their son was delayed and they had him assessed together with all the other cousins. This father said that he might have noticed that something was wrong but did not want to accept or acknowledge it.

Table 4.12 Time when experimental parents first noticed their child's problem.

PROBLEM FIRST NOTICED	*Indiv subjects*		*Couples*	
	No	*%*	*Mo*	*Fa*
Less than one year	7	23%	4	4
One to six years	14	47%	3	2
First school years	6	20%	0	0
Didn't notice anything	3	10%	1	2
Total	**30**	**100%**	**8**	**8**

When the subjects were asked what had made them suspicious, 12 parents (nine mothers, three fathers) stated that the child's delayed milestones had caused anxiety (Table 4.13).

Table 4.13 Factors arousing suspicion.

FACTORS	*Indiv subjects*		*Couples*	
	No	*%*	*Mo*	*Fa*
Delayed milestones	12	40%	4	3
Failed at school	5	17%	0	0
Family member pointed out	3	10%	1	2
Child had fits	1	3%	0	0
Aware of family "problem"	1	3%	1	0
None	8	27%	2	3
Total	**30**	**100%**	**8**	**8**

The parents were asked how long they waited from the time they noticed that the child was different to the time they received the diagnosis of FMR (see table 4.14). The data comparing the couples' responses suggested that mothers perceived a shorter waiting period than the fathers did.

Table 4.14 Time between first observing problems and diagnosis.

TIME ELAPSED	*Indiv subjects*		*Couples*	
	No	*%*	*Mo*	*Fa*
Up to one year	8	27%	2	2
One to three years	6	20%	3	1
Three or more years	8	27%	2	3
No information	8	26%	1	2
Total	**30**	**100%**	**8**	**8**

The parents described many different feelings while awaiting the diagnosis. These included being traumatised and hurt, feeling like it was the end of the world, and acceptance. Some mothers (3) asked "why me?" and others (3) denied the fact that there was a problem (3). Examples of the responses were:

> "Why me, why him, I questioned everything, I thought I did something wrong, I felt guilty"

> "It was not easy to accept, a father wants a son to buy bikes and cars, I denied it, I thought he was just slow".

Some described feelings of hopefulness: "I thought he could be cured". Mothers also described anger, anxiety, guilt, sadness, isolation, felt a sense of responsibility and were upset. One mother said:

> "I was accused of wanting my child to walk before he could crawl, no child opens his mouth and speaks properly, I was told, I refused to put him in a normal school and the Transvaal Education Department wanted to take us to court".

There were three fathers who accepted the situation, one stated:

> "We accepted it before we had him because my sister-in-law had a child with a problem, so we knew the risk we were taking".

Other fathers described feelings of hurt, disappointment, trauma and denial, eg. "I denied the problems, life went on fairly normally, it was only slight developmental delay".

After receiving the diagnosis of FMR, the parents described similar feelings. Some mothers (6) felt guilty once they knew how FMR was inherited. Examples of their responses included:

> "I was bitter, I blamed myself, if I had known I was a carrier I would never have had children, I think my husband blames me, I had a lot of hate towards our affected son",
>
> "I felt guilty, I took it worse than my husband, I worried that he would not be accepted, I overreacted and bought the best educational toys, my son's appearance had to be perfect so no-one could suspect that their was something wrong with him".

However another mother was relieved of her guilt by knowing how FMR is inherited, and she stated that,

> "Nothing could have been done to prevent this".

Some mothers felt uncertain (3), and three were relieved at having a diagnosis,

> "I am sad that they will not get better, but also happy that I know what the diagnosis is" (a mother with an affected boy and girl)

There were three mothers who regretted not knowing anything about FMR before planning to have children. Feelings of the world tumbling down, bitterness, hurt, even hate for the child, shame, shock, and upset were described. Again, some mothers asked "why me?" and were angry, some were unhappy and sad (4), one felt inferior and again some lived in hope.

There were four fathers who accepted the situation, one stated "the diagnosis came so late, we already knew what he was capable of". One had feelings of uncertainty with questions such as: "will he catch up, or learn to drive a car, or will he be able to hold down a job?" One father with two affected boys also expressed feelings of bitterness and anger,

> "I was extremely bitter and angry when I realized the implications of FMR. It is not cut and dried but very variable, we don't know how they will develop".

One father experienced denial and stated that "there was a time when I did not believe the diagnosis because he looks just like his twin sister". Another father hoped for the best:

"I was hopeful that something could be done, eg a miracle cure, that FMR could be medically repaired and the insert could be returned to its normal size".

4.7.3 PERSONAL CHANGES

The subjects were asked whether they thought they had changed as a person after having the index child, and if they had, how they had changed. The parents in both groups gave similar answers, about half (57%) thought that they had changed. Some experimental subjects thought that they had changed for the better and stated: "I am more understanding, caring and accepting, I am less selfish and I have changed my attitude towards the handicapped" (mother); "I never liked children and never wished to have any, but now I am loving and a very considerate person" (mother). Other experimental subjects reported negative changes: "I had high expectations for my children, now I take each child as they come" (mother); "I have become less confident, insecure and easily worried " (mother); "My whole life has changed, I have become very bitter and angry, my religion has changed and I don't believe in God any more" (father); "The whole household has changed, other people's remarks about my son are humiliating and you become hard" (mother).

The majority of subjects did not think their ambitions had changed (21, 70% in both groups). The remaining subjects stated that they had changed their ambitions and two parents of children with FMR had made appropriate adaptations: "I started my own business so that my son will always have a place to work" (father) and "I wanted to form a support group" (father). However, a normal child also created changes eg: "my life revolves around our son, I work to keep him at University" (father); "I stopped working to look after the children" (mother); "I fell pregnant, and I was unable to go back to school" (mother); and "I was very career orientated, but after the children I am not" (Afrikaans mother).

4.7.4 FAMILY PLANNING

The majority of subjects in both groups reported that they did not want more children.

As can be seen in Table 4.15 there was no consensus among experimental or control couples and experimental fathers were more likely than their wives not to want more children, while control mothers were more likely than their husbands not to want more children.

Table 4.15 Plans for future children.

MORE CHILDREN	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Yes	2	7%	2	7%	1	0	1	2
No	14	47%	20	67%	2	5	7	5
Unsure	1	3%	1	3%	0	0	0	1
Not applicable*	13	43%	7	23%	5	3	0	0
Total	**30**	**100%**	**30**	**100%**	**8**	**8**	**8**	**8**

* These were couples who had been sterilized.

The reasons provided by the subjects for not wanting more children are listed in Table 4.16. Different answers were obtained from the subjects in the two groups. Some subjects were unable to have more children because they have been sterilized. Some experimental subjects (all mothers) were worried about having another child with FMR (four, 13%). In the control group, the subjects stated that they had completed their families (14, 56%), that they were too old (seven, 20%) and that they were unable to reproduce (six, 23%). Again, perhaps surprisingly, there was no consensus between the partners in the couples and fathers did not mention sterilization etc, as often as mothers did. Only one parent among the couples stated that FMR was the reason he did not want more children.

Table 4.16 Reasons for not wanting more children.#

REASONS	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Completed family	8	27%	14	47%	1	3	3	3
Because of FMR	4	20%	-	-	-	1	-	-
Financial	1	3%	6	20%	-	-	0	2
Too old	3	10%	7	23%	1	1	2	1
Problems*	10	33%	4	10%	5	3	3	0
Sterilized	3	10%	1	3%	-	-	0	0
Other	0	-	2**	7%	0	0	0	0

\# Several subjects gave more than one response
* Includes one control woman who had two miscarriages
** "no patience", "too much work"

4.7.5 PRENATAL DIAGNOSIS AND SELECTIVE ABORTION

The two groups were asked slightly different questions to obtain the information on prenatal diagnosis and selective abortion. The experimental subjects were asked whether they would request prenatal diagnosis (PND) and termination of pregnancy (TOP) for FMR in future pregnancies. The control subjects were asked whether they would want to know of any fetal abnormalities in future pregnancies and whether they would request a TOP if the fetus was affected. The responses are shown in Tables 4.17 and 4.18.

More than half the subjects in both groups (22, 73% experimental group and 20, 67% in the control group) would request PND. Although a few more control parents than parents in the experimental group were unsure whether they would request this procedure, the difference was not significant. In the couples women were more likely to state that they would request PND than their partners, but this was only a trend, the sample was too small for statistical testing.

Table 4.17 Subjects' views on prenatal diagnosis.

PND	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Yes	22	73%	20	67%	7	5	6	5
No	4	10%	6	20%	1	2	3	2
Unsure	1	3%	4	13%	0	0	0	1
No answer*	3	13%	0	-	0	1	0	0
Total	**30**	**100%**	**30**	**100%**	**8**	**8**	**8**	**8**

* one father and one mother who returned a postal questionnaire did not respond and one father was not aware of the diagnosis of FMR and was not asked about PND.

Some of the responses provided by the subjects in the experimental group included: "although I cannot live without my son, I will not bring another like him into the world" (mother); "to prepare myself" (mother); "I would not be able to take the suspense I would want to know" (father); "not sure, in theory I will but don't know in practice" (mother).

Some examples of the responses of the controls included: "don't want to subject an abnormal child to this world" (mother); "if I know, I can decide what I want to do, having an abnormal child will disrupt our family life" (mother); "just to prepare myself" (mother); "it is a good thing to know, because to be forewarned is to be forearmed" (father); "what can you do, I will keep the baby" (father); "don't want to know, it is nature, we must not interfere" (mother); "a child is part of you, one should accept it as it is" (mother).

All the subjects who reported that they would request PND, would not necessarily terminate an affected pregnancy (See Table 4.18). For example, 22 experimental mothers would request PND but only 18 (82%) of this group would have a TOP, while 20 control mothers would request PND but only 10 (50%) would ask for TOP. Significantly more parents of children with FMR would request TOP for a FMR fetus (18, 60%) than would control parents (10, 33%) with a fetus diagnosed with unspecified fetal abnormalities (χ^2

= 5.05, $p < 0.05$). Significantly more parents in the control group were unsure what they would do if a pregnancy was affected (14, 47%) compared to parents of children with FMR (only two) ($\chi^2 = 8.99$, $p < 0.005$). There was no consensus among couples again and the trend suggested that fathers were less likely to request TOP than mothers.

Table 4.18 Subjects' views on termination of pregnancy.

TOP	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Yes	18	60%	10	33%	5	4	3	1
No	7	23%	6	20%	2	3	2	3
Unsure	2	7%	14	47%	1	0	3	4
No answer*	3	10%	0	-	0	1	0	-
Total	**30**	**100%**	**30**	**100%**	**8**	**8**	**8**	**8**

* includes father and mother who completed postal questionnaires and one father was not asked about TOP.

The responses, the experimental subjects provided, included: "the child does not stand a chance to have a full and really happy life" (mother); "it is unfair to bring a child into the world when society does not accept them" (mother); "they are capable of doing a lot of things, FMR is not so bad that I would terminate a pregnancy if a fetus is affected" (father); "I am anti-abortion, it is a life, you get a child for a reason, you will not get a child if God doesn't think you can cope" (father); "it is a big decision, I do not want to be in that position, I do not want my daughter to go through all that" (mother).

Examples from the control group included: "our neighbours have two children with Cerebral Palsy and I know what it is all about, I will not be able to handle it" (mother); "the quality of life of abnormal children is not the best, it is better to have a normal child" (mother); "institutions are expensive, from normal family to abnormal child could cause major problems" (mother); "I am against termination unless it is in the mother or the child's best interest" (father); "the defect would have to be very serious, I would not terminate for Down syndrome" (mother): "it is against my religious beliefs" (father).

Those who were unsure stated; it is "difficult, I do not know, it is warranted in some instances" (mother); "unsure, I would consider a termination according to the prognosis" (father); "unsure, I don't know what I will do in the situation" (mother).

4.7.6 ADVICE TO OTHER PARENTS

The parents of children with FMR were asked what advice they would give to another person in a similar position. The responses of the mothers and fathers were similar, there was just one father who felt that he could not really answer this question, since he was still struggling to come to terms with the diagnosis.

Some mothers emphasised that the child and it's limitations should be accepted, and they would advise other parents as follows:

> "Has it's ups and downs, your biggest disappointment is wanting them to achieve and then not having them meet your expectations, accept them for what they are".
>
> "Accept their limitations, keep them happy and do not expect too much of them".
>
> "Accept the problem, the quicker the better, it will not go away, give the child lots of love and attention and don't exclude them from the rest of the family".
>
> "Accept them for what they are, their capabilities and achievements, all they really want is love and care".

Other mothers emphasized the necessity for patience, support, and care for the affected child:

> "Patience and understanding when reprimanding, ignore many things"
>
> "Support the child and give them lots of love, and do not spoil them"
>
> "Have lots of patience, guide them, and teach them to participate in household chores"

Other responses included;

> "Parents should support each other, it is particularly hard on the father" (from a mother);
>
> "One must have all the tests, do not have a child with FMR, it is unfair on them"

(mother)

Examples of some of the fathers' responses were as follows:

> "Do not give them special treatment, integrate them into the family and treat them as normal"
>
> "Carry on as normal, do not neglect the other children in the family"
>
> "Give the child a lot of support, treat the child as if normal"
>
> "Go for Genetic testing"
>
> "Accept it, live with it"
>
> "Go for advice. Each child is different. Do not give up hope, accept the situation and make the best of it. Never loose faith. Love the children and accept the responsibility and accept the will of God"

4.7.7 SUMMARY

In this section the effects of having a child with FMR on the parents were investigated. Most of the parents became aware of the problems during the child's preschool years and usually because of the delayed milestones. The parents then waited an average of 2.2 years (ranged from one month to 11 years) before a final diagnosis was made. The feelings parents described during the waiting period included anger, anxiety, guilt, isolation and denial. Fathers appeared to be slightly (but not significantly) more accepting of the situation than mothers, although they also experienced feelings of denial and hurt. After receiving the diagnosis some mothers reported that they felt guilty once they realised how FMR was inherited, one however, was relieved of her guilt.

About half of the subjects felt they had changed as a person after having had a child (either with or without FMR). Some changes were positive, for example the subjects became more understanding, caring and/or accepting, and some were negative for example some became bitter and/or angry.

Most subjects did not think their ambitions had changed after the birth of the child.

However, some experimental and control parents made appropriate adaptations; one experimental father started his own business so that his son would always have a place to work; and one control mother works to keep her son at university.

The majority of experimental and control subjects did not want more children. The reason most often stated by experimental subjects was: that their family was completed or they were worried about having a child with FMR. The reasons control subjects stated included: that they had completed their families; or that they were too old. A few more experimental subjects would request prenatal diagnosis in future pregnancies than controls. Significantly more experimental subjects would request selective abortion ($\chi^2 = 5.05$, $p < 0.05$) compared to controls, and significantly more control subjects were unsure about this compared to the parents with children with FMR ($\chi^2 = 8.99$, $p < 0.005$).

In the final part of this section, the experimental subjects reported what advice they would give to other parents with a child with FMR. Their advice included; accept the child and it's limitation, have patience, support them, integrate the child into family, do not give them special treatment.

4.8 THE EFFECTS OF THE INDEX CHILD ON THE PARENTS' MARITAL RELATIONSHIP

4.8.1 INTRODUCTION

The marital relationship and how it was affected by having a child with FMR was investigated. The data provide information on the aspects of the child that caused friction between husband and wife, how they viewed their relationship, and whether it had changed since the birth of their child with FMR.

4.8.2 ASPECTS THAT CAUSE FRICTION

Parents were asked who made the decisions regarding the children, whether they had any disagreements and which decisions regarding the child caused them to argue. In both

groups the parents reported that decisions regarding the child were made together in most cases. More control subjects reported that decisions were made together, however the difference between the groups was not significant. The results are shown in Table 4.19.

Table 4.19 Parental decision-making regarding the children.

DECISION-MAKER	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Mother	5	25%	6	21%	3	1	0	3
Together	14	70%	21	75%	5	6	8	5
Father	1	5%	0	-	0	1	0	0
Child himself *	0	-	1	4%	0	0	0	0
Total **	**20**	**100%**	**28**	**100%**	**8**	**8**	**8**	**8**

* The 'child' is aged 23 years
** Only 20 Exp and 28 Cnt subjects of the 30 subjects in each group were currently living with their partners

As might be expected, both groups reported that they sometimes had disagreements regarding the child. However, there was no consensus among the 8 couples. In the experimental group more mothers (6) than fathers (2) admitted to sometimes having disagreements and in the control group more fathers (6) than mothers (4) admitted such disagreements. The numbers were too small for statistical testing.

The major source of disagreement was discipline (nine, 60% experimental and 16, 72% control subjects). Other sources reported by the experimental parents included: education, the future of the child, overprotectiveness of one of the parents, and things that resulted in a change in the child's routine. Sources reported by the control parents included: parents' views on which of the child's activities should take priority, reading of pornographic books, partner interferes in disciplining, and father taking the son for drinks.

4.8.3 TIME SPENT TOGETHER

The subjects with partners were asked how often they went out as a couple without the children and if they were satisfied with the amount of time that they and their partners

spent together. Most subjects went out together either regularly or occasionally and there was little differences in the pattern of responses between the two groups.

When asked whether they were satisfied with the time they spent together, most subjects in the experimental group were (12, 60%). One mother stated "we are too busy to go out more, to maintain our sanity we have to go out at least once a week". The two fathers who were satisfied with the amount of time they spent with their wives said the following: "I prefer to watch television and videos with the whole family at home". Most control parents were also satisfied (18, 64%) and some of their responses included: "I want my family around me"; and "we do not have enough money".

The experimental subjects that were not satisfied with the amount of time that they spent with their partners (two mothers and five fathers) had the following to say: "not really, we have to accept that we have no-one to leave our son with" (father); "one needs time to work on your relationship, you should not neglect this because the children come first" (mother). The control subjects (six mothers and four fathers) provided similar responses: "we would like to go out more, but we have no-one to look after the children" (mother); and "I am not satisfied, but it will come right, this is a time of your life that you have to sacrifice, your children take up your time" (father).

The mothers who had partners (12 of the 20 experimental subjects and 20 of the 21 control subjects) were asked whether they were satisfied with the amount of help they received from their partners in doing the housework (only mothers were asked since no fathers were performing these duties). The majority of mothers in the two groups were satisfied, however twice as many mothers in the control group (16, 80%) compared to mothers in the experimental group (8, 67%) were satisfied with the help they received (not statistically significant). Three experimental mothers were not satisfied, and an older mother with four children of whom one boy has FMR said "this is a sore point, my husband's solution is to pay someone else to do the extra work, he will not do the work himself" another mother, also with one affected son said "I have my moments when I go on strike". Two of the four control mothers who were not satisfied reported that: the husband instructs the son to do the work; and that the husband's work keeps him busy.

4.8.4 THE SUBJECTS' RELATIONSHIP

Subjects with partners (16 female and eight male experimental and 20 and 9 control subjects respectively) were asked to describe their relationship with their spouse and to comment on whether they thought their relationship had changed and if so in which way it had changed, after having the index child. Four of the experimental group mothers and one divorced control father answered this question in retrospect, although they were not living with their partners at the time of the interview (two were widowed, one separated and one single). The majority of the parents in both groups described their relationship as being good (see table 4.20).

Table 4.20 Subjects' opinions of their marital relationship.

RELATIONSHIP	*Individual subjects*				*Couples*			
	Exp group		*Cnt group*		*Exp group*		*Cnt group*	
	No	*%*	*No*	*%*	*Mo*	*Fa*	*Mo*	*Fa*
Very Good	6	25%	3	10%	2	1	3	0
Good	12	50%	18	63%	4	5	4	7
Fair	2	8%	7	24%	2	1	1	1
Bad	4	16%	1	3%	0	1	0	0
Total	**24**	**100%**	**29**	**100%**	**8**	**8**	**8**	**8**

Some examples of the responses given by the subjects in the experimental group include: "very good, I have a very understanding husband"; "we have our normal ups and downs, after all, no marriage is perfect" (father); "bad as soon as he realised our son was not OK" (single mother); "extremely tense, this is because of FMR, we fight a lot and we have talked about divorce" (husband), his wife said; "it can be very good, my husband is the domineering one and I am quiet and sensitive". Again partners perceptions of their marital relationship showed little consensus.

The control group's responses included: "although we understand one another, we are still different people and we do fight sometimes" (mother); "not as good as I would like it to be, he lost his job twice in one year" (mother).

Over half the subjects in the two groups (13, 54%, experimental and 19, 64%, controls) thought their relationship had not changed since the birth of the index child. The remaining subjects thought their relationship had changed, except for one experimental mother who was unsure. Some of these subjects reported positive changes, for example: "better and worse in certain aspects" (experimental father); "in some respects it has brought us closer"; and "I cannot say in what way, I have stopped searching for answers and I was able to communicate my feelings about our son better" (experimental mother). In one control couple both partners stated that having a child brought them closer together.

Other experimental couples reported negative changes: "it put a lot of strain on our relationship, I blamed myself and thought my husband blamed me, I could not come to terms with the situation" (wife), and her husband said "better and worse in certain aspects"; and another couple stated "our relationship was never tense like this, with so much fighting and quarrelling" (husband), and "we have more fights due to our two affected boys, I feel as if everything is my fault and my husband and his whole family blames me" (wife). A single mother said "he hated this pregnancy, he did not want the child and blamed me for everything". The control subjects also had some negative responses: "things are not as calm as they used to be, we fight over F" (mother); and a couple stated: "we have less time for each other" (wife), and "there are probably more pressures, the children need your attention" (husband).

Finally the subjects who were divorced or separated, were asked why they thought this had happened. The answers for the experimental group were as follows:

> "I couldn't get a permanent job, so I could not pay lobolla" (bride-price) (a divorced father)
>
> "confidential reasons, not because of my affected son" (separated mother)
>
> "he walked out as soon as he noticed they were not normal, he blamed me" (separated mother)
>
> "he made another girl pregnant" (separated mother)
>
> "because of M, he does not want people to know she is his child" (single mother)
>
> "because of the affected children" (divorced mother)

The reason for the one divorced father in the control group was:

"she changed her job and the new one required that she travelled a lot"

4.8.5 SUMMARY

The relationship between the parents was evaluated by examining aspects that caused friction, satisfaction with the partner, and changes in the relationship. The pattern of responses in the two groups was similar and there were no statistically significant differences.

In both groups most of the parents reported that the decisions regarding the child were made together (70% experimental and 75% controls), but that they had disagreements regarding child rearing, mostly over discipline. These disagreement were obvious from the partners' responses since in many instances they were discordant.

Most subjects reported that they had enough time alone with their partners. In general, the mothers were satisfied with the amount of help they received from their partners.

The majority of subjects described their relationship as good (75% experimental and 73% controls). The majority of subjects reported that their relationship had not changed since the birth of the child (54% experimental and 64% controls). Some of those who reported that it had changed thought it was a positive change, for example they had become closer. But, other subjects reported negative changes, such as, more fights over the child. Negative changes were also reported by subjects in the control group. Of the eight subjects who were divorced or separated, three reported that the affected child was the reason.

4.9 THE HELP PROVIDED TO THE SUBJECTS IN THE EXPERIMENTAL GROUP

4.9.1 INTRODUCTION

The final questions in the interview schedule were put to the experimental group only. This section was concerned with how the diagnosis of FMR was made, the professional help and support the parents received, and whether they wanted contact with other parents of children with FMR.

4.9.2 DIAGNOSIS

In most cases the subjects stated that a paediatrician was responsible for making the diagnosis of FMR (see Table 4.21), although even on this matter couples were not all in agreement.

Table 4.21 Parents' reports on who made the FMR diagnosis.

WHO MADE THE DIAGNOSIS	*Indiv subjects*		*Couples*	
	No	*%*	*Mo*	*Fa*
Paediatrician	18	60%	6	3
Genetic counsellor	8	27%	2	4
Other*	3	10%	0	1
Not told	1	3%	0	0
Total	**30**	**100%**	**8**	**8**

* Including one neurologist and two doctors.

At the time of the diagnosis, 13 (43%) subjects had questions about the child's future and a few parents were concerned about the genetics (6, 20%). Table 4.22 shows the results.

Table 4.22 Information requested by the parents at the time of the diagnosis.*

INFORMATION REQUESTED	*Ind subjects*		*Couples*	
	No	*%*	*Mo*	*Fa*
Prognosis	13	43%	4	6
Inheritance	6	20%	3	1
Treatment, management, education	6	20%	3	1
Further information	1	3%	0	0
How to help others	1	3%	0	1
None	9	30%	1	1

* Some parents gave more than one response

Some of the responses given by the parents included: "I wanted to know the prognosis, and how far he is expected to develop mentally" (mother): "I wanted to know if she would deteriorate or get better, I was concerned about her future, would she get married and have children, and have a normal life" (father); "I wanted to know where it came from, what it is, how to "fix" children and if they would marry, I had endless questions" (mother); "I did not want to know anything, I was too shocked" (mother)

The majority of the parents (17 out of 26, 80%) reported that their questions were answered. One father stated: "I was impressed with the Doctor, he was very knowledgable". Parents who reported that their questions were not answered stated, for example: "only some questions were answered" (mother); "all was so new, things became clearer as he grew up" (mother).

4.9.3 GENETIC COUNSELLING

Half (17, 57%) the parents reported that they had had genetic counselling. When comparing the responses within the eight couples, six mothers and five fathers reported that they had counselling. Husband and wife disagreed in one case. However, the majority of those who had genetic counselling reported that it was a positive experience (see table 4.23)

Table 4.23 Parental views on the genetic counselling experience.

GENETIC COUNSELLING (IN JOHANNESBURG)	*Indvid subjects*		*Couples*	
	No	*%*	*Mo*	*Fa*
Had counselling	17	57%	6	5
Pos experience[1]	11	65%	4	2
Neg experience[2]	3	17.5%	2	0
No information	3	17.5%	0	3
No counselling	13	43%	2	3
Total	**30**	**100%**	**8**	**8**

Some of the positive responses given included: "it helps to get to terms with the diagnosis if you understand what FMR is all about" (mother); "it is nice to know what is wrong" (mother); "we got good advice, it also lessened my guilt" (mother); "we were told more about the syndrome, especially the realities, we needed it" (mother). and some of the negative responses included: "annoying, we did not get any information, we were referred" (mother); "it was a waste, they didn't know anything" (mother); "I cried too much and didn't understand anything" (mother).

4.9.4 CONTACT WITH OTHER PARENTS

Parents were asked whether they had any contact with other parents with children with FMR and how they experienced this or if they had not, if they would like to meet other parents. Less than half (14, 47%) of the subjects had contact with other families with children with FMR. Couples' responses were similar in this case.

The parents who had contact with other affected families were asked how they felt about it. The following responses were obtained:

> "My sister also has an affected child, it helps because you can relate to each other" (mother)
>
> "It is nice to speak to someone in the same position to the one that you are in"(mother)
>
> "It was very helpful because I learned from it" (mother)

"It was good that I was not alone" (mother).

Those subjects who did not have contact were asked whether they would like to meet other parents with children with FMR. Some of the mothers responses were as follows:

"It would have been nice to have had support"

"I would like to share and compare problems"

Two fathers stated:

"I do not need this, but my wife would benefit from it"

"It would be interesting"

The parents were finally asked whether they would join a FMR support group and almost all of the subjects would (25, 83%). There was just one father who stated that he was not interested and four parents (two mothers and two fathers) who stated that they might join a support group.

4.9.5 SUMMARY

The professional help subjects received was generally from the person who made the diagnosis. In most cases this was a paediatrician (60%) and most parents were satisfied (80%) with the help they received.

About half (57%) of the subjects reported that they had genetic counselling. The majority of those who had counselling reported that it was a positive experience, making it easier to come to terms with the diagnosis.

About half of the subjects reported that they had contact with other families and within couples there was agreement. Finally most of the subjects (83%) would like to join a support group.

4.10 COMMENTS

In the last open-ended item the subjects were asked to add any comments or thoughts. Several subjects commented that schooling was one area they were concerned about:

> "the biggest problem is schooling, the children mimic others so they need a normal environment"
>
> "Should I send him to boarding school, or keep him here?"
>
> "we moved to Johannesburg so that our son could be in a good school, we did not want to send him away"
>
> "it is difficult to find a suitable centre for FMR children, finding a pre-school is probably the worst, there are limited facilities for the children"

Some parents emphasized the need for awareness regarding FMR in schools, doctors and the public:

> "there is a lack of knowledge about children with FMR in the community, it should be explained to the schools and teachers" (mother)
>
> " doctors should be educated, FMR scares people. People are very ignorant"

There were some subjects who felt they would benefit from more counselling and/or a support group. Two families with adults with FMR had to deal with sexuality issues. Both males were sterilized since the parents were worried that they would produce offspring. One mother said that her son does not associate sex (he watches pornographic videos) with reproducing.

4.11 SUMMARY

In this chapter the results of the analysis of the data obtained from the experimental and control group subjects are presented. The two groups of subjects consisted of 22 families (matched by ethnic group, age and sex of the oldest affected child and the number of siblings) which included 21 female and nine male subjects, totalling 30 individual subjects in each. In the 22 experimental families there were a total of 31 affected children (26 males and five females).

According to the aims of the study the major findings can be summarized as follows. The relationship between the FMR child and his siblings was generally good. Although more experimental than control parents reported a bad relationship with some communication problems and some resentment between the siblings it was not statistically significant. Most parents reported that the siblings were aware of the FMR diagnosis and some stated that it affected their relationship with the affected sib, in some cases positively and in others negatively. The majority of normal siblings, according to the parents, did not feel neglected. Significantly more experimental than control parents rated their child's relationship with their friends as poor ($\chi^2 = 9.48$, $p < 0.005$), and significantly more children with FMR had no friends according to the parents ($\chi^2 = 4.83$, $p < 0.05$).

The parents' relationship with the children could generally be described as good. All the parents (except one father) could think of something about their child that they liked. Surprisingly more experimental parents than control parents ($\chi^2 = 7.38$, $p < 0.01$) reported that they liked their children's happy, loving, caring and thoughtful nature. However, there were some aspects that parents disliked about their children with FMR, especially their tempers, destructiveness and the difficulty in controlling them. Significantly more parents of children with FMR reported this than did controls ($\chi^2 = 15.44$, $p < 0.001$). Control parents described other aspects they disliked in their normal children. The marital relationship between the parents was generally good and the two groups' reports were similar. The parents did however have disagreements about the children, but only 3 out of 8 experimental parents claimed that they got divorced or separated because of the children. Slightly (but not significantly) more experimental parents thought that their relationship had changed after having the children than parents in the control group. Some parents described being closer as a result, and others that fighting and arguing had increased.

Most experimental parents observed their child's problems prior to schooling but waited up to three years, for a diagnosis. During this waiting period they described having feelings of anxiety, anger, guilt and isolation. When they received the diagnosis similar feelings were described, with more guilt (especially in mothers) when they learned how FMR was inherited. The fathers also described feelings of hurt and disappointment,

however it seems like fathers were more accepting of the situation than the mothers.

A few more experimental subjects would request PND in future pregnancies compared to controls (not significant). On the other hand significantly more experimental subjects would request TOP if the fetus were diagnosed with FMR ($\chi^2 = 5.05$, $p < 0.05$). Also significantly more control parents were unsure whether they would request TOP if the fetus were found to be affected with congenital abnormalities ($\chi^2 = 8.99$, $p < 0.005$).

Most parents reported that they received professional help from the diagnosing doctor which, in most cases, was a paediatrician (60%) and parents were mostly satisfied with this service. Only 47% of parents had genetic counselling and less than half had contact with other families, but most described both these experiences as positive. Most parents would have liked some support and the majority would like to join a FMR parent support group.

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1 INTRODUCTION

In this chapter, the results obtained from the analysis of the data will be discussed and compared with the available reports in the literature. Each of the family relationships which have been investigated in the study will be examined separately. These relationships include those between the parents and affected children, between the children and their siblings and peers, and between the parents themselves. The parents' feelings about their situation will also be discussed. The limitations of the study will be outlined, recommendations regarding the implications of the findings will be made and conclusions drawn.

5.2 THE SAMPLE

5.2.1 THE PARENTS

The sample size for the present study was 60 subjects, 30 were in the experimental group (parents of children with FMR) and 30 in the control group (parents of normal children). This sample compares well with the sample sizes reported on in studies on FMR conducted by Meryash (1989) and Meryash and Abuelo (1988). In his study on perception of burden among women at risk for having a child with FMR, Meryash (1989) investigated 16 women who had a child with FMR, 15 women who were related to individuals with FMR, but who did not have an affected child, and 63 women with no known increased risk of giving birth to a child with FMR or any other birth defect. Meryash and Abuelo (1988) studied the counselling needs of 32 women at risk for bearing a child with FMR. However, the present sample is small in comparison to the 181 families with Down syndrome children studied by Byrne *et al.* (1988) and the 104 families with a child with Down syndrome studied by Gath (1978). However, Gath only chose 30 families with

Down syndrome children, out of the 104 families, and 30 control families with a normal child for in depth study. Further, of the 127 families from all parts of South Africa with children with FMR known to the researcher only 30 subjects were accessible and willing to participate in the present study. Both fathers (nine) and mothers (21) were included in the present study, as mothers are usually the focus of research and very little data are available on fathers' views and experiences of having a child with a disability. As one of the purposes of the present study was to provide a basis and identify possible areas for further research on families with children with FMR, the small sample available was thought to be adequate.

When the control group was selected, they were matched with the subjects of the experimental group for the sex and age of the children, ethnic group and family size. It was considered important to match the two groups by ethnic origin since cultural differences influence attitudes toward disability, family life and raising children. It was also for this reason that families with children with FMR from most major ethnic groups were included. Further, as the present study was concerned with family issues and relationships the age and sex of the index children, and family size, were chosen as additional matching criteria. The two groups were almost perfectly matched for all these criteria. Gath (1978) used the same criteria in her study on Down syndrome and the family, but she also controlled for socioeconomic status, the fathers' occupation and home neighbourhood. Although this procedure was not feasible in the present study, the two groups compared quite well with respect to income level, type of living arrangements and education levels.

5.2.2 THE TWO GROUPS OF CHILDREN

When the control group was selected the age and sex of the control child was matched with the first-born child with FMR. Only the firstborn children were evaluated by the parents (even where parents had two affected children). There were 22 index children in the families with children with FMR and 22 matched controls, with 19 males and three females in each group, so that the sex ratio in both groups was identical. The average age of the index children in the experimental group (only the first-born affected child in the

family) was 16.7 years whereas the average age of the children in the control group was 15.7 years. Statistically there is no significant difference between the average ages of the children with FMR and the matched children in the control group. The ordinal position of the children in the two groups was also similar.

Most of the parents (52%), when assessing how many of the behavioral characteristics associated with FMR (maximum score was 28) they perceived their children to show, gave their children a low moderate score (10-14), only one child had a very high score (24). This emphasised that although all the children had FMR, not all of them showed all the characteristics thought to be common in such patients. The commonest characteristics shown in the affected individuals in the present study were short attention span, emotional outbursts and shyness. The least common characteristics reported by the parents, were: rocking, tactile defensiveness and self-mutilation. The present study is in agreement with Hagerman *et al.* (1991) who reported that short attention span appeared at a high frequency in young FMR males (all 15 males studied) and Hagerman and Sobesky (1989) who stated that many affected individuals have a history of shyness or difficulties with social interaction. The findings in the present study regarding tactile defensiveness (found in 36% of affected individuals) is in contrast with Hagerman *et al.* (1991) who claim that 79% (11/15 males studies) showed tactile defensiveness. However, it should be noted that Hagerman's results were based on objective assessments and not subjective parental observations as in the present study.

Further, 10 children were evaluated by both their parents, and mostly the two parents responded similarly, however four parents responses differed to such an extent that the two fathers assessed the child as more severely affected than their partners. This emphasized that mothers and fathers may perceive their child's problems differently. According to Cunningham and Davis (1985) there is evidence that fathers have a less optimistic view, than mothers, about their mentally disabled children. They suggest that such a finding can be explained by the fact that fathers have to go out to work and consequently have less time to observe their child's behaviours and achievements. The trend observed in this study supports Cunningham and Davis' findings.

The activities most of the children with FMR enjoyed included physical activities such as kicking a ball, running around and playing football and watching television. The control

children also enjoyed similar activities, and in addition they enjoyed going to movies and reading. The activities reported in the experimental group are similar to those described by Davie and co-workers 1984 in their observational study of three to five year old normal children (cited by Byrne *et al.* 1988). The authors found that these normal children spent most of their time engaged in watching television, gross motor activities, pretend play and looking at books. The largest group of children (average age 16.7 years) in the present study were older than the group studied by Davie, yet they enjoyed similar activities to the younger children. This finding suggests that the play activities of children reflect their developmental rather than their chronological age. The difference between developmental and chronological age in children with FMR has implications for educational integration and according to Byrne *et al.* (1988:46): "... we should not expect success if we insist on a rigid adherence to chronological-age streaming".

5.3 FAMILY RELATIONSHIPS

5.3.1. THE RELATIONSHIPS BETWEEN THE CHILD WITH FMR AND HIS PARENTS.

The relationship between the child and his parents was evaluated by investigating child management, feelings towards the child and burden on the parents. About half of the experimental parents had management concerns. This finding was in keeping with Byrne *et al.* (1988) study on parents with children with Down syndrome in which 46% of parents had management concerns. Byrne also found that the concerns did not pass with time and that they were still problematic two or three years later. As parents of children with Down syndrome also reported management concerns, these are not associated only with FMR but could occur in any family with a child with mental disability, or, perhaps, any other disability.

The control group subjects also had concerns but they were different to those expressed by the experimental subjects. The parents of children with FMR reported more long term concerns such as: finding an appropriate school for the child, financial worries, dependence of the child on the mother, and what the future holds for the children.

However, the control subjects mentioned more immediate concerns such as their child's quick temperedness, lack of confidence, reading difficulties at school, how to assert discipline, not taking education seriously and wasting money. Meryash (1989) in his study on the perception of at-risk women of the burden of raising a child with FMR, found that the mothers with affected children reported that finance and the education of their child were among their greatest problems.

Most parents in both groups in the present study used verbal punishment most often to discipline their children (87% experimentals and 93% controls), while 53% in both groups used physical punishment. This is very different from Byrne *et al.* (1988) results where only 47% of mothers with children with Down syndrome studied in England used verbal punishment and the majority, 91%, used physical punishment. A trend observed in the present study when comparing the couples' responses, was that more experimental mothers (7/8) used physical punishment more often than their partners did, while more control fathers (6/8) used this method more often than did their wives. Cohen (1962) stated that parents of children with mental disability were often anxious about discipline and had concerns about putting restrictions on "defenceless" children, and therefore they tended to give them special allowances. Five parents in the present study reported that they were more patient and made allowances for the child with FMR, one mother said she treated her affected son with "cottonwool gloves". However, these parents were in the minority, and more than half (57%) of the parents in the present study reported that they did not treat their children differently to their other children. Similarly, Byrne *et al.* (1988) found that 47% of mothers did not treat their child with Down syndrome differently to the other children in the family.

All the parents in the two groups rewarded good behaviour verbally. One method parents of children with FMR used that the parents in the control group did not, was giving the child special privileges. It was interesting to find that significantly more ($\chi^2 = 5.10$, $p < 0.05$) control parents rewarded good behaviour by hugs and kisses (14, 47%) compared to experimental parents (four, 13%). The reason why parents of children with FMR might not reward good behaviour by hugs and kisses, might be due to tactile defensiveness or a dislike of being touched in the affected children. In a comparison between each parent's

response to their own child on items 12 (Does your child dislike being touched?) and 29.1 (How do you praise your FMR child's good behaviour?), it was found that of the 14 parents who reported that their child disliked being touched, sometimes or often, only two mothers rewarded good behaviour by physical touching (both having reported that their child only sometimes disliked being touched).

Half the experimental subjects stated that they enjoyed their children's happy, loving, caring and thoughtful nature and reported this significantly more often than did the control parents ($\chi^2 = 7.38$ $p < 0.01$). This finding is in keeping with Maes *et al.* (1992) who found that the temperament of 58 mentally retarded FMR males was different from that of 58 FMR negative mentally retarded males, and that the FMR males were positive people with an openness to social contact and attention. This report of positive temperament however, seems to be in contrast to the autistic-like behaviours (avoidance of eye and tactile contact) reported in some FMR individuals (Maes *et al.* 1992). Maes *et al.* found that less than 10% of FMR individuals showed social indifference such as, not reaching out when reached for and not being responsive to other people's facial expressions. It is therefore important to note that the social interactions of FMR individuals may not be characterised by impairments in social responsivity or empathy, as might have been expected due to the association of autistic-like features with FMR. One example given by a mother of a 24 year old male in the present study illustrates his empathic nature:

"when I had a migraine once, he wanted to know what was wrong, and when I told him, he made me a cup of tea and brought it and a pain killer to me in bed"

The experimental parents in the present study reported that they disliked their children's bad tempers, destructiveness, and the fact that their children were difficult to control, significantly ($\chi^2 = 15.44$ $p < 0.001$) more often than did the controls. As children with FMR have behavioural difficulties, which include temper tantrums (Braden 1991a) and emotional outburst and stubbornness (Maes *et al.* 1992), it was expected that their parents would report this more than parents of normal children. However, caution should be taken in assuming that these difficulties are unique to families with children with FMR, since it is still debatable as to whether such problems are specific to the syndrome or are

associated with mental retardation irrespective of cause.

As Byrne *et al.* (1988) found in their study on mothers of children with Down Syndrome, the mothers in the present study were the main caregivers of the affected child. According to Roeyers and Cloetens (1995) fathers of children with mental retardation reported that they assumed more responsibility for child care and household tasks than did fathers of children with autism or normal children. Although this was not apparent in the small sample examined in the present study, couples with children with FMR were more likely, than the parents of normal children, to go together to take the child to the doctor. Although the results did not reach statistical significance, more siblings in the experimental group helped with caregiving than siblings in the control group. This trend is in agreement with that reported by Gath (1985) who stated that older sisters, particularly, could be burdened with the care of the retarded child.

Byrne *et al.* (1988) reported that only 16% of mothers felt that their child with Down Syndrome created major difficulties and almost prevented family outings entirely, while most subjects did not acknowledge these problems. Most of the families with a child with FMR in the present study also included their affected children on outings. Only one couple reported that the children's behavioural problems made it "a nightmare" for them to go out.

5.3.2 THE SIBLING RELATIONSHIPS

All the children, except for one in the experimental and one in the control group, had siblings. About half (54%) the parents reported that the child with FMR related well to the siblings. Similarly Byrne *et al.* (1988) found that the relationship of children with Down syndrome with their siblings was generally good and 72% got on well together. However, the relationship was characterised by some problems in 14% of cases and 3% had marked problems. Although more subjects in the present study stated that there were problems compared to those in the control group, this was only a trend. The problems included impatience, lack of communication, fighting and bullying.

In the majority of cases (67%) in the present study, the siblings were aware of the diagnosis of FMR, and in about two thirds of the families this knowledge altered the relationship, sometimes for the better and sometimes for the worse. One mother reported that her daughter went through a resentful stage towards her affected brother because she was worried that in the future when she had children they might also be affected.

Gath (1985) found that the normal siblings in her study were not always adversely affected by having a sibling with Down syndrome. Further, parental reports suggested more ill-effects on the siblings than the siblings' self reports. Cunningham (1982) reported that siblings of a child with Down syndrome benefitted from growing up with the child and that they could become tolerant, understanding and mature in dealing with others. In the present study a few parents of children with FMR also reported that the siblings were more tolerant and protective of the affected child.

The majority of parents in the present study did not think that the siblings of the child with FMR felt excluded. Gath (1985) also found that, although earlier studies showed that the normal siblings might suffer from less parental care and attention, this was because of poor provision of services for handicapped children, and that where such services are available normal siblings are no more likely to be neglected emotionally or physically than any other group of children.

5.3.3 THE RELATIONSHIPS BETWEEN THE CHILD WITH FMR AND HIS FRIENDS

More experimental children (six, 20%) than controls (none) had no friends and this was a significant difference ($\chi^2 = 4.83$, $p < 0.05$). The friends the children in the experimental group mentioned were mostly neighbours or from school, while the controls had a wider range of friends. Similarly, Byrne *et al.* (1988) found that 60% of children with Down syndrome, aged between two and 10 years, had at least one friend and the friends were mostly children of neighbours (58%), only 11% had friends at school.

Significantly more parents in the experimental group (13, 43%) than controls stated that

there were problems as to how the children with FMR related to their friends ($\chi^2 = 9.40$, $p < 0.005$). Similarly, Byrne *et al.* (1988) reported that there were problems in peer relationships in 39% of their sample of children with Down syndrome. The problems they mentioned that were also reported by the parents in the present study, included teasing and behaviour problems such as damaging toys or hitting the friends. It is not really surprising that a child who shows behavioural problems would have difficult peer relationships and any child with such problems, might be expected to have disharmony with the peer group.

5.3.4 THE RELATIONSHIP BETWEEN THE PARENTS

The relationship between the parents was evaluated by investigating aspects that caused friction, the amount of time spent together without the children, and how they described their relationship. Most experimental and control parents reported that decisions regarding the child were made together and that they sometimes had disagreements. The majority of subjects in both groups reported that discipline was the aspect that they disagreed about most. Byrne *et al.* (1988) had similar findings. They reported that 61% of parents with children with Down syndrome had disagreements and that these were mostly over discipline, schooling, and short-term care.

Most parents reported that they went out occasionally or regularly, there was little difference between the two groups and most subjects were satisfied with the time they spent together. There were five fathers and two mothers who were not satisfied and said that the children with FMR prevented them from spending more time together. Similarly, Byrne *et al.* (1988) reported that 62% of parents with Down syndrome children were content with the frequency of outings and that only 15% of those who would like to go out more often felt that the child with Down syndrome prevented them. Some of the mothers of children with Down syndrome were concerned about baby sitters and whether they would cope in an emergency, and two families in the present study had similar concerns.

The majority of the parents in both groups described their relationship as "good", and only 16% stated that it was "bad". According to Gath (1978), 30% of parents with children with Down syndrome in her study had a "bad" overall rating of the marital relationship,

and Byrne *et al.* (1988) stated that 7% of their parents of affected children reported "bad" relationships.

Less than half the parents in both groups thought their relationship had changed after the birth of the index child. Positive and negative changes were reported in both groups. About a quarter of the experimental subjects said the child with FMR had brought them closer together and enriched their marriage, while another quarter reported that the child had put a strain on their marriage and it had become tense. In comparison, McConkie-Rosell *et al.* (1997) found that 64% of the 28 females they studied with a child with FMR felt that their relationship with their husband had changed as a result of the diagnosis, and 72% indicated a positive and 27% a negative change. Byrne *et al.* (1988) findings also showed more positive than negative changes: 30% of parents with a child with Down syndrome reported changes for the better and 14% changes for the worse.

Finally the seven subjects who were divorced or separated, were asked why they thought this had happened. In this small group three claimed that the affected child was the reason for the marital break-up. One couple, still married, were experiencing stress at the time of the study. The wife felt that the husband and his family blamed her and they were constantly fighting. In his study in the USA, Meryash (1989) found that the 16 women with children with FMR reported that their relationship with their husbands was among the least problematic areas for the women. Most (81%) of these women were still married to the father of their affected child. Similarly, Gath (1985) found that only 10% of marriages between parents of children with Down syndrome had broken down after the birth of the child. This is in contrast with studies which have found that having a severely mentally handicapped child has a negative influence on marital relationships (Farber 1959).

According to Gath (1985) it is the initial trauma of having a child with a disability, rather than the wear and tear of looking after them, that is so devastating to the marital relationship. The evidence for this statement comes from studies of families who have fostered or adopted handicapped children, particularly those with Down syndrome. These volunteer families do not have a high rate of marital disharmony but instead appear to have particularly strong personalities and stable relationships. Gath (1978:66) states "... the

advent of the mongol baby was not as likely to mar a good marriage as to turn a moderate or shaky one into a poor one.", and Byrne *et al.* (1988:77) "...there does not appear to be a direct relationship between having a child with Down syndrome in the family and the marriages suffering."

5.4 THE PARENTS' FEELINGS

5.4.1 WHILE AWAITING A DIAGNOSIS

The time period between when parents became aware of a problem and when they received the diagnosis of FMR ranged from one month to 11 years. The subjects described a great number of feelings during this period. Mothers reported feeling traumatised, hurt, feeling like it was "the end of the world", and then acceptance. Some asked "why me?", and some denied the fact that there was a problem. Some described feelings of anger, anxiety, guilt, heart break, isolation, responsibility, upset, and some were accused of overreacting. Fathers also described feelings of hurt, disappointment, traumatisation and denial.

Hinze and Ravh (1990) reported that the parents of three to six year old mentally disabled children, in their study, sought examinations of the child and initiated supportive and therapeutic measures, during the period when they suspected something was wrong. However, both mothers and fathers showed emotional strain. Some of the parents tried to evade facing the problems by denial of the facts and trivializing the problems, and mothers showed emotional upset more clearly than fathers. The authors state, however that care should be taken in interpreting these findings as they do not prove that fathers, or men in general, can take more emotional strain, they suggest that men may have gender-specific convictions about how self-controlled they should be.

5.4.2 AT THE TIME OF THE DIAGNOSIS

After being given the diagnosis of FMR, the parents had similar feelings to those they described during the waiting period. More mothers felt guilty once they knew how FMR was inherited. Some subjects felt uncertain and others were relieved at having a diagnosis.

Some regretted not knowing anything about FMR before planning to have children. Feelings of the "world tumbling down", bitterness, hurt, even hatred for the child, shame, shock, and upset were described. Again, some asked "why me?" and were angry, some were unhappy and sad, one felt inferior, and some lived in hope.

The small group of fathers appeared mostly to accept the situation but they might not have expressed their feelings fully. Some had feelings of uncertainty with questions such as: will he catch up, or learn to drive a car, or go to work? Some were very concerned with the child's future. Fathers also expressed feelings of bitterness, anger and denial, but some hoped for the best.

According to Hinze and Ravh (1990), in their study on parents with children with mental disability, the diagnosis marked the end of the period of suspicion, and mothers had more reactions of emotional strain, particularly disappointment and depression, than fathers did. Further, the fathers showed a greater readiness to rationally accept the diagnosis. This was also observed in the present study, however care should be taken not to generalise from these findings, since the sample may have been biased by the fathers' willingness to participate, and those who did might have accepted their child's disorder.

Price-Bonham and Addison (1978) in their study on parents with mentally disabled children, showed that fathers had more concerns about future problems whereas mothers were more emotional. These results are similar to those found in the present study, in which the fathers were concerned about the child's future. The mothers on the other hand were more emotional and described feelings of hurt and sorrow.

The feelings parents reported in the present study, during the waiting period and at the time of the diagnosis, are similar to those associated with the bereavement or grief process as described by Kübler-Ross (1970), Antley *et al.* (1984), Cunningham and Davis (1985) and Garguilo (1985). According to Kessler and Kessler (1988) the occurrence of genetic disease is accompanied by one of the more severe psychological traumas and the parents often show various symptoms, including depression and other grief reactions.

5.4.3 PERSONAL CHANGES

The parents in the two groups gave similar responses to the item on personal changes and about half in each group (57%) thought that they had changed after the birth of the index child. Most experimental and control subjects reported that they were now more understanding, accepting, stronger, less selfish and more patient, although some experimental subjects reported being insecure, bitter, angry and hard. Cohen (1962) stated that parents of a handicapped child often become more sensitive to the needs of others. Byrne *et al.* (1988) also found that 74% of parents of children with Down syndrome stated that they had changed, and become less self-centred and less concerned with trivia.

The majority of parents in both groups did not think their ambitions had changed after the birth of the index child. The few who admitted to changing their ambitions had made constructive adaptations to their situation, such as wanting to start a support group and starting their own business. However, a few control parents had also made adaptations, such as working to keep the child at university, or stopping work to look after the children.

5.4.4 PRENATAL DIAGNOSIS AND SELECTIVE ABORTION

Many parents from both groups did not plan more children (47% experimental and 67% controls). In the present study, parents of children with FMR, reported that they did not want more children because: they had completed their families and had been sterilized or, in a few cases, they would not consider it due to having a child with FMR. Mothers in the control group reported that they had completed their families, were too old, and/or had financial constraints. Curtis *et al.* (1994) showed, in their study on the reproductive histories of 27 known or possible FMR carrier women, that these women carefully considered their reproductive choices. One aspect which influenced their decision to have more children was the risk of being a carrier. Several women postponed pregnancy until their risk of being a carrier of FMR was reduced to non-carrier status. McConkie-Rosell *et al.* (1997) found that 67% of the women with a child with FMR did not have more children after the birth of the affected child, because of their risk.

In the present study, many subjects in both experimental (73%) and control (67%) groups would request prenatal diagnosis in a future pregnancy. Meryash and Abuelo (1988), in their study of 32 women at risk for having children with FMR, also found that most (81%) women would request PND. McConkie-Rosell *et al.* (1997) found that 82% of the women they studied would have used PND if it had been available.

Of the subjects who reported that they would request prenatal diagnosis there were some (mostly controls) who would not terminate if an affected fetus was diagnosed. However, nearly twice as many experimental parents (18, 60%), who had the experience of an affected child, would terminate an affected pregnancy, compared to control parents (10, 33%) ($p < 0.05$). Also significantly more control parents than experimental parents were unsure what they would do about termination if an affected fetus was diagnosed ($p < 0.05$). The trend of these findings are in keeping with those of Meryash and Abuelo (1988). They found that 39% of women who had a child with FMR would terminate a pregnancy if the next fetus was affected. However, of the women at risk, but who did not have child with FMR, only 14% would request TOP and 71% were unsure whether they would request a termination.

Meryash (1989) found that women who were willing to abort an affected fetus perceived the raising of a child with FMR to be a greater burden than those who would not abort. The author found that the women who gave birth to a child with FMR underwent an adjustment process which resulted in the perception of a somewhat lesser burden than that they would have expected prior to having an affected child. However, the women with an affected child were still more likely to opt for TOP, and several women requested sterilization. Therefore, the women still considered the problems associated with FMR so great that they were unwilling to risk a recurrence. It is thus apparent that the perception of burden and caring for a child with FMR and the experience of having raised an affected child are important variables which can influence a woman's attitude towards PND and TOP.

Ekwo *et al.* (1987) studied the attitudes of 252 women towards the acceptance of amniocentesis and the perceived burden of having a child with facial abnormalities,

physical handicap, mental retardation, early death and prolonged illness. The authors found that the women perceived prolonged illness in their child as most burdensome and facial abnormalities as least burdensome. Further, the perceived burden associated with having a child with prolonged illness or early death were considered the most serious, and that associated with physical handicap and facial abnormalities least serious, and mental retardation fell in between the two groups. In their examination of the relationship between perceived burden and the acceptance of amniocentesis, they found that women who accept amniocentesis were more likely to perceive congenital malformations as burdensome. These women were most worried about having a child with mental retardation or prolonged illness, however those who rejected amniocentesis were worried more about having a child with prolonged illness. The number of living children the women had correlated with their perception of the consequences of congenital malformation, and women with fewer living children regarded congenital malformations as more burdensome than women with more living children. A family history of Down syndrome was also inversely related to the perception of burden, and women with no family history of Down syndrome tended to view congenital malformations as burdensome. Beeson and Golbus (1985) studied 26 women at risk for X-linked conditions (haemophilia A and Duchenne muscular dystrophy) and reported that women who had lived with affected children were unwilling, whereas those who had not were more willing, to risk the birth of an affected child.

Another aspect that plays a role in parents decisions to have PND and TOP, is the parents' perception of the risk. Parents translate their risk into binary form - I will or I will not have an affected child (Lippman-Hand and Fraser 1979). Therefore the decision making process of parents in such situations are complex and the perceived burden, the experience of caring for the child and understanding of risks play a role in their decisions regarding PND and TOP. Beeson and Golbus (1985:113) state that: "When actual decisions concerning PND and TOP are examined, they indicate that: (1) parents may not perceive themselves as engaging in a weighing of alternatives or making decisions at all, (2) the potential consequences are seen in binary rather than probabilistic terms, and (3) the decisions centre on perceived social consequences rather than primarily on biomedical data and abstract values."

5.5 THE PARENTS' USE OF PROFESSIONAL HELP

In most cases parents (60%) reported that a paediatrician was responsible for making the diagnosis of FMR in their child, with a medical geneticist making the diagnosis in 27% of cases. Parents stated that they had had questions about the prognosis and about the inheritance of the condition. The majority of the parents (80%) reported that their questions were answered satisfactorily. According to Meryash and Abuelo (1988), in their study on the counselling needs in FMR families, the issues the women thought most important and that should be discussed during genetic counselling were: availability of treatment, risk to their children of having a mentally retarded child, future functioning of the affected individuals in the family, and availability of PND. The least important issues were: making a diagnosis of FMR in other mentally disabled family members, risks to the subjects' siblings of having an affected child, what to tell relatives about FMR, and whether there were many other children and families with FMR. Altogether 57% of parents reported that they had had genetic counselling and 65% stated that it was a positive experience. Levy (1990) also reported that overall 85% of the 105 subjects he studied in Johannesburg felt that their expectations were met and that they were satisfied with the genetic counselling they received. However, according to Lippman-Hand and Fraser (1979), parents may feel ambiguity about the cause and prognosis of a condition and the impact of having an affected child. They suggest that this may leave some parents dissatisfied with genetic counselling and when a counsellor is unable to supply answers to the parents, they may devalue the consultation. Levy's (1990) study is not strictly comparable with the latter since he had fewer subjects who had had genetic counselling because of an affected child, and therefore fewer parents who may have felt the "ambiguity" described by Lippman-Hand and Fraser (1979).

Nearly half (47%) of the parents in the present study reported that they had been in contact with other families with children with FMR and that it was a positive experience. Those subjects who had not met other parents with children with FMR reported that they would like to do so. Almost all of the subjects stated that they would like to join a support group. Cohen (1962) said that parents who have successfully faced their problems can offer a special kind of help to other parents, which professionals cannot provide. Roeyers

and Cloetens (1995:8) are in agreement and they state the following: "...a number of families with a child with a handicap functioned successfully. They may have developed coping strategies that can be taught to others who are overwhelmed by stress. Parent contact groups, that bring together parents of children with the same handicap, can play an important role in this respect".

5.6 CONCLUSIONS RELATED TO THE AIMS OF THE STUDY

The key findings from the study are reported below acccording to the aims of the study.

5.6.1 THE RELATIONSHIP BETWEEN CHILDREN WITH FMR AND THEIR PARENTS, SIBLINGS AND FRIENDS, AND THE PARENTAL RELATIONSHIP.

The first aim of the study was to investigate the relationships in families with FMR and identify areas in which the experimental group differed significantly from the control. The first significant finding was that fewer parents of children with FMR than controls rewarded good behaviour in their child physically, probably due to the tactile defensiveness of the affected individuals. Secondly, half the parents of children with FMR appeared to enjoy their child's positive temperament (Meas *et al.* 1992 showed a similar finding), however this could be due to some overcompensation for the disorder. Thirdly, many experimental parents disliked the behavioural problems of their affected child. However, since children with mental disability due to other causes may also show similar behaviour problems, the effect of these problems on the family may not be unique to parents of children with FMR.

The results on the evaluation of the sibling relationship showed that the children with FMR mostly related well to their sibs. Further, in some siblings knowledge of FMR altered their relationship with the affected child, either for the better or for worse. Generally, however parents reported that the normal siblings were accepting, tolerant and protective of the child with FMR and that they did not feel excluded.

The relationship between the children with FMR and their peers appeared to be more affected by the disorder than the sibling relationship. The children with FMR had significantly fewer friends and more problems in their peer group relationships than did the normal controls. Similar problems were found in children with Down syndrome particularly in those who displayed behavioral difficulties (Byrne *et al.* 1988).

The evaluation of the relationship between the parents showed that, although parents of children with FMR had disagreements (which were mostly over discipline) most of the parents were content with their relationship and with the time they spent together. Some subjects reported that their relationship had changed after they had had their child with FMR, the experience enriched it in some cases and caused strain in others. Having a child with FMR therefore does not necessarily have a negative impact on the marital relationship. However the issues involved in whether the impact will be positive or negative are complex and to predict which marriages might dissolve is almost impossible. According to Byrne and Cunningham (1985) a combination of factors, such as the life-cycle stage, family interpretation of their situation, and the integration of the family prior to the birth of the disabled child are associated with the extent of the stress the situation imposes on the marriage.

5.6.2 PARENTS' FEELINGS ABOUT RECEIVING THE DIAGNOSIS IN THEIR CHILD, PRENATAL DIAGNOSIS AND SELECTIVE ABORTION.

The second aim of the project was to study how parents reacted to the diagnosis and their views on PND and TOP. The parents of children with FMR described feelings of denial, anger, shock, and sadness during the waiting period between the onset of observable symptoms and the time when the diagnosis was made. These feelings are characteristic of the process through which parents mourn the loss of a normal child.

The majority of the parents of children with FMR in this study did not want more children and the majority would request PND and TOP for affected fetuses in any future pregnancy. Significantly more parents of children with FMR than controls would

terminate a pregnancy if an affected fetus was diagnosed. The experience of raising a child with FMR therefore appears to play an important role in the decision to have prenatal diagnosis and termination if the fetus is affected.

5.6.3 THE PROFESSIONAL HELP THE PARENTS USED.

The third aim of the project was to investigate what professional help the parents utilized. The subjects generally received the diagnosis of FMR from a paediatrician and their concerns at the time included a need for further information about the prognosis and inheritance of FMR. The majority of the subjects had had genetic counselling and were satisfied with the service they received.

Half of the subjects had had contact with other families with children with FMR and those who had not met such families stated that they would like to do so. Further, almost all the subjects expressed the desire to join a parent support group.

5.7 LIMITATIONS OF THE STUDY

Various limitations of the study became clear during the course of the project:

1. As the sample size was quite small, the conclusions drawn may not be applicable to all families of children with FMR. However this was the maximum number of subjects which could be ascertained within the time constraints of this project.
2. The response rate was low (20%), mostly due to difficulty in tracing the potential subjects. Also, there could have been some self selection bias and only those who had successfully adjusted to their situation and were willing and capable of thinking about and discussing it might have volunteered to participate.
3. Only a few fathers participated and they were probably also a self selected and somewhat biased sample. However since not much research has been carried out on fathers it was worth including them.
4. The information that was gathered relied on parental self reports and parental perceptions, which could have been inaccurate (for example, regarding their child's symptoms). Also as this was a retrospective study the subjects might not have

remembered all the facts about their past experiences and feelings, and their perceptions could have become distorted over time. This however is a limitation applicable to many such psychosocial studies.

5. Emotional problems have been documented in FMR females with normal IQ's and those with mental retardation. It has been shown that affected females may show "blinders effect" in interviews which means that they may not incorporate past information into current situations and that they may minimize problems (Sobesky *et al.* 1994b). For this reason, in the present study, the experimental group, which consists of mothers of affected children who may be carriers of a FMR gene, may not be strictly comparable to the control group, which consists of mothers with normal children. The lower level of education in the experimental group may reflect the carrier or mildly affected FMR status of these subjects. The findings of the study therefore need to be considered with regard to this background.

5.8 RECOMMENDATIONS

5.8.1 THE GENETIC COUNSELLING SERVICE FOR FAMILIES WITH A MEMBER WITH FMR

The subjects in the present study found genetic counselling worthwhile and therefore it is important that the families with children with FMR receive such counselling. As one subject stated regarding her counselling experience:

"we were told more about the syndrome, especially the realities, we needed it"

Genetic counselling for FMR should be provided in a non-directive manner and follow the internationally accepted aims of genetic counselling (cited in Kessler:xvi 1979) and should address the following aspects:

1. The medical and social aspects: these include the features, behavioural problems, the possibility of intellectual disability, and treatment options such as medications which might alleviate some of the behavioural abnormalities, for example hyperactivity. The education options should also be outlined as these are of particular concern to the parents as shown in this study.

2. The genetic aspects: FMR is a complex disorder and parents need to understand the inheritance pattern and the nature of the gene defect to be able to alleviate their guilt feelings, such as "what did I do wrong?". As FMR is inherited in a X-linked fashion there are implications for future children and other family members. The risks to offspring and other relatives of having a child with FMR need to be explained clearly to the couple. Understanding of risks is important as they affect the parents future childbearing decisions and plans.
3. Available options: Parents need to know what tests are available to diagnose the disorder, and the advantages and disadvantages of PND. Parents who did not want children, because of their risk of having a child with FMR, may plan another pregnancy if PND and selective TOP for affected fetuses were available.
4. Emotional support: this is very important for clients during genetic counselling sessions. The parents receive information that is challenging to their whole being, and as a counsellor one must be aware of their reactions to the diagnosis and this new information. Empathic counselling should be provided in at least one or two follow-up sessions after the initial counselling. This process will ensure that the parents understand all the medical and genetic aspects, as well as the options open to them, should allow them to ask more questions about aspects that they did not understand, and should provide them with support and guidance.
5. Appropriate referral is a necessary adjunct to genetic counselling. FMR children frequently require speech therapy, developmental assessment psychiatric or psychological help, as well as special education, and they should be referred to the appropriate centres from the genetic counselling clinic.

5.8.2 FORMATION OF A SUPPORT GROUP

The present study found that the majority of parents would like to meet others parents and they would join a support group. Such a group can provide emotional and psychological support, socializing opportunities, valuable information about FMR and educational and other resources, and act on behalf of the special needs children. Also by working together families and professionals can improve community attitudes toward children with special needs (Jewell-Smart 1992).

In starting a support group several aspects should be considered. Initially a motivated person, preferably a parent, is needed to get the group going, and time must be allowed for the parents to get actively involved. A needs assessment should be conducted among the members and the type of group, ie family alone or family and professionals, should be considered.

The purpose of the support group would be to (Jewell-Smart 1992):

1. allow families with a common diagnosis to meet and share ideas.
2. help families to understand the special needs of their children and how best to meet those needs.
3. share knowledge regarding community resources to enhance their children's development.
4. receive needed support and knowledge from professional caregivers and other families especially new families.
5. assist families in moving beyond their initial reaction after receiving a diagnosis.
6. encourage opportunities for the families to meet in an atmosphere that encourages deep and personal sharing of concerns.
7. provide information about the disorder to members, professionals and the public.

During the present study to meet the needs of the subjects a support group was formed by the writer and another professional. Although no parent has yet been identified to run the group it is presently providing some of these functions.

5.8.3 PUBLIC EDUCATION

> "there is a lack of knowledge about children with FMR in the community, it should be explained to the schools and teachers" (mother in the present study)

A few parents mentioned that the doctors and the public were not aware of FMR. Also, for some parents, it took years before they received a diagnosis, which emphasises that information about FMR is probably lacking and should be made more available.

Both academic departments of Human Genetics and the Human Genetics section of the Department of Health, as well as support groups could play a part in providing community education. Support group members, in conjunction with the experts at the academic centres and the Department of Health, could draw up and provide pamphlets explaining what FMR is and circulate them widely. The support group could also compile a regular newsletter which would keep the members up to date with the new research findings and send information and perhaps personal stories to popular magazines. They could also organise regular meetings and awareness days. These activities would not only keep the affected families up to date, but educate the lay public and the professionals.

5.8.4 FURTHER RESEARCH

1) In the present study a few differences between the behaviour of the fathers and mothers with regard to their FMR child were identified for example, the use of physical or verbal punishment and perceptions of the severity of the disorder in the child. As only nine fathers participated the findings might not be generalizable to all fathers of children with FMR. A larger sample of fathers, as well as mothers, of children with FMR should therefore be investigated to assess whether these results would hold true in a larger group.

2) In the present study it was found that of the 11 parents that reported tactile defensiveness in their child only two rewarded good behaviour with physical touching. This aspect could be explored in more detail in a larger sample and methods of dealing with this somewhat negative behaviour pattern might be investigated.

3) The literature study revealed that different effects on the siblings of an affected child are reported when the data are collected from either the parents or the siblings themselves. The present study only included parents' reports and siblings' self reports could be studied in a future project. Also only subjective parents perceptions of the family relationships were studied, objective assessments of family dynamics may be worthwhile including in a future study. Furthermore the

perceptions of parents and siblings could be compared in more detail and the needs of siblings for a support group could be investigated.

5.9 SUMMARY AND CONCLUSION

From the present study it can be concluded that the relationship between the individuals with FMR and their parents was affected to some extent due to the presence of the disorder in the child. Many parents were concerned about managing their financial affairs and the child's education, and some were more lenient with their affected children and made some allowances because of their disorder. The parents had to cope with their children's behavioural problems, such as destructiveness and bad tempers, and some did not praise good behaviour with physical affection possibly due to the tactile defensiveness associated with the condition. However, some of the parents reported that their children had positive temperaments and were happy and caring.

The relationship between the children with FMR and their normal siblings was generally good and the normal sibs were accepting, tolerant and protective of the affected child. The relationship between the children with FMR and their peers was, however more adversely affected. The FMR children had significantly fewer friends and more problems in their peer relationships than the normal control children did.

The marital relationship of the subjects was affected in various ways by the presence of the child with FMR. Although the parents had disagreements (mostly over discipline), most were content with their relationship and the time they spent together. Some reported that the experience had enriched their relationship and brought them closer and others admitted that it had put a strain on the marital relationship.

As in other individuals who have experienced loss, parents of children with FMR, described feelings similar those associated with the bereavement process, after the diagnosis. The experience of having a child with FMR appeared to influence the subjects' child-bearing decisions, and the experience of caring for an affected child appeared to sway their decisions in favour of requesting PND and TOP. Most of the subjects in the

present study had genetic counselling and were satisfied with service. Half had had contact with other families and those who had not stated that they would like to meet other families.

From the results obtained in the present study, it can be concluded that family dynamics are disturbed by the presence of a child with FMR. Counsellors and therapists who work with these families should therefore be aware of the subtle effects of the syndrome on family relationships. Also the findings show that couples appreciate appropriate genetic counselling, and that parent support groups should be initiated for the essential support that can be provided only by a peer group. Information regarding the syndrome should be made available to the public so that in future the diagnosis is made earlier in the life of the child. Further research may be conducted to investigate the differences observed in the responses obtained from mothers and fathers, to explore the relationship between tactile defensiveness and rewarding good behaviour, and to investigate and compare the parents and siblings' perceptions of the effects of FMR on the siblings, and perhaps to assess the needs for sibling groups. In these ways a better service could be provided to these families who have to live with the effects of having a child with FMR, their problems can be understood and ameliorated, and the quality of their lives improved.

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APPENDIX A

Letters of approval from the University of the Witwatersrand's Postgraduate Committee and clearance certificate from the Committee for Research on Human Subjects.

UNIVERSITY OF THE WITWATERSRAND. JOHANNESBURG

Division of the Deputy Registrar (Research)

COMMITTEE FOR RESEARCH ON HUMAN SUBJECTS (MEDICAL)
Ref: R14/49 van der Colff

CLEARANCE CERTIFICATE PROTOCOL NUMBER M 940716

PROJECT Fragile X syndrome: a family study

INVESTIGATORS Miss T M van der Colff

DEPARTMENT Human Genetics, SAIMR

DATE CONSIDERED 940729

DECISION OF THE COMMITTEE *

Unconditionally approved.

DATE 940831

CHAIRMAN. ..... (Professor P E Cleaton-Jones)

* Guidelines for written "informed consent" attached where applicable.

c c Supervisor: Professor J Kromberg
Dept of Human Genetics, SAIMR

Works2\other\heclear\ 940716

==========

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and ONE COPY returned to the Secretary at Room 10001, 10th Floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee.

DATE...1/9/94.....SIGNATURE .....

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Faculty of Medicine

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

7 York Road, Parktown, 2193 South Africa • Telegrams Witsmed • Telephone (011) 647-1111 • Fax: (011) 643-4318

Student Number: 9311574/G
Degree: mm043

12 June 1995

Mrs T M Wessels (nee van der Colff)
365 van den Heever Street
Erasmia 0183
PRETORIA

Dear Mrs Wessels,

APPROVAL OF PROTOCOL ENTITLED, "FRAGILE X SYNDROME: A FAMILY STUDY"

I should like to advise you that the protocol that you have submitted for the degree of MSc(Med) has been approved by the Postgraduate Committee at its recent meeting, for continuation of your candidature, subject to ethics approval being obtained.

Professor J G Kromberg of the Department of Human Genetics has been appointed as your supervisor. You are asked to maintain regular contact with your supervisor who must be kept advised of your progress.

Please note that all candidates for higher degrees must make reference in their research reports to the clearance number of the relevant ethics committee. The final title, when submitting the research, should comply with the above title, and a signed declaration, noting that the work has been your own and not submitted to any other University, must also be included.

Yours sincerely,

MRS G GABRIEL
FACULTY OFFICER (POSTGRADUATE)
FACULTY OF MEDICINE

cc: Professor T Jenkins
Professor J Kromberg

APPENDIX B

Cover letters from DNHPD

DEPARTMENT OF HEALTH
DEPARTEMENT VAN GESONDHEID
Republic of South Africa

UMNYANGO WEZEMPILO
LEFAPH LA MAPHELO
Republiek van Suid Afrika

Faks: (012) 21-5392
Fax:
Teleks:
Telex:
Telefoon: (012) 312-0221
Telephone:

Telegramadres: "SAGWEP"
Telegraphic adress:
Privaatsak X828
Private Bag
0001 Pretoria

Hallmark Building, Proes Street
Navrae • Enquiries: Miss S Aucamp
Verwysing • Reference: Genetic Services
19/3/6/2

CONFIDENTIAL

To the Specific Family

Dear parent/family member

CONCERNING THE FRAGILE (X) SYNDROME

As a result of your, or a member of your family's, previous contact with a genetics nurse of the Department of Health in connection with a Fragile-X-syndrome diagnosis, you or a member of your family is on the Genetic Services address list in order to facilitate communication regarding the syndrome. If you have no knowledge of this, then please ignore this letter and accept our apologies for any unnecessary anxiety this letter may have caused you.

Fragile-X-syndrome is an inherited condition due to a fragile site on the X chromosome. This syndrome is associated with learning disabilities ranging from mild learning problems to mental handicap. Boys are affected more often than girls. No one is to blame and it can not be prevented or cured.

You have probably already received a letter from the Department of Health informing you of the study undertaken by the Department of Human Genetics of the University of the Witwatersrand on the experiences and perceptions of a family with a Fragile-X affected member. We would like to stress that you are under no obligation to participate in this project. The only reason we would like you to take part in the study is so that other families in the same situation as you can benefit from your experience.

We want to assure you that all information in our data base, including your details, is strictly confidential. The letter that you have received was addressed and sent to you by Genetic Services in the Department of Health. Your address will not, under any circumstances, be revealed to any person or institution. The only way that researchers can contact you is if you make contact with them from your side.

You will also soon be receiving a questionnaire which you are welcome to fill in and complete if you so desire. If you have any queries or remarks to make regarding the project you can contact **Miss T van der Colff at (011) 489 9228** or **(011) 489 9224 (office hours)** or **after hours at (011) 440 2966**. If you have any questions regarding the syndrome you can contact Genetic Services for more information.

Yours sincerely

Aucamp

DIRECTOR-GENERAL
Date: 03/10/94

GW 1/6.1.3

DEPARTMENT OF HEALTH
DEPARTEMENT VAN GESONDHEID
Republic of South Africa

UMNYANGO WEZEMPILO
LEFAPHA LA MAPHELO
Republiek van Suid-Afrika

Faks: (012) 21-5392
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Telex:
Telefoon: (012) 312-0221
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Telegramadres: "SAGWEP"
Telegraphic address:
Privaatsak X828
Private Bag
0001 Pretoria

Hallmark Building, Proes Street
Navrae • Enquiries: Miss S Aucamp
Verwysing • Reference: Genetic Services
19/3/6/2

CONFIDENTIAL

To the Specific Family

Dear parent/family member

CONCERNING THE FRAGILE (X) SYNDROME

Enclosed, please find the questionnaire mentioned in our previous letter to you. We would once again like to assure you that the matter is treated as strictly confidential and that you are under no obligation to participate in the study. We would, nevertheless, encourage you to consider taking part so that others in your situation may benefit from your experiences. If you decide to take part, please place the completed questionnaire in the addressed envelope and return it.

If you have not received our previous letter and would like to know more about the project, please do not hesitate to contact Genetic Services for more information. We appreciate your cooperation in this regard.

Yours sincerely

DIRECTOR-GENERAL
Date: 01/12/94

APPENDIX C

Introductory letter to postal questionnaire (experimental group)

THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

SCHOOL OF PATHOLOGY
Department of Human Genetics

PO Box 1038, Johannesburg, 2000
Tel: +27-11-489-9000

Hospital Street, Johannesburg
Fax: +27-11-489-9226
+27-11-489-9209

Professor T Jenkins	489-9210	Dr TJL de Ravel	489-9212	Dr M Ramsay	489-9214
Professor JGR Kromberg	489-9213	Dr A Krause	489-9219	Dr AB Lane	489-9221

INTRODUCTORY LETTER TO POSTAL QUESTIONNAIRE

Dear Parents

I am a post graduate Masters student at the Department of Human Genetics at the University of the Witwatersrand and the South African Institute for Medical Research. As part of fulfilment of my degree I am undertaking a study on Fragile X Syndrome.

My aim is to explore the effects that the diagnosis of Fragile X in a child has on the family, including the parents and siblings. Although much research has been done on Fragile X Syndrome, the focus has largely been on the genetic and diagnosis aspects. There remains a great need to explore the psychological and social issues which surround Fragile X Syndrome.

What I hope to accomplish with this study is to identify the problems to see if there are some that all families share, and therefore to assess whether families would benefit from the formation of a support group under the auspices of the South African Inherited Disorders Association (SAIDA).

The relevant information will be gathered by means of a postal questionnaire. You should receive this within two weeks after receiving this letter. The introductory letter and questionnaire is also available in afrikaans. Please contact me if you would like an Afrikaans copy.

I assure you that this study is completely confidential and that your names will not be connected to your answers.

Your participation in this study will be greatly appreciated.

Yours sincerely,

T Wessels
MSc(Med) Student

APPENDIX D

Cover letter for postal questionnaire (experimental group)

THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

SCHOOL OF PATHOLOGY
Department of Human Genetics

PO Box 1038, Johannesburg, 2000
Tel: - 27-11-489-9000
Hospital Street, Johannesburg
Fax: - 27-11-489-9226

Professor T Jenkins	489-9210	Dr TJL de Ravel	489-9212	Dr M Ramsay	489-9214
Professor JGR Kromberg	489-9213	Dr A Krause	489-9219	Dr AB Lane	489-9221

COVER LETTER FOR POSTAL QUESTIONNAIRE

RESEARCH TITLE: Fragile X syndrome: a family study.
SUPERVISOR: Professor JGR Kromberg.

Dear Respondent

Attached to this letter are two questionnaires about your experiences of being a parent with a child with Fragile X syndrome, one should be completed by the Mother and the other by the Father.

The questionnaires are divided into 6 sections and should take 30 to 45 minutes to complete. While you are responding to the questions it is very important that you remember that there are no right and wrong answers. You should give your own answers based on what you have experienced.

I assure you that this study is a confidential one. Your name will not appear anywhere in the write-up of the report. Where you are asked to give you children's names it is purely to assist me in interpreting the answers. You will notice that the questionnaires are number coded, this is to check on who responded. It is necessary for you to consent to participating in this study and I have therefore included a consent form for you to sign.

If you are interested in the outcome of the study, please fill in the relevant section at the end of the consent form.

When you have completed the questionnaire and filled in the consent form, please place them both in the stamped, addressed envelope provided, and return it to me as soon as possible.

Your participation in the study is much appreciated and it will help us to learn more about the Fragile X syndrome and its effects on the family.

Your sincerely

T Wessels
MSc(Med) Student

APPENDIX E

Introductory letter to interview (experimental group)

THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

SCHOOL OF PATHOLOGY
Department of Human Genetics

PO Box 1038, Johannesburg, 2000
Tel: +27-11-489-9000

Hospital Street, Johannesburg
Fax: +27-11-489-9226
+27-11-489-9209

Professor T Jenkins	489-9210	Dr TJL de Ravel	489-9212	Dr M Ramsay	489-9214
Professor JGR Kromberg	489-9213	Dr A Krause	489-9219	Dr AB Lane	489-9221

INTRODUCTORY LETTER TO INTERVIEW

Dear Parent/Parents

I am a post graduate Masters student at the Department of Human Genetics at the University of the Witwatersrand and the South African Institute for Medical Research. As part of fulfilment of my degree I am undertaking a study on Fragile X Syndrome.

My aim is to explore the effects that the diagnosis of Fragile X in a child has on the family, including the parents and siblings. Although much research has been done on Fragile X Syndrome the focus has largely been on the genetic and diagnosis aspects. There remains a great need to explore the psychological and social issues which surround Fragile X Syndrome.

What I hope to accomplish with this study is to innvestigate the problems, and identify those that many families share. I would also like to assess whether families would benefit from the formation of a support group under the auspices of the South African Inherited Disorders Association (SAIDA).

The relevant information will be gathered by means of an interview schedule. The interview will be conducted using a schedule of questions, with each parent/partner separately and will take approximately 45 minutes. I will contact you to arrange a suitable time.

I assure you that this study is completely confidential and that your names will not be connected to your answers.

The more parents that participate in the study, the more insight into the problems that families with Fragile X children experience, could be gained. I would therefore appreciate it if you could inform any other parents of Fragile X syndrome children that you may know, about this study. They could contact me telephonically at:

(011) 489 9228 or 489 9224 (office hours) or
(011) 440 2966 (after hours)

Your participation in this study will be greatly appreciated.

Yours sincerely,

T Wessels
MSc(Med) Student

APPENDIX F

Cover letter for interview (experimental group)

THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

SCHOOL OF PATHOLOGY
Department of Human Genetics

PO Box 1038, Johannesburg, 2000
Tel: +27-11-489-9000
Hospital Street, Johannesburg
Fax: -27-11-489-9226

Professor T Jenkins	489-9210	Dr TJL de Ravel	489-9212	Dr M Ramsay	489-9214
Professor JGR Kromberg	489-9213	Dr A Krause	489-9219	Dr AB Lane	489-9221

COVER LETTER FOR INTERVIEW

RESEARCH TITLE: Fragile X syndrome: a family study.
SUPERVISOR: Professor JGR Kromberg

Dear Respondent

Your willingness to participate in this study is greatly appreciated.

I will conduct an interview, by asking each parent alone a series of questions about his/her experiences of being a parent with a child with Fragile X syndrome.

The interview will take between 30 and 45 minutes to complete. While you are responding to the questions it is very important to remember that there are no right or wrong answers. You should give your own answers based on what you have experienced.

I assure you that this study is a confidential one. Your name will not appear anywhere in the write-up of the report. Where you are asked to give you children's names it is purely to assist me in interpreting the answers. It is necessary for you to give your consent to participate in this study and I have therefore attached a consent form for you to sign.

If you are interested in the outcome of the study, please fill in the relevant section at the end of the consent form.

Your participation in the study will help us to learn more about the Fragile X syndrome and its effects on the family.

Your sincerely

T Wessels
MSc(Med) Student

APPENDIX G

Questionnaire (Schedule A) used in the experimental group

FRAGILE X SYNDROME: A FAMILY STUDY

QUESTIONNAIRE/INTERVIEW **No ____**

SECTION 1 - PERSONAL DETAILS.

1. What is your sex ?
(Please tick appropriate box)

Male [ ]

Female [ ]

2. What is your date of birth ?

_____/_____/_____

Day Month Year

3. What is your marital status ?
(Please tick appropriate box)

Single	[ ]	Divorced	[ ]
Living with a partner	[ ]	Widowed	[ ]
Married	[ ]	Other (Specify)_____	[ ]

4. What is your religion ?
(Please tick appropriate box)

Catholic	[ ]	Muslim	[ ]
Protestant	[ ]	Hindu	[ ]
Jewish	[ ]	Other (Specify)_____	[ ]

5. Are you ..... ?
(Please tick appropriate box)

Black	[ ]	Indian	[ ]
White	[ ]	Other (Specify)_____	[ ]
Coloured	[ ]		

6. What is the highest level of education obtained ?
(Please tick appropriate box)

Std 5 or lower	[ ]	Technicon	[ ]
Std 6 to Std 10	[ ]	University	[ ]
Technical college	[ ]	Other (Specify)_____	[ ]

7. What is your occupation ? (eg. Domestic worker, lawyer, doctor etc.)

_____

7.1. If you are employed do you work ?
(Please tick appropriate box))

Full time [ ]

Part time [ ]

Other (Specify) [ ] _____

7.2. If you are employed what is your income per year ?
(Please tick appropriate box)

Less than R20 000 [ ]

R20 000 to R48 00 [ ]

R48 000 to R60 000 [ ]

Over R60 000 [ ]

8. Are you living in ?
(Please tick appropriate box)

Your own house [ ]

Rented house [ ]

Own apartment [ ]

Rented apartment [ ]

Other (Specify)_____ [ ]

SECTION 2 - DETAILS OF THE CHILDREN IN THE FAMILY.

9. List all your children, starting with the oldest, in the table below. Specify their date of birth (D.O.B.) and sex. (Please write down their names to avoid confusion).

Names	D.O.B.	Sex
1.		
2.		
3.		
4.		
5.		
6.		

10. Which of the following schools has/have your child/children with Fragile X syndrome (FXS) attended ?
(Please tick appropriate box)

Child's name	Normal school	Special class in normal school	Remedial school	Special school	Not attended school
1.	☐	☐	☐	☐	☐
2.	☐	☐	☐	☐	☐
3.	☐	☐	☐	☐	☐

11. If any of your children diagnosed with Fragile X syndrome has finished school, is/are the affected child/children working ?
(Please tick appropriate box)

	Yes	No
1.	☐	☐
2.	☐	☐
3.	☐	☐

11.1 If yes, where is/are the child/children with Fragile X syndrome working ?
(Please tick appropriate box)

	Normal employment	Sheltered employment
1.	☐	☐
2.	☐	☐
3.	☐	☐

12. The table below shows some of the characteristics found in children with Fragile X syndrome. Not all children show all of these characteristics all at the same time. The aim of this question is to establish to which extent your child/ children show these characteristics.

Tick NEVER (N) if your child does not show a specific characteristic.

Tick SOMETIMES (S) if your child shows a specific characteristic only sometimes.

Tick OFTEN (O) if your child shows a specific characteristic a lot.

There is space provided for you to evaluate each child separately. If you have more than one child with Fragile X syndrome, please write in your children's names.

for example:

CHARACTERISTICS	NAME	N	S	O
Does your child hurt him/herself ?	1. Mandy			
	2. Mike			
	3.			

CHARACTERISTICS	NAME	N	S	O
Is your child hyperactive ?	1.			
	2.			
	3.			
Does your child get bored easily ?	1.			
	2.			
	3.			
Does your child hurt him/herself ?	1.			
	2.			
	3.			
Does your child rock from side to side or backwards and forwards ?	1.			
	2.			
	3.			
Does your child bite his/her hands ?	1.			
	2.			
	3.			

CHARACTERISTICS	NAME	N	S	O
Does your child flaps his/her hands ?	1.			
	2.			
	3.			
Is your child shy ?	1.			
	2.			
	3.			
Does your child have difficulties with socialising ?	1.			
	2.			
	3.			
Does your child dislike being touched ?	1.			
	2.			
	3.			
Does your child have emotional outbursts ?	1.			
	2.			
	3.			
Does your child avoid making eye contact ?	1.			
	2.			
	3.			
Does your child speak without completing his/her sentences ?	1.			
	2.			
	3.			
Does your child repeat words, phrases or topics over and over ?	1.			
	2.			
	3.			
Does your child speak very fast ?	1.			
	2.			
	3.			

13. What is/ are your child/ children with fragile X' favourite activity ?

_____

_____

_____

14. What games does your child/children with fragile X like playing?

_____

_____

_____

SECTION 3 - EFFECTS ON THE FAMILY

SECTION 3.1 - THE CHILD: HIS/HER FRIENDS AND SIBLINGS.

If you only one child, only answer the first four questions (question 15, 16, 17, 18)

15. Evaluate your Fragile X child's/ children's friendships by ticking the appropriate box. My child has.....

Child's name	A lot of friends	A few friends	No friends
1.	☐	☐	☐
2.	☐	☐	☐
3.	☐	☐	☐

If you have more than one child with Fragile X syndrome please answer the following four questions (question 16, 17, 18, and 19) **only** for your **oldest** child with Fragile X syndrome.

16. Who are your fragile X child's friends ? (for eg. neighbours, relatives)

_____

_____

_____

17. How does your child with fragile X relate to other children ?

_____

_____

_____

18. How do the other children relate to your child with Fragile X ?

_____

_____

_____

_____

19. How does your child with Fragile X relate to his/her brothers and sisters ?

_____

_____

_____

_____

20. How do your other children relate to your Fragile X child/ children ?

_____

_____

_____

_____

21. Are your other children aware that their brother/sister has Fragile X syndrome ?
(Please tick appropriate box)

Yes [ ]

No [ ]

Sort off [ ]

21.1 Describe how this effects their relationship ?

_____

_____

_____

_____

22. Are there any problems in their (Fragile X child with his/ her brothers and sisters) relationships ?
(Please tick appropriate box)

Yes [ ]

No [ ]

22.1 If yes, what sort of problems do they experience ?

_____

_____

_____

_____

23. Do your other children play with your Fragile X child/ children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

23.1 If yes, what sort of games do they play?

_____
_____
_____
_____

24. Are their times when your other children do not want to play with your Fragile X child/ children ?
(Please tick appropriate box)

Often [ ]

Sometimes [ ]

Never [ ]

24.1 Please give reasons to your answer.

_____
_____
_____
_____

25. Do you think your other children feel left out ?
(Please tick appropriate box)

Yes [ ]

No [ ]

25.1 If yes, why do you think so ?

_____
_____
_____
_____

SECTION 3.2 - THE CHILD/ CHILDREN AND THE PARENTS

26. Do you have concerns about management of your Fragile X child/ children ?
(Please tick appropriate box)

Child's name	No concerns	Some concerns	Many concerns
1. _____	☐	☐	☐
2. _____	☐	☐	☐
3. _____	☐	☐	☐

If you have more than one child with Fragile X syndrome please answer the following questions (question 27, 28, 29, 30, and 31) **only** for your **oldest** child with Fragile X syndrome.

27. If there are concerns, what are they ?

_____

_____

_____

_____

28. How do you discipline your fragile X child ?
(Please tick all the appropriate boxes)

Physical punishment (eg. spanking) [ ]

Time out (eg. send to room for a period of time) [ ]

Verbal punishment (eg. scolding) [ ]

Threats (eg. if you don't..., I will....) [ ]

Withdrawal of privileges (eg. not allowed to watch favourite TV program) [ ]

Other (Specify)_____ [ ]

29. Do you praise your Fragile X child's good behaviour ?
(Please tick appropriate box)

Often [ ]

Sometimes [ ]

Never [ ]

29.1 If you do, how is this done ?

_____
_____
_____
_____

30. Which particular aspects about your Fragile X child, if any do you like ?

_____
_____
_____
_____

31. Which particular aspects about your Fragile X child, if any do you dislike ?

_____
_____
_____
_____

Only answer question 32 if you have more than one child.

32. Do you think you treat your Fragile X child differently to your other children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

32.1 If yes, explain why do think so ?

_____
_____
_____
_____

33. Who does most of the child-related tasks like dressing, washing, and feeding of the fragile X child/ children ?
(Please tick all the appropriate boxes)

Mother [ ] Family member (Specify)_____ [ ]

Father [ ] Other (specify)_____ [ ]

If you have ticked more than one box, answer only question 33.1

If you have ticked only one box, answer only questions 33.2 and 33.3.

33.1 Please describe how the child-related tasks are accomplished.

_____
_____
_____
_____
_____

33.2 Does the person mentioned in question 33 receive any help in managing the Fragile X child ?
(Please tick appropriate box)

Yes [ ]

No [ ]

33.3 If yes, who helps and how often ?

_____
_____
_____
_____

34. Who plays with the fragile X child/ children most of the time ?
(Please tick appropriate box)

Mother [ ] Family member (Specify)_____ [ ]

Father [ ] Other (specify)_____ [ ]

35. Who is responsible for taking the fragile X child/ children to hospital, doctor or therapy visits most of the time ?
(Please tick appropriate box)

Mother [ ] Family member (Specify)_____ [ ]

Father [ ] Other (specify)_____ [ ]

If you have ticked more than one box, answer question 35.1

35.1 Please explain who the responsibilities are shared.

_____

_____

_____

Only answer question 36 if you have more than one child.

36. If you had to answer questions 33, 34, and 35 again but this time for one of your children without Fragile X syndrome, would you have given the same answers ?
(Please tick appropriate box)

Yes [ ]

No [ ]

36.1. If no, explain how you would have answered differently ?

_____

_____

_____

37. Do you have family outings with you Fragile X child/ children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

37.1 If yes, how often and what kind of things do you do ?

_____

_____

_____

37.2 If no, what are the reasons for this ?

_____

_____

_____

38. Do you have family outings without your Fragile X child/ children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

38.1 If yes, how often and what kind of things do you do ?

_____

_____

_____

38.2 If no, what are the reasons for this ?

_____

_____

_____

SECTION 3.3 - EFFECTS ON THE PARENTS

39. When did you first notice that there was something wrong with your child/ children ?

_____

_____

_____

_____

40. How long did it take from first noticing that there was something wrong to the final diagnosis?

_____

_____

_____

_____

41. Describe what you went through during this stage.

_____

_____

_____

_____

42. How did you feel after you were told that your child/ children had fragile X syndrome ?

_____

_____

_____

_____

43. Do you think that you are the same sort of person you were before you had a Fragile X child/ children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

43.1 If no, describe how you have changed.

_____
_____
_____
_____
_____

44. Do you have enough time to yourself for doing your own thing ?
(Please tick appropriate box)

Yes [ ]

No [ ]

44.1 If no, what is the reason for this.

_____
_____
_____
_____
_____

45. Do you think that your ambitions have changed after you had a Fragile X child/ children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

45.1 If yes, how have they changed.

_____
_____
_____
_____
_____
_____

46. Do you want more children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

Unsure [ ]

46.1 Please give reasons for your answer.

_____

_____

_____

_____

47. If you/ your wife were to fall pregnant would you want to know whether the fetus has Fragile X sydrome ?
(Please tick appropriate box)

Yes [ ]

No [ ]

Unsure [ ]

47.1 Please give reasons for your answer.

_____

_____

_____

_____

48. If you/ your wife were to fall pregnant and you were told that the fetus had Fragile X syndrome would you want to terminate the pregnancy ?
(Please tick appropriate box)

Yes [ ]

No [ ]

Unsure [ ]

48.1 Please give reasons for your answer.

_____

_____

_____

_____

49. What advice would you give other parents who are in a similar position to the one that you were in ?

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

SECTION 3.4 - THE MARITAL RELATIONSHIP

50. Who makes the decisions regarding your Fragile X child/ children ?
(Please tick appropriate box)

You [ ]

Your spouse [ ]

Together [ ]

51. Do you disagree about decisions that have to be made about the Fragile X child/ children ?
(Please tick appropriate box)

Never [ ] Often [ ]

Sometimes [ ] Always [ ]

52. Which decision regarding your Fragile X child/ children causes you and your spouse to quarrel ? (eg. decisions about discipline, or to which school a child should go to)

_____
_____
_____

53. How often do you and your spouse go out alone ?

_____
_____
_____

53.1 Are you satisfied with this ? Why or why not ?

_____

_____

_____

54. Are you satisfied with the amount of help that you receive from your spouse/partner in doing the housework and caring for the children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

54.1 Describe your feelings about this.

_____

_____

_____

55. How would you describe you and your spouse's relationship ?

_____

_____

_____

56. Do you think your relationship with you spouse has changed after you have had your Fragile X child/ children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

56.1 If yes, how did it change ?

_____

_____

_____

57. If you are divorced or separated, why do you think this happened ?

_____

_____

_____

_____

_____

_____

SECTION 4 - HELP PROVIDED.

58. Who diagnosed your child/ children as having Fragile X syndrome ?
(Please tick appropriate box)

Family Doctor	[ ]	Genetic counsellor	[ ]
Paediatrician	[ ]	Other (Specify)_____	[ ]
Obstetrician/Gynaecologist	[ ]		

59. What questions did you have at the time of the diagnosis ?

_____
_____
_____
_____
_____

60. Were these questions answered by the person who made the diagnosis ?
(Please tick appropriate box)

Yes [ ]

No [ ]

60.1 If no, who answered your questions ?

_____
_____
_____
_____

61. Did you and your spouse have genetic counselling ?
(Please tick appropriate box)

Yes [ ]

No [ ]

61.1 If yes, what is your feelings about this ?

_____
_____
_____
_____

62. Have you been in contact with other parents who also have a Fragile X child/ children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

62.1 If yes, what is your feelings about this ?

_____

_____

_____

_____

62.2 If no, would you like to meet other parents ?

_____

_____

_____

_____

63. Would you be interested in joining a fragile X support group ?
(Please tick appropriate box)

Yes [ ]

No [ ]

64. Please add any comments or thoughts.

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

65. This form has been completed by.....

Mother [ ]

Father [ ]

THANK YOU FOR YOUR TIME !!

APPENDIX H

Informed consent (experimental group)

THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

SCHOOL OF PATHOLOGY
Department of Human Genetics

PO Box 1038, Johannesburg, 2000
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Fax: +27-11-489-9226
+27-11-489-9209

Professor T Jenkins	489-9210	Dr TJL de Ravel	489-9212	Dr M Ramsay	489-9214
Professor JGR Kromberg	489-9213	Dr A Krause	489-9219	Dr AB Lane	489-9221

No:_____

INFORMED CONSENT

RESEARCH TITLE: Fragile-X syndrome: a family study.

RESEARCHER: Tina-Marié Wessels (Msc(Med) Student, Department of human genetics)

SUPERVISOR: Professor JGR Kromberg

I _____ (Name), _____(Age in years), consent to participate in a study, which involves the completion of either a questionnaire, or an interview regarding my experiences as being a parent of a Fragile-X child.

I understand what the study involves, and that I have the right to withdraw consent at any time.

Signature of Subject: _____

Date: _____

I would like to receive a summary of the report when it is finished:
(Please tick appropriate box)

Yes [ ]

No [ ]

APPENDIX I

Cover letter for interview (control group)

THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
SCHOOL OF PATHOLOGY
Department of Human Genetics

PO Box 1038, Johannesburg, 2000 Hospital Street, Johannesburg
Tel: + 27-11-489-9000 Fax: - 27-11-489-9226

Professor T Jenkins	489-9210	Dr TJL de Ravel	489-9212	Dr M Ramsay	489-9214
Professor JGR Kromberg	489-9213	Dr A Krause	489-9219	Dr AB Lane	489-9221

COVER LETTER FOR INTERVIEW

RESEARCH TITLE: Fragile X syndrome: a family study.
Normal control group

SUPERVISOR: Professor JGR Kromberg

Dear Respondent

Your willingness to participate in this study is greatly appreciated.

I will conduct an interview, by asking each parent alone a series of questions about his/her experiences of being a parent.

The interview will take between 30 and 45 minutes to complete. While you are responding to the questions it is very important to remember that there are no right or wrong answers. You should give your own answers based on what you have experienced.

I assure you that this study is a confidential one. Your name will not appear anywhere in the write-up of the report. Where you are asked to give you children's names it is purely to assist me in interpreting the answers. It is necessary for you to give your consent to participate in this study and I have therefore attached a consent form for you to sign.

If you are interested in the outcome of the study, please fill in the relevant section at the end of the consent form.

Your sincerely

T Wessels
MSc(Med) Student

APPENDIX J

Questionnaire (Schedule B) used in the control group

FRAGILE X SYNDROME: A FAMILY STUDY
NORMAL CONTROL GROUP

QUESTIONNAIRE/INTERVIEW **No ___**

SECTION 1 - PERSONAL DETAILS.

1. What is your sex ?
(Please tick appropriate box)

Male [ ]

Female [ ]

2. What is your date of birth ?

_____ / _____ / _____

Day Month Year

3. What is your marital status ?
(Please tick appropriate box)

Single	[ ]	Divorced	[ ]
Living with a partner	[ ]	Widowed	[ ]
Married	[ ]	Other (Specify)_____	[ ]

4. What is your religion ?
(Please tick appropriate box)

Catholic	[ ]	Muslim	[ ]
Protestant	[ ]	Hindu	[ ]
Jewish	[ ]	Other (Specify)_____	[ ]

5. Are you ..... ?
(Please tick appropriate box)

Black	[ ]	Indian	[ ]
White	[ ]	Other (Specify)_____	[ ]
Coloured	[ ]		

6. What is the highest level of education obtained ?
(Please tick appropriate box)

Std 5 or lower	[ ]	Technicon	[ ]
Std 6 to Std 10	[ ]	University	[ ]
Technical college	[ ]	Other (Specify)_____	[ ]

7. What is your occupation ? (eg. Domestic worker, lawyer, doctor etc.)

_____

7.1. If you are employed do you work ?
(Please tick appropriate box))

Full time [ ]

Part time [ ]

Other (Specify) [ ] _____

7.2. If you are employed what is your income per year ?
(Please tick appropriate box)

Less than R20 000 [ ]

R20 000 to R48 00 [ ]

R48 000 to R60 000 [ ]

Over R60 000 [ ]

8. Are you living in ?
(Please tick appropriate box)

Your own house [ ]

Rented house [ ]

Own apartment [ ]

Rented apartment [ ]

Other (Specify)_____ [ ]

SECTION 2 - DETAILS OF THE FRAGILE X CHILD/ CHILDREN IN THE FAMILY.

9. List all your children, starting with the oldest, in the table below. Specify their date of birth (D.O.B.), sex and whether or not they have been diagnosed as having Fragile X syndrome (FXS). (Please write down their names to avoid confusion).

Names	D.O.B.	Sex	FXS	
			Yes	No
1.				
2.				
3.				
4.				
5.				
6.				

10. What is your index's child favourite activity ?

_____

_____

_____

11. What games does your index child like playing?

_____

_____

_____

SECTION 3 - EFFECTS ON THE FAMILY

SECTION 3.1 - THE CHILD: HIS/HER FRIENDS AND SIBLINGS.

If you only have one child, only answer the first four questions (question 13, 14, 15, 16)

12. Evaluate your index child's friendships by ticking the appropriate box.
My child has.....

Child's name	A lot of friends	A few friends	No friends
1.	☐	☐	☐
2.	☐	☐	☐
3.	☐	☐	☐

13. Who are your index child's friends ? (for eg. neighbours, relatives)

_____

_____

_____

14. How does your index child relate to other children ?

_____

_____

_____

15. How do the other children relate to your index child ?

16. How does your index child with relate to his/her brothers and sisters?

17. How do your other children relate to your index child ?

18. Are there any problems in their (index child with his/ her brothers and sisters) relationships ?
(Please tick appropriate box)

Yes [ ]

No [ ]

18.1 If yes, what sort of problems do they experience ?

19. Do your other children play with your index child ?
(Please tick appropriate box)

Yes [ ]

No [ ]

19.1 If yes, what sort of games do they play?

20. Are their times when your other children do not want to play with your index child ?
(Please tick appropriate box)

Often [ ]

Sometimes [ ]

Never [ ]

20.1 Please give reasons to your answer.

_____

_____

_____

_____

21. Do you think your other children feel left out ?
(Please tick appropriate box)

Yes [ ]

No [ ]

21.1 If yes, why do you think so ?

_____

_____

_____

_____

SECTION 3.2 - THE CHILD/ CHILDREN AND THE PARENTS

22. Do you have concerns about management of your index child ?
(Please tick appropriate box)

Child's name	No concerns	Some concerns	Many concerns
1.	☐	☐	☐
2.	☐	☐	☐
3.	☐	☐	☐

23. If there are concerns, what are they ?

_____

_____

_____

_____

24. How do you discipline your index child ?
(Please tick all the appropriate boxes)

Physical punishment (eg. spanking) [ ]

Time out (eg. send to room for a period of time) [ ]

Verbal punishment (eg. scolding) [ ]

Threats (eg. if you don't..., I will....) [ ]

Withdrawal of privileges (eg. not allowed to watch favourite TV program) [ ]

Other (Specify)_____ [ ]

25. Do you praise your index child's good behaviour ?
(Please tick appropriate box)

Often [ ]

Sometimes [ ]

Never [ ]

25.1 If you do, how is this done ?

_____

_____

_____

_____

26. Which particular aspects about your index child, if any do you like ?

_____

_____

_____

_____

27. Which particular aspects about your index child, if any do you dislike ?

_____

_____

_____

_____

Only answer question 29 if you have more than one child.

28. Do you think you treat your index child differently to your other children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

28.1 If yes, explain why do think so ?

_____

_____

_____

_____

29. Who does most of the child-related tasks like dressing, washing, and feeding of the index child ?
(Please tick all the appropriate boxes)

Mother [ ] Family member (Specify)_____ [ ]

Father [ ] Other (specify)_____ [ ]

If you have ticked more than one box, answer only question 29.1

If you have ticked only one box, answer only questions 29.2 and 29.3.

29.1 Please describe how the child-related tasks are accomplished.

_____

_____

_____

_____

_____

29.2 Does the person mentioned in question 33 receive any help in managing the index child ?

(Please tick appropriate box)

Yes [ ]

No [ ]

29.3 If yes, who helps and how often ?

_____

_____

_____

_____

30. Who plays with the index child most of the time ?

(Please tick appropriate box)

Mother [ ] Family member (Specify)_____ [ ]

Father [ ] Other (specify)_____ [ ]

31. Who is responsible for taking the index child/ children to hospital, doctor or therapy visits most of the time ?

(Please tick appropriate box)

Mother [ ] Family member (Specify)_____ [ ]

Father [ ] Other (specify)_____ [ ]

If you have ticked more than one box, answer question 31.1

31.1 Please explain who the responsibilities are shared.

_____

_____

_____

Only answer question 32 if you have more than one child.

32. If you had to answer questions 29, 31, and 31 again but this time for one of your other children, would you have given the same answers ?

(Please tick appropriate box)

Yes [ ]

No [ ]

32.1. If no, explain how you would have answered differently ?

_____
_____
_____

33. Do you have family outings with you index child ?
(Please tick appropriate box)

Yes [ ]

No [ ]

33.1 If yes, how often and what kind of things do you do ?

_____
_____
_____

33.2 If no, what are the reasons for this ?

_____
_____
_____

34. Do you have family outings without your index child ?
(Please tick appropriate box)

Yes [ ]

No [ ]

34.1 If yes, how often and what kind of things do you do ?

_____
_____
_____

34.2 If no, what are the reasons for this ?

_____
_____
_____

SECTION 3.3 - EFFECTS ON THE PARENTS

35. Do you think that you are the same sort of person you were before you had your index child? (Please tick appropriate box)

Yes [ ]

No [ ]

35.1 If no, describe how you have changed.

_____
_____
_____
_____
_____

36. Do you have enough time to yourself for doing your own thing ? (Please tick appropriate box)

Yes [ ]

No [ ]

36.1 If no, what is the reason for this.

_____
_____
_____
_____
_____

37. Do you think that your ambitions have changed after you had your index child ? (Please tick appropriate box)

Yes [ ]

No [ ]

37.1 If yes, how have they changed.

_____
_____
_____
_____
_____
_____

38. Do you want more children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

Unsure [ ]

38.1 Please give reasons for your answer.

_____
_____
_____
_____

39. If you/ your wife were to fall pregnant would you want to know of abnormalities in the fetus?
(Please tick appropriate box)

Yes [ ]

No [ ]

Unsure [ ]

39.1 Please give reasons for your answer.

_____
_____
_____
_____

40. If you were told that the fetus is abnormal would you want to terminate the pregnancy ?
(Please tick appropriate box)

Yes [ ]

No [ ]

Unsure [ ]

40.1 Please give reasons for your answer.

_____
_____
_____
_____

SECTION 3.4 - THE MARITAL RELATIONSHIP

41. Who makes the decisions regarding your index child ?
(Please tick appropriate box)

You [ ]

Your spouse [ ]

Together [ ]

42. Do you disagree about decisions that have to be made about the index child ?
(Please tick appropriate box)

Never [ ] Often [ ]

Sometimes [ ] Always [ ]

43. Which decision regarding your index child causes you and your spouse to quarrel ? (eg. decisions about discipline, or to which school a child should go to)

_____

_____

_____

44. How often do you and your spouse go out alone ?

_____

_____

_____

44.1 Are you satisfied with this ? Why or why not ?

_____

_____

_____

45. Are you satisfied with the amount of help that you receive from your spouse/partner in doing the housework and caring for the children ?
(Please tick appropriate box)

Yes [ ]

No [ ]

45.1 Describe your feelings about this.

_____

_____

_____

46. How would you describe you and your spouse's relationship ?

_____

_____

_____

47. Do you think your relationship with you spouse has changed after you have had your index child ?

(Please tick appropriate box)

Yes [ ]

No [ ]

47.1 If yes, how did it change ?

_____

_____

_____

48. If you are divorced or separated, why do you think this happened ?

_____

_____

_____

_____

_____

_____

49. Please add any comments or thoughts.

50. This form has been completed by.....

Mother [ ]

Father [ ]

THANK YOU FOR YOUR TIME !!

APPENDIX K

Informed consent (control group)

THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

SCHOOL OF PATHOLOGY
Department of Human Genetics

PO Box 1038, Johannesburg, 2000
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Hospital Street, Johannesburg
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Professor T Jenkins	489-9210	Dr TJL de Ravel	489-9212	Dr M Ramsay	489-9214
Professor JGR Kromberg	489-9213	Dr A Krause	489-9219	Dr AB Lane	489-9221

No:_____

INFORMED CONSENT

RESEARCH TITLE: Fragile-X syndrome: a family study.
Normal control group.

RESEARCHER: Tina-Marié Wessels (Msc(Med) Student, Department of human genetics)

SUPERVISOR: Professor JGR Kromberg

I _____ (Name), _____ (Age in years), consent to participate in a study, which involves the completion of either a questionnaire, or an interview regarding my experiences as being a parent.

I understand what the study involves, and that I have the right to withdraw consent at any time.

Signature of Subject: _____

Date: _____

I would like to receive a summary of the report when it is finished:
(Please tick appropriate box)

Yes [ ]

No [ ]

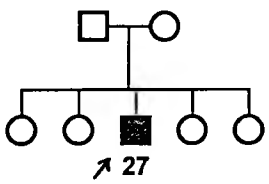
APPENDIX L

The pedigrees of the 22 families from the experimental group and their matched control families

THE 22 FAMILIES FROM THE EXPERIMENTAL GROUP AND THEIR MATCHED CONTROL FAMILIES

Experimental group

1)



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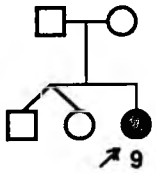

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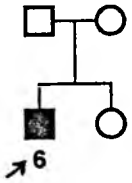

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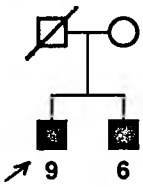

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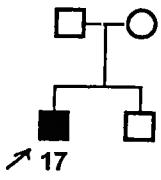

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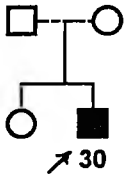
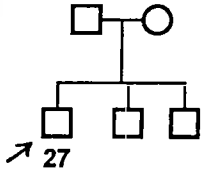


Control group

1)



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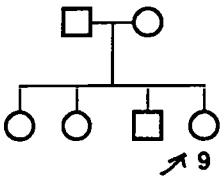

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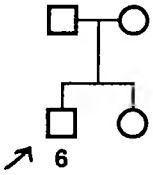

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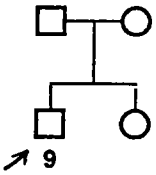
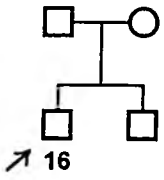
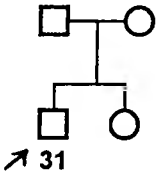


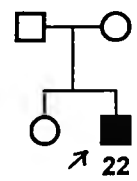
5)



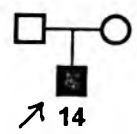
6)



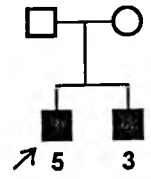
7)



8)



9)



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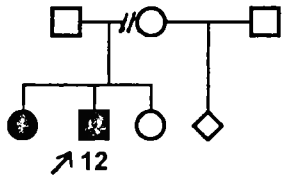

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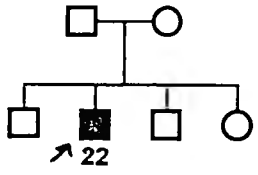

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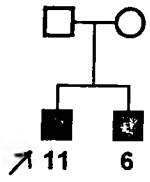

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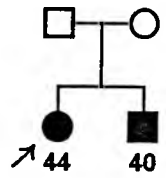

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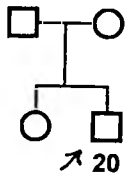

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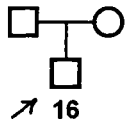

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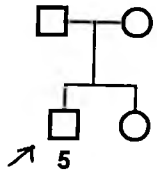

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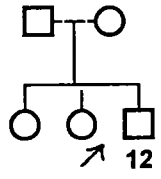

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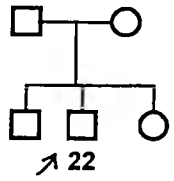

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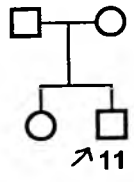

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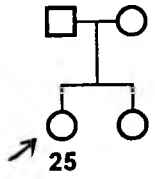

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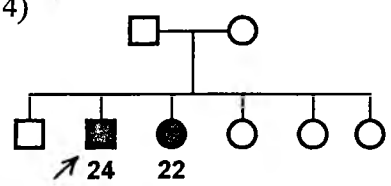

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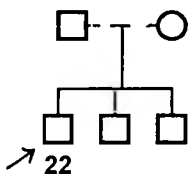

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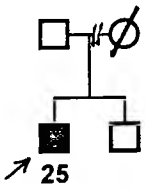

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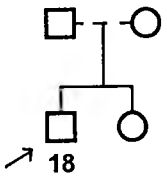

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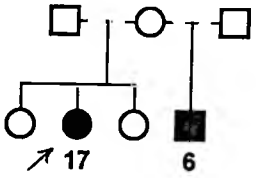

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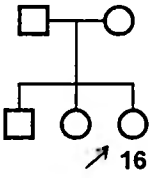

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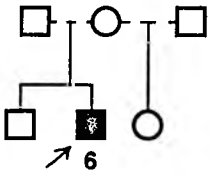

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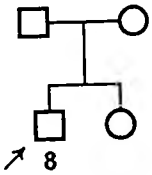

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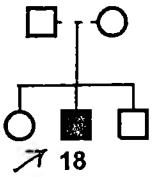

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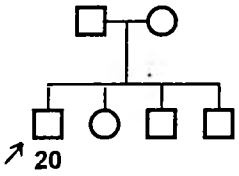

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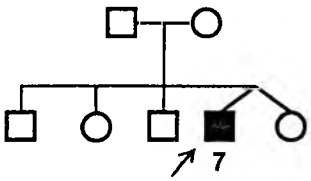

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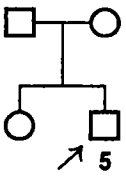

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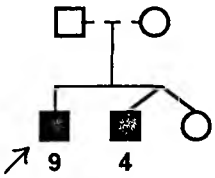

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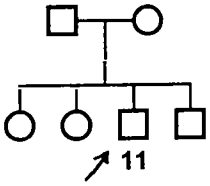

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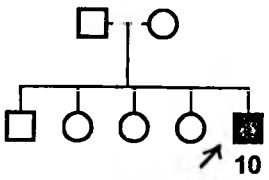

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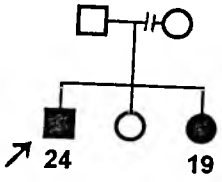
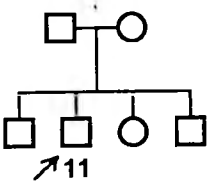


Families:

1 to 13 - Caucasoid
14 to 18 - African
19 to 21 - Coloured
22 - Indian

21)



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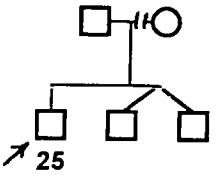

Families:

1 to 13 - Caucasoid
14 to 18 & 22 - African
19 to 21 - Coloured